

A prospective evaluation to define optimal surgical strategies in the management of complex pancreatic injuries based on the analysis of patients treated at a major South African academic institution.

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Dedication

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The data presented in the literature review of this thesis are based in part on the following publications by the author or as co-author

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Abstract

In order to address crucial existing limitations in the assessment and analysis of pancreatic injuries due to the lack of robust data and deficient surgical strategies, this thesis focused on priority topics to resolve existing unanswered and under-researched questions in the management of complex pancreatic injuries. Each of the twelve clinical studies in this thesis evaluated a specific aspect of pancreatic trauma based on the detailed analysis of prospective granular data from a large cohort of patients treated in an academic surgery and trauma centre with substantial experience in civilian operative trauma care in which standard and uniform protocols were applied.

1. The Pancreatic Injury Mortality Score (PIMS) study derived and validated a novel organ-specific risk prediction score calculated from five variables, age >55, shock on admission, a vascular injury, number of associated injuries and pancreatic grade of injury. Cut-off scores were used to generate three risk groups with increasing rates of mortality in low (PIMS 0-4), medium (PIMS 5-9), and high risk (PIMS 10–20) groups. PIMS is simple, quick and easily understandable, increases clinical risk prediction for patients with complex pancreatic injuries and can be used as a benchmark for survival. This original PIMS is a comprehensive and validated tool which accurately predicts post-operative mortality progressively across its range of scores based on easily accessible data points.

2. The factors predicting morbidity and death in patients undergoing surgery for pancreatic trauma was examined using logistic regression analyses in the largest and most comprehensive single centre series to date. Bivariate logistic regression analysis showed that 9 factors, age, RTS, presence of shock, need for a transfusion, volume of blood transfused, damage control surgery, AAST grade of pancreatic injury, an associated vascular injury and a repeat laparotomy were significant predictors of morbidity. In the final multivariate logistic regression analysis model however only 2 variables, AAST grade of pancreatic injury and a repeat laparotomy were significant predictors of morbidity. When factors associated with mortality were considered, logistic regression analysis found that 11 variables, age, RTS, the presence of shock, patients who required a major blood transfusion, the median number of units transfused, the need for a damage control laparotomy, AAST grade 3,4,5 pancreatic injuries, associated vascular injuries, the number of associated injuries, postoperative complications and days in ICU were significant. However in the final stepwise multivariate logistic regression analysis model only 5 variables, age, shock, median number of units transfused and the presence of associated complications were significant factors associated with mortality.

3. The outcome after pancreatoduodenectomy for Grade 5 pancreatic injuries using established HPB techniques of resection and reconstruction adapted for trauma was critically evaluated in this study. Nineteen of 426 patients with pancreatic injuries underwent a pancreatoduodenectomy. Nine

patients had associated inferior vena cava or portal vein injuries. Five patients had an initial damage control procedure and underwent a definitive operation at a median of 15 hours later when stable. Twelve patients underwent a pylorus-preserving pancreatoduodenectomy and seven had a standard Whipple resection. Three patients with APACHE II scores of 15, 18, 18 died post-operatively of multi-organ failure. All 16 survivors developed post-operative complications which included Dindo-Clavien grade I (n = 1), grade II (n = 7), grade IIIa (n = 2), grade IVa (n = 6) complications. Factors complicating surgery were shock on admission, number of associated injuries, coagulopathy, hypothermia, gross bowel oedema and traumatic pancreatitis. This study showed that a pancreatoduodenectomy is a life-saving procedure in the small cohort of stable patients with non-reconstructable pancreatic head injuries and that a pylorus-preserving pancreatoduodenectomy is technically feasible and safe in the trauma situation.

4. This study used robust methodology and objective and reproducible endpoints to define specific criteria for selection of the type of surgery including initial damage-control surgery(DCS) and pancreatoduodenectomy for complex combined pancreatoduodenal injuries (CPDIs). Seventy-five patients with CPDI, underwent 161 operations (range 1 to 9 operations). Twenty-nine patients with complex CPDI underwent DCS and 46 had definitive treatment during the initial operation. Nineteen had a pancreatoduodenectomy, either during the initial operation (n=13) or after

DCS (n=6). Mortality was related to associated vascular injuries overall ($p<0.01$), major visceral venous injuries ($p<0.011$), and the combination of vascular plus the total number of associated organs injured ($p<0.046$). Despite using DCS in CPDIs, morbidity (84%) and mortality (28%) remain substantial. Careful selection of patients undergoing pancreatoduodenectomy resulted in 84% survival. Associated vascular injuries, major visceral venous injuries, and combined vascular and associated organs injured influenced outcomes and mortality.

5. The role of damage control surgery (DCS) in 79 patients to determine factors influencing mortality was evaluated in this original study. Fifty-nine (74.7%) patients had AAST grade 3, 4 or 5 pancreatic injuries. The 79 patients had a total of 327 associated injuries (mean: 3 per patient, range 0-6) and underwent a total of 187 (range 1-7) operations. Vascular injuries (60/327, 18.3%) occurred in 41 patients. Twenty seven (34.2%) patients died without having a second operation. The remaining 52 patients had two or more laparotomies (range 2-7). Overall 28 (35%) patients underwent a pancreatic resection either during DCS (n=18) or subsequently as a secondary procedure (n=10) including a Whipple (n=6) when stable. Overall 43 (54.4%) patients died. Despite the magnitude of their combined injuries and the degree of physiological insult, DCS salvaged 45% of critically injured patients who later underwent definitive pancreatic surgery. Mortality was related to associated vascular injuries overall, major visceral venous

injuries and combined vascular and total number of associated organs injured.

6. Outcome after initial DCS and subsequent pancreatoduodenectomy and reconstruction with particular appraisal of the advantages of delaying resection in unstable patients with associated major vascular injuries to assess optimal operative sequencing was evaluated in this study. During the 20-year study period, 312 patients were treated for pancreatic injuries of whom 14 underwent a pancreatoduodenectomy. Six of the 14 patients were *in extremis* with exsanguinating venous bleeding and non-reconstructable AAST grade 5 pancreatoduodenal injuries and underwent DCS followed by delayed pancreatoduodenectomy and reconstruction when stable. The mean operating room time was 113 minutes, range 90-140 m vs 335 minutes, range 260-395 minutes ($p < 0.01$). During the second laparotomy 5 patients had a pylorus-preserving pancreatoduodenectomy and one a standard Whipple resection. Four of the six patients survived.

7. The 6-scale Accordion Severity Grading System (ASGS) metrics was used for the first time in this study to benchmark the spectrum and severity of complications after pancreatic resection for trauma. Applying univariate logistic regression analysis, mechanism of injury, RTS < 7.8 , shock on admission, DCS, increasing AAST grade and type of pancreatic resection were significant variables for complications. Multivariate logistic regression analysis however showed that only age and type of pancreatic resection

(PD) were significant. The detailed outcome analysis provided may serve as a reference for future institutional and international comparisons.

8. This study critically evaluated morbidity and mortality after distal pancreatectomy for major pancreatic injuries and assessed the severity of pancreas-specific postoperative complications using objective, reliable, and reproducible internationally accepted graded classification systems. Overall mortality in 107 patients was 12%, 16% for gunshot injuries, 8% for blunt trauma and 0% in patients who had stab wounds. Eighty patients had a post-operative complication. A pancreatic leak (n=26) was the most common pancreatic related complication. Median postoperative stay in 28 patients with no or grade I complications was 9 days; in 11 patients with grade II complications was 18 days; in 14 grade IIIa, 31 days; in 19 grade IIIb, 38 days; in 8 grade IVa, 33 days in 14 grade IVb, and in 13 grade V the duration of postoperative stay was 14 ± 39.4 days. Overall mortality for distal pancreatectomy was 12%. Pancreatic leak was a common cause of morbidity. Length of hospitalisation increased with increasing Clavien–Dindo severity grading. There was a significant difference in the duration of hospitalization in patients with no or grade I complications compared to those with grade II-IV injuries ($p < 0.05$).

9. This novel study critically evaluated the efficacy of endotherapeutic pancreatic duct stenting and transmural cyst drainage in the management of delayed complications after major pancreatic injuries. Of 27 patients with delayed complications related to an initial pancreatic injury, 16 had non-

resolving symptomatic pancreatic pseudocysts, 10 had persistent pancreatic fistulae and 1 had a symptomatic duct stricture. Fourteen patients with grade 2a, 3a, 3b or 4c main pancreatic duct injuries were successfully treated endoscopically with either pancreatic duct stenting or pseudocyst drainage while 13 patients with grade 4a or 4b duct injuries who had complete duct division with a disconnected duct syndrome failed endoscopic management and required surgical intervention. The 27 patients underwent a total of 49 endoscopic procedures (47 elective, 2 emergency) of whom 4 developed complications related to the endoscopic treatment. All 4 resolved, 2 after urgent endoscopic re-intervention. In this analysis the new proposed Cape Town pancreatic ductal injury grading classification showed a close correlation with outcome after endoscopic and operative intervention.

10. To test the hypothesis that much of the morbidity and mortality after a major pancreatic injury is due to collateral damage to adjacent vital organs and in their absence, isolated pancreatic injuries (IPI) should have a significantly lower complication and death rate, this study assessed outcome and injury-specific factors after an IPI. Of 49 patients with an IPI, 34 (70%) underwent urgent surgery, 20 of whom had a distal pancreatectomy and 14 had external drainage of the pancreatic injury. Fifteen (30%) patients presented with a non-resolving pancreatic pseudocyst or fistula; five had grade 4A or 4B ductal injuries and underwent surgery, 10 with 3A and 3B ductal injuries were successfully managed

endoscopically. Fifty-five percent had post-operative morbidity. Two patients (4%) died of non-pancreatic-related causes. While overall mortality is low after an IPI, morbidity is high. Two-thirds of patients required operative intervention and one-third were treated endoscopically. The degree of pancreatic ductal injury determined whether endoscopic intervention was effective.

11. This study examined the factors associated with morbidity and mortality in 78 patients who had a laparotomy for a stab wound of the pancreas. Sixty-five patients had AAST grade I or II injuries and 13 had grade III, IV or V pancreatic injuries. Eight (10.3%) of 78 patients had an initial damage control operation. Sixty nine (84.6%) patients had drainage of the pancreas only, six had a distal pancreatectomy and one had a Whipple resection. Most pancreas-related complications occurred in patients with AAST grade III injuries; 8 patients (10.2 per cent) developed a pancreatic fistula. Four (5.1%) patients died. Grade of pancreatic injury (AAST grade I–II vs grade III–V injuries; $p < 0.001$), RTS ($p < 0.007$, OR 5.01, 95% CI 1.46-17.19), presence of shock on admission ($p = 0.022$, OR 3.31, 95% CI 1.16-9.42), need for a blood transfusion ($p < 0.001$, OR 6.46, 95% CI 2.40-17.40) or repeat laparotomy ($p < 0.001$) had a significant influence on the development of general complications. This analysis showed that although mortality was low after pancreatic stab wounds, morbidity was high. Significant predictors of morbidity in this study were an increasing AAST grade of pancreatic

injury, a high revised trauma scale, shock on admission to hospital, the need for a blood transfusion and a repeat laparotomy.

12. This analysis evaluated for the first time how techniques for pancreatic, biliary and gastric anastomoses need to be modified for reconstruction after a pancreatoduodenectomy for trauma. Twenty patients underwent a PD. Six had an initial damage control procedure. Thirteen had a pylorus-preserving PD and 7 a standard Whipple resection because injury to the pylorus precluded a pylorus-preserving resection. Twelve patients had a pancreatojejunostomy and 8 a pancreatogastrostomy, 3 of whom had a duodenojejunal hepaticojejunal sequence of anastomoses to allow endoscopic biliary stent retrieval. Pancreatic and biliary reconstructions performed under adverse conditions after a trauma PD required a variety of technical modifications. The pylorus does not have to be sacrificed and posterior gastric implantation is a safe option for an oedematous pancreas. This study confirms that delayed resection and reconstruction after damage control is feasible with a reasonable prospect of survival. This study demonstrated that a pylorus-preserving pancreatoduodenectomy is feasible in selected patients and that pylorogastric resection is only necessary when dictated by the extent of injury. A practical argument has been advanced that a pancreatogastrostomy may be a safer option than a pancreatojejunostomy when conventional anastomoses are high-risk due to oedematous tissues. These techniques do not need to be used in all pancreatoduodenal injuries requiring resection, but should be applied and

adapted to the severity of the situation. The data emphasize that complex pancreatic injuries result in significant postoperative morbidity and are best managed collaboratively by trauma and HPB surgical teams.

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CHAPTER 1

Introduction and pancreatic injury overview

Major injuries of the pancreas are among the most complex operative challenges surgeons are likely to encounter during a trauma laparotomy. Although pancreatic injuries are relatively uncommon, considerable morbidity and mortality may result if associated vascular and duodenal injuries are present or if the extent of the injury is underestimated or intervention is delayed (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006, Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008). Prognosis is influenced by the cause and complexity of the pancreatic injury, the amount of blood lost, the duration of shock, the rapidity of resuscitation and the quality and appropriateness of the surgical intervention (Krige 1995, Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001, Chrysos, Athanasakis et al. 2002, Kao, Bulger et al. 2003, Krige 2006). Early mortality results from uncontrolled or massive bleeding due to associated vascular and adjacent organ injuries (Farrell, Krige et al. 1996, Krige 2004) while late mortality is generally a consequence of infection or multiple organ failure. A main pancreatic duct injury may be occult and if neglected can lead to major complications including pseudocysts, fistulae, pancreatitis, sepsis and secondary haemorrhage (Lewis, Krige et al. 1993, Farrell, Krige et al. 1996, Krige 2004, Potoka, Gaines et al. 2015). The principles of management of pancreatic trauma include the need for early diagnosis and accurate definition of the site and extent of injury to facilitate

optimal intervention (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006, Girard, Abba et al. 2016, Iacono, Zicari et al. 2016, Ho, Patel et al. 2017). The gravity of major pancreatic injuries and the potentially serious complications necessitate a comprehensive and multidisciplinary approach to treatment (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006, Subramanian, Dente et al. 2007). This overview appraises the spectrum of pancreatic injuries and outlines the mechanisms of injury, clinical and laboratory diagnosis, classification, imaging techniques, operative management, outcome and intervention for postoperative complications.

1.1 Incidence

Although the pancreas is injured in less than 3% of severe abdominal injuries (Krige 1995, Krige 2004, Degiannis, Glapa et al. 2008, Potoka, Gaines et al. 2015) recent data show an increasing incidence due to both high-speed automobile accidents and civil violence involving increasingly dangerous weapons (Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008). In North American and South African cities, penetrating abdominal injuries from gunshot wounds are the most common cause of pancreatic trauma, while in Western Europe, Great Britain and Australia blunt injuries due to road traffic accidents predominate (Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008, Potoka, Gaines et al. 2015, Girard, Abba et al. 2016). This geographical variation in aetiology results in considerable disparity in the reported severity and type of pancreatic injuries (Krige, Beningfield et al. 2005, Potoka, Gaines et al. 2015).

1.2 Mechanism of injury

The unique anatomic features of the pancreas influence the site and type of injury. The proximity of major vascular structures and surrounding viscera adds to the complexity of pancreatic injuries. Leakage of pancreatic exocrine secretions due to duct disruption exacerbates the mechanical effects of direct pancreatic trauma, with resultant peri-pancreatic oedema and tissue and fat necrosis (Potoka, Gaines et al. 2015, Girard, Abba et al. 2016, Iacono, Zicari et al. 2016). The nature and consequence of penetrating injuries depend on the type and kinetic energy tissue dissipation of the wounding agent (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Penetrating injuries with adjacent contusions occur in single-fragment missile wounds, while high energy transfer injuries to the head and neck cause severe pancreatic damage and can injure the common bile duct, portal vein, IVC, gastroduodenal, right and middle colic vessels which compound the effect of the pancreatic trauma. Isolated injuries and those due to blunt trauma may pose particular diagnostic problems due to the initial lack of physical signs (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006, Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008).

1.3 Associated injuries

Isolated injuries to the pancreas are uncommon (Krige 1995, Krige, Beningfield et al. 2005). The incidence of associated injuries exceeds 95% with a mean of 3.5 organs injured (Stone, Fabian et al. 1981, Feliciano, Martin et al. 1987, Jurkovich and Carrico 1990, Akhrass, Yaffe et al. 1997, Fleming, Collier et al. 1999). These associated injuries cause most of the

morbidity and mortality in patients with pancreatic trauma. The organs most commonly injured are the liver (42%), stomach (40%), major vessels (35%), thoracic viscera (31%), colon and small bowel (29%), central nervous system and spinal cord, skeleton and extremities (25%) and duodenum (18%) (Lucas 1977, Krige 1995, Krige, Beningfield et al. 2005, Krige 2006, Potoka, Gaines et al. 2015, Iacono, Zicari et al. 2016). The management of combined injuries to the pancreas and duodenum is complex, especially when devitalized tissue and associated damage to contiguous vital structures including the bile duct, portal vein, vena cava, aorta or colon are present (Moore, Cogbill et al. 1990, Subramanian, Dente et al. 2007, Potoka, Gaines et al. 2015, Iacono, Zicari et al. 2016). Colonic injuries are more common after penetrating than blunt trauma and increase the risk of postoperative sepsis (Potoka, Gaines et al. 2015). Penetrating injuries result in injuries to retroperitoneal vessels in a third of patients (Jurkovich and Carrico 1990).

1.4 Classification of injuries

Comparisons between various forms of treatment are difficult to analyse because isolated pancreatic injuries are infrequent, experience in most centres is limited and there is no universally acceptable injury classification system (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Although several classifications have been used in the past, the AAST pancreatic injury grading score is currently the most widely used (Table 1) (Moore, Cogbill et al. 1990). The injury grade in the AAST classification is primarily determined by the presence or absence of a main pancreatic duct injury

and the anatomic location of the injury within the pancreas. This grading system is clinically useful since the management of a pancreatic injury is dependent on the presence or absence of a main pancreatic duct injury and the anatomic location of injury (Potoka, Gaines et al. 2015).

Table 1 The AAST Classification of Pancreatic Injury

Grade 1	Superficial laceration or minor contusion without duct injury
Grade 2	Major laceration contusion without duct injury or tissue loss
Grade 3	Distal transection or parenchymal injury with duct injury
Grade 4	Proximal transection (to the right of the superior mesenteric vein) or parenchymal injury involving ampulla
Grade 5	Massive disruption or obliteration of pancreatic head

The American Association for the Study of Trauma classification of pancreatic injuries has five grades depending on the severity and location of parenchymal and duct disruption.

1.5 Diagnosis

Delay in diagnosis and intervention is an important cause of increased morbidity and mortality. The retroperitoneal position of the pancreas contributes to delay in diagnosis as clinical signs may be subtle and late in onset (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Blunt trauma to the pancreas may be clinically occult, and parenchymal and duct injury may go unrecognized both during initial evaluation and during surgery (Chrysos, Athanasakis et al. 2002). Awareness of these factors and recognition of the mechanism of injury should therefore lead to a high index of suspicion for pancreatic injury.

Serum amylase levels correlate poorly with the presence or absence of pancreatic trauma (Potoka, Gaines et al. 2015). Amylase levels may be normal in severe pancreatic damage or may be elevated when no demonstrable injury to the gland has occurred. The incidence of hyperamylasaemia in patients with proven blunt pancreatic trauma ranges from 3-75% (Potoka, Gaines et al. 2015). Conversely, in patients with hyperamylasaemia after blunt abdominal trauma, the pancreas has been found to be injured in anything from 10-90% of patients (Potoka, Gaines et al. 2015). Measuring serum amylase levels more than 3 hours after blunt trauma may avoid false negative results in pancreatic injuries, and a serially rising serum amylase level in a patient with abdominal tenderness and pain is a better indicator of pancreatic injury (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Other causes for a raised serum amylase level after blunt trauma to be considered include acute alcohol intake, bowel infarction or injury to duodenum, stomach or small bowel (Krige 1995).

1.6 Imaging

1.6.1 Plain Abdominal Radiographs

Specific features on plain radiographs of the abdomen may raise suspicion of pancreatic trauma, especially when signs of duodenal injury are present (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Gas bubbles in the retroperitoneum, adjacent to the right psoas muscle, around the kidneys or anterior to the upper lumbar vertebrae as seen on frontal or cross-table radiographs may indicate a duodenal injury (Jurkovich and Carrico 1990,

Krige 1995, Krige, Beningfield et al. 2005). Free intraperitoneal gas may also be present. Fractures of the transverse processes of the lumbar vertebrae are collateral evidence of significant retroperitoneal trauma (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Other indirect signs of pancreatic injury are displacement of the stomach or transverse colon by haemorrhage or oedema, or a general "ground-glass" appearance (Lucas 1977, Jurkovich and Carrico 1990). Oral iodinated contrast may demonstrate a duodenal leak, with or without distortion of the duodenal C-loop.

1.6.2 Ultrasound

Ultrasound imaging as part of the initial assessment of trauma patients is an effective and reliable imaging technique for assessing the presence of free abdominal fluid, which is most likely to be due to blood (McKenney, Nir et al. 1996). Focussed abdominal sonography in trauma (FAST) is useful as the initial imaging modality, but directed ultrasound evaluation of pancreatic trauma is frequently difficult due to the associated abdominal injuries, overlying bowel gas, obesity or subcutaneous emphysema (McKenney, Nir et al. 1996, Cirillo and Koniaris 2002).

1.6.3 Computerized Tomography

Computerized tomography (CT) is the radiological investigation of choice for diagnosis and evaluation of pancreatic injury in polytrauma patients and is both more sensitive and specific than ultrasonography (Mullinix and Foley 2004, Kumar, Panda et al. 2016). The main indications for CT are in haemodynamically stable patients with abdominal pain or tenderness

following trauma who have a suspected pancreatic injury, and in the assessment of late complications of pancreatic trauma. An intravenous iodinated contrast bolus provides the optimal contrast enhancement of the pancreas necessary to identify subtle parenchymal lacerations. The CT findings of post-traumatic pancreatitis are time-dependent and may not be evident on scans performed immediately after injury (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). The features of injury or post-traumatic pancreatitis are focal or diffuse pancreatic enlargement, oedema and peripancreatic fat stranding, thickening of the anterior pararenal fascia, with or without acute fluid collections in or around the pancreas (Mullinix and Foley 2004). Other non-specific CT findings of pancreatic trauma include blood or fluid tracking along the mesenteric vessels, fluid in the lesser sac, or fluid between the pancreas and splenic vein (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006).

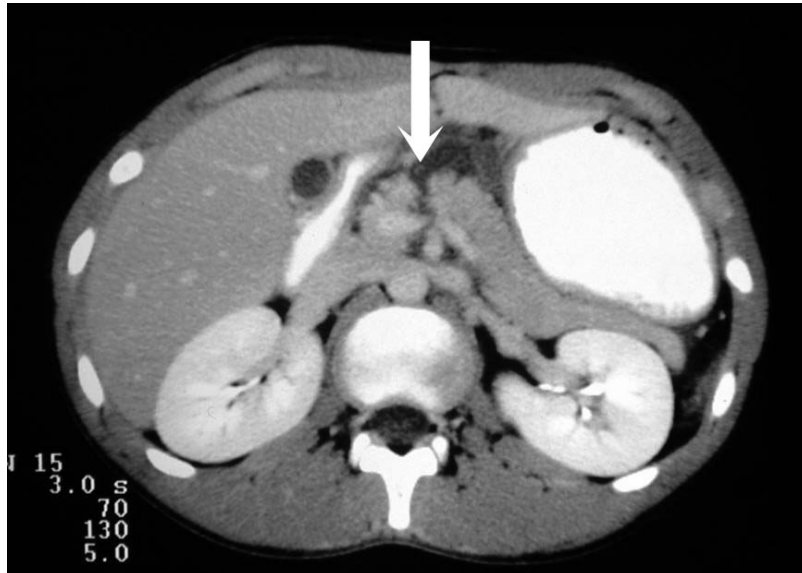
The features of pancreatic trauma may however be subtle, particularly in the immediate post-injury period and in adults with minimal retroperitoneal fat. Pancreatic contusions may appear as low-attenuation or heterogeneous focal or diffuse enlargements of the pancreas (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Pancreatic lacerations may be seen as linear, irregular, low-attenuation areas within the normal parenchyma. Unless the two edges of a fracture or transected pancreas are separated by low-attenuation fluid or haematoma, the diagnosis of pancreatic transection may be difficult to recognise on CT (Krige 1995,

Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Common CT pitfalls in diagnosing pancreatic injury include fluid in the lesser sac or adjacent unopacified bowel mimicking focal pancreatic enlargement or contusion, or streak artefacts or focal fatty replacement of pancreatic parenchyma simulating a pancreatic laceration (Krige 1995). Other CT findings that mimic pancreatic injury include blood or fluid tracking around the pancreas from injuries to the adjacent duodenum, spleen or left kidney, pelvic haematoma tracking superiorly in the retroperitoneum and retroperitoneal oedema from vigorous intravascular volume resuscitation (Patel, Spencer et al. 1998).

The ability of CT to accurately diagnose pancreatic injury depends on the quality of the CT scanner, the technique used, the experience of the observer and the timing of the examination in relation to the injury (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Within 12 hours after injury, CT scans may be normal in a significant proportion of cases due to an obscured fracture plane, overlying or intervening blood or close apposition of the edges of the pancreatic injury. Repeat scanning 12 to 24 hours after the injury may reveal an obvious injury which was initially subtle (Figure 1). The overall imaging sensitivity in detecting all grades of pancreatic injury has been estimated at 80%, but major ductal injury detection has been reported to be as low as 43%, even with modern imaging techniques (Patel, Spencer et al. 1998). Further analysis of missed injuries also suggests that CT is inaccurate in grading the degree of

pancreatic injury and often a lower grade of injury is diagnosed by CT than is found at laparotomy (Patel, Spencer et al. 1998, Cirillo and Koniaris 2002, Mullinix and Foley 2004, Kumar, Panda et al. 2016).

Figure 1



CT scan showing fracture (arrow) of the pancreatic neck

1.6.4 Magnetic resonance cholangiopancreatography (MRCP)

MRCP is a valuable additional imaging modality which provides an accurate and rapid means of assessing the pancreatic duct. T2-weighted MRCP sequences depict the fluid-filled pancreatic and bile ducts as high-signal structures (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). As opposed to ERCP where trans-papillary injection of contrast is needed to depict the pancreatic duct, with an associated risk of subsequent pancreatitis, MRCP is non-invasive and no contrast is needed (Fulcher, Turner et al. 2000). MRCP findings indicating injury to the pancreatic duct include focal disruption or interruption of the duct, focal or diffuse dilation of

the upstream duct and communication between the duct and intrapancreatic or peripancreatic fluid collections. Unlike retrograde pancreatography, MRCP is able to provide additional useful information concerning the upstream pancreatic duct architecture and injury, even without continuity with the downstream duct (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006).

The development of rapid MR imaging techniques and MR-compatible physiologic monitoring and ventilation devices allows imaging to be performed on patients with acute injuries, although it may still be logistically difficult (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Even though several different acquisitions are usually performed, scans can be completed in less than 10 minutes which is an important advantage for a severely injured patient. Some MRCP sequences do not require breath-holding, with little degradation of image quality even if the patient is unable to cooperate fully. Special sequences may also suppress artefact formation from metallic objects such as surgical clips and bullet fragments (Fulcher, Turner et al. 2000).

1.6.5 Endoscopic retrograde cholangiopancreatography (ERCP)

Until the availability of MRCP, ERCP was the most accurate method of defining a pancreatic duct injury by demonstrating extravasation of contrast from the duct (Figure 2) (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994). Pre-operative ERCP is seldom feasible in severe pancreatic trauma, as most patients require urgent laparotomy for bleeding or associated

injuries (Sugawa and Lucas 1988, Blind, Mellbring et al. 1994). ERCP in stable patients after blunt trauma to the pancreatic head or neck may also be technically difficult due to distortion of recognizable mucosal landmarks, including the papilla, caused by intramural haematoma or surrounding peripancreatic oedema (Sugawa and Lucas 1988). The concept of intra-operative ERCP to define pancreatic duct anatomy is appealing as it avoids opening the duodenum and performing a potentially difficult operative cannulation of the papilla during laparotomy (Blind, Mellbring et al. 1994). However, even in centres with the necessary expertise, the logistic difficulties involved in performing an emergency intra-operative ERCP can outweigh the potential benefits. Frequently the urgency of dealing with collateral vascular, visceral and solid organ injuries precludes an intra-operative ERCP. In addition, the patient's supine position, the need for high quality X-ray facilities and the necessity for complete visualisation of the pancreatic duct add to the technical difficulties (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006).

Figure 2



ERP showing duct occlusion (arrow) at the pancreatic neck

ERCP is an invasive procedure associated with complications, including pancreatitis in 3% of patients. The results are operator-dependent, and failure to cannulate the ampulla or completely fill the pancreatic duct may occur in up to 10% of patients (Whittwell, Gomez et al. 1989). Patients in whom a minor duct injury is demonstrated on the pancreatogram but without leakage beyond the pancreatic capsule (i.e. a contained leak) can be treated non-surgically (Takishima, Hirata et al. 2000, Kim, Lee et al. 2001). Confirmation of major ductal injury with extravasation requires operative intervention in most patients, unless duct continuity is present and facilities exist to place an endoscopic pancreatic duct stent (Takishima, Horiike et al. 1996, Thomson, Krige et al. 2014).

1.7 Management

The initial management of the patient with pancreatic trauma is similar to that of any patient with severe abdominal injury (Krige 1995, Farrell, Krige et al. 1996, Krige, Beningfield et al. 2005, Krige 2006). Primary management includes maintaining a clear airway, urgent resuscitation and ventilatory and circulatory support (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006, Potoka, Gaines et al. 2015). Venous access, blood group and crossmatch, volume replacement, measurement of haemoglobin concentration, white cell count, packed cell volume, urea, creatinine, electrolytes and blood gases should be rapidly obtained (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). A nasogastric tube and urinary catheter are essential (Krige 1995, Krige, Beningfield et al. 2005). The mechanism

and type of injury are determined while the physical examination and resuscitation are in progress. In patients with blunt abdominal trauma, information should be sought regarding the mechanism of injury and the vector of force (e.g. steering wheel, bicycle or motorcycle handlebar, sports injury or assault). The injury may seem trivial or innocuous and the initial clinical assessment may be misleading with scant signs because of the retroperitoneal location of the pancreas. Urgent laparotomy is required in all patients with evidence of major intraperitoneal bleeding, associated visceral trauma, or peritonitis (Farrell, Krige et al. 1996).

1.7.1 Laparotomy

A long midline incision provides optimal exposure (Krige 1995, Farrell, Krige et al. 1996, Krige, Beningfield et al. 2005, Krige 2006). In the presence of shock and haemoperitoneum, the first priority is to identify the source of bleeding. Immediate survival is dependent upon successful control and repair of major vascular injuries (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). The inaccessible retropancreatic positions of the superior mesenteric and splenic arteries and veins and portal vein make proximal and distal clamping or circumferential control of individual vessels impractical during massive bleeding. Rapid initial control is therefore best obtained by surgical packing or digital pressure. Early duodenal mobilization and bimanual compression of the bleeding site is helpful if there is suspicion of a major portal or superior mesenteric vein injury (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Vigorous resuscitation with blood and blood components should continue until bleeding has been

stunched and normovolemia achieved. Attention is then directed to other priority visceral injuries before dealing with the pancreatic trauma (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006).

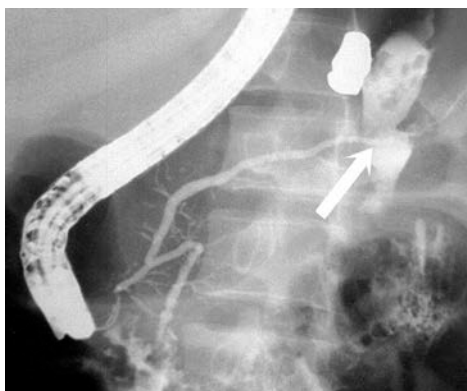
1.7.2 Intraoperative evaluation of the pancreas

In most patients with penetrating trauma, the diagnosis of pancreatic injury is made at laparotomy (Krige 1995, Fleming, Collier et al. 1999, Krige, Beningfield et al. 2005, Krige 2006, Ho, Patel et al. 2017). Minor contusions or lacerations of the pancreatic substance do not usually require further definitive treatment, but this decision can only be made after careful local exploration to exclude a major pancreatic duct injury. Determining the presence and extent of a pancreatic injury intraoperatively requires adequate exposure of the pancreas, determination of the integrity of the pancreatic parenchyma and more importantly the status of the major pancreatic duct (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). This may be complicated by the extent and severity of associated injuries. Gross inspection and palpation of the pancreas alone can be misleading as a retroperitoneal or subcapsular haematoma and peripancreatic oedema may mask major parenchymal and duct injuries (Iacono, Zicari et al. 2016). Clues suggesting the presence of a pancreatic injury include a lesser sac fluid collection, retroperitoneal bile-staining and crepitus or haematoma overlying the pancreas at the base of the transverse mesocolon or visible through the gastrohepatic ligament (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Fat necrosis of the omentum or retroperitoneum may be present if there has been undue delay before the laparotomy (Krige 1995,

Krige, Beningfield et al. 2005, Krige 2006). With such findings, complete visualisation of the gland and accurate determination of the integrity of the pancreatic duct is crucial, remembering that failure to recognize a major pancreatic duct injury is the principal cause of postoperative morbidity.

Intra-operative features indicating a major pancreatic duct injury include a transected pancreas, a visible duct injury, a laceration involving more than half of the width of the pancreas or a large central perforation (Iacono, Zicari et al. 2016). All penetrating wounds should be traced through their entire intra-abdominal course to exclude pancreatic or other visceral injury (Rotondo, Schwab et al. 1993, Ho, Patel et al. 2017). Intra-operative evaluation of the head of the pancreas includes assessment of the integrity of the main pancreatic duct, whether the pancreatic head or duodenum are devitalized, the presence and extent of duodenal injury, whether the ampulla is disrupted, if the bile duct is intact or whether a vascular injury has occurred (Figure 3)

Figure 3



ERP via minor papilla demonstrating distal pancreatic fistula (arrow) after an abdominal gunshot injury (bullet*)

1.7.3 Operative cholangiopancreatography

Several radiological methods of intra-operative assessment of biliopancreatic ductal integrity have been used (Krige 1995, Krige, Beningfield et al. 2005). The easiest and most convenient is to perform a conventional operative cholangiogram through the cystic duct after removing the gall bladder, or alternatively, by inserting a 25 gauge butterfly needle into the common bile duct and injecting 10 ml of full strength water soluble iodinated contrast with fluoroscopic control (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). The images obtained may be useful to assess the intrapancreatic bile duct, the integrity of the ampulla and continuity of the pancreatic duct if there is contrast reflux into the pancreatic duct. In the presence of an associated open duodenal injury, the papilla may be conveniently accessible and should then be located (Krige and Thomson 2011). A soft 5Fr paediatric feeding tube can also be used for operative pancreatography by cannulating the ampulla of Vater. A skilled endoscopist may be of assistance in performing an intra-operative ERCP if logistics permit (Thomson, Krige et al. 2014).

1.8 Treatment

1.8.1 Grade 1: Contusions and lacerations without duct injury

Seventy per cent of pancreatic injuries are minor and include contusions, haematomas and superficial capsular lacerations without an underlying major ductal injury (Table 1). Control of bleeding and simple external drainage without repair of capsular lacerations are sufficient treatment (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). A

closed silastic suction drain is preferred, as pancreatic secretions are more effectively controlled, skin excoriation at the drain exit site is reduced, and bacterial colonization is less of a risk than when a sump or gravity drain is used (Jurkovich and Carrico 1990, Patton, Lyden et al. 1997).

1.8.2 Grade 2: Distal injury with duct disruption

Injury to the neck, body or tail of the pancreas with major lacerations or transections and associated pancreatic duct injury is best treated by left pancreatectomy (Figure 3) (Patton, Lyden et al. 1997, Ho, Patel et al. 2017). Optimal management of the divided pancreatic duct and the resection margin after distal pancreatectomy remain controversial. Oversewing or stapling the transected end of the pancreas and using simple methods to buttress or seal the cut margin are sufficient and have not led to increased fistula formation (Krige and Thomson 2011).

1.8.3 Grade 3: Proximal injury with probable duct disruption

It is especially important to exclude a pancreatic duct injury in trauma to the head of the pancreas (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Injuries to the head of the pancreas that do not involve the main pancreatic duct are best managed by simple external drainage (Figure 3). Even if there is a suspected isolated pancreatic duct injury (as may occur with a localized penetrating injury), provided there is no devitalisation and the ampulla is intact, external drainage of the injured area is often the safest option (Degiannis, Levy et al. 1996, Patton, Lyden et al. 1997). A controlled fistula thus created either resolves spontaneously or

may later require elective internal drainage after definition of the exact site of duct leakage (Girard, Abba et al. 2016, Iacono, Zicari et al. 2016).

1.8.4 Grades 4/5: Combined major pancreaticoduodenal injuries

Severe combined pancreatic head and duodenal injuries are uncommon, and usually result from gunshot wounds or blunt trauma with other associated intra-abdominal injuries. In determining the best option for patients with combined injuries, it is crucial to define the integrity of the common bile duct, pancreatic duct and ampulla as mentioned earlier and the viability of the duodenum (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). The presence of bile staining in the retroperitoneum or around the lower bile duct in the hepatoduodenal ligament is confirmation of bile duct injury or ampullary avulsion (Krige and Thomson 2011). If the duodenal injury involves the third or fourth part of the duodenum remote from the ampulla and there is concern about ductal integrity, a duodenotomy opposite the papilla can be used to evaluate the ductal system (Krige 1995, Krige, Beningfield et al. 2005).

If the common bile duct and ampulla are shown to be intact, the duodenal laceration is repaired and the pancreatic injury treated according to the site of the injury. As with grade 3 injuries, division or damage to the main pancreatic duct and parenchyma near the junction of head and neck are optimally managed by resection of the neck, body and tail (Figure 1.3). A penetrating injury of the pancreatic head without devitalisation is best treated by careful drainage of the area (Krige 1995, Krige 2004, Krige,

Beningfield et al. 2005, Krige 2006). Localized ischaemia at the site of the duodenal injury should be debrided before primary duodenal closure, and if there is concern about the integrity of the duodenum, decompression using a carefully placed nasogastric tube in the duodenal loop is useful (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006).

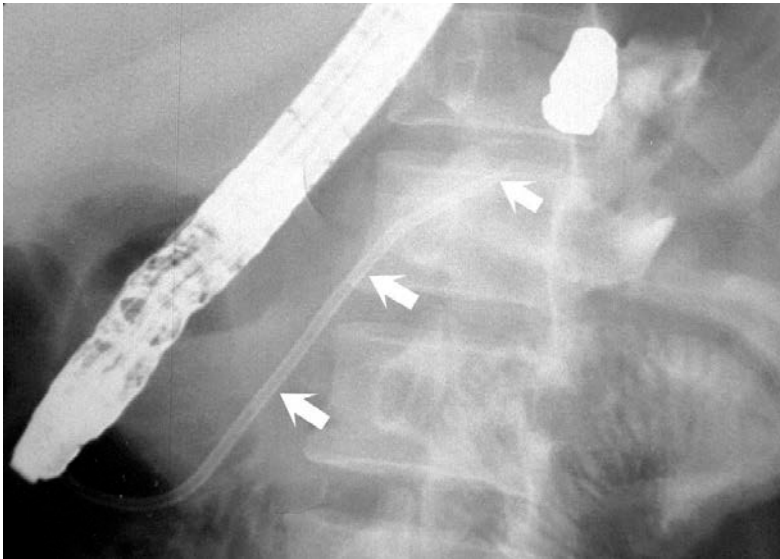
With a severe injury to the duodenum in association with a lesser pancreatic head injury, some authors advise diversion of gastric and biliary contents away from the duodenal repair. Several complex techniques have been described in the past to deal with this situation, including diversion using either a duodenal "diverticulisation" or a "pyloric exclusion" procedure (Berne, Donovan et al. 1974, Vaughan, Frazier et al. 1977). In a small number of selected patients, pyloric exclusion has proved useful in managing severe duodenal injuries combined with pancreatic head injuries in which a Whipple procedure is not justified (Vaughan, Frazier et al. 1977). Most experts believe, however, that the same objectives can be achieved by less complex procedures and in this situation primary duodenal closure is used with external catheter drainage near the site of the repair, a diverting gastrojejunostomy without closure of the pylorus and a fine-bore silastic nasojejunal feeding tube (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006).

1.9 Pancreaticoduodenectomy

Reconstruction may not be possible in some combined injuries of the proximal duodenum and head of the pancreas with extensive tissue

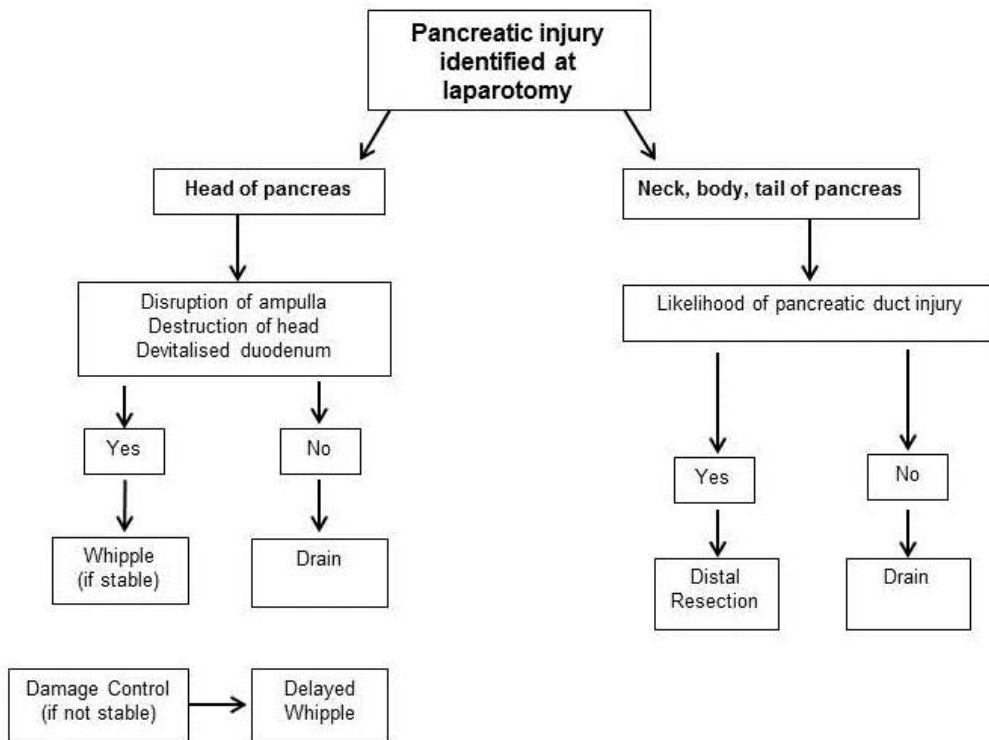
devitalisation, or with complete disruption of the ampulla involving the proximal pancreatic duct and distal common bile duct, or avulsion of the duodenum from the pancreas (Figure 4) (Krige 1997, Asensio, Petrone et al. 2003). In these situations, the only rational option is resection (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Pancreaticoduodenectomy (PD) has the advantage of removing all injured tissue and allows reconstruction of the digestive tract and preservation of pancreatic function (Krige 1997). The decision to resort to PD is based upon the extent of the pancreatic injury, the size and vascular status of any duodenal injury, the integrity of the distal common duct and ampulla of Vater, and the status of the major peripancreatic vascular structures and the experience of the surgeon (Figure 5). PD may be necessary in 1-2% of isolated pancreatic injuries and in up to 10% of combined pancreaticoduodenal injuries (Krige 1997, Asensio, Petrone et al. 2003, Krige, Nicol et al. 2014, Krige, Kotze et al. 2016). The need for resection is usually obvious at first sight when there is massive destruction with gross devitalisation of the duodenum or pancreatobiliary, duodenal and ampullary disruption is present. Blunt trauma may result in a near-complete *de facto* PD (Krige, Nicol et al. 2014, Krige, Kotze et al. 2016).

Figure 4



Endoscopically placed pancreatic stent (arrows) to treat fistula shown in Fig 1.3

Figure 5



Management algorithm for pancreatic injury

The technique of an emergency PD for trauma is modified if the patient is hypotensive with active bleeding from around the pancreas (Krige 1997). Factors complicating resection and predicting poor outcome are shock on admission, the number of associated injuries, coagulopathy, hypothermia, marked jejunal oedema and traumatic pancreatitis (Krige, Nicol et al. 2014). Technical problems in the reconstruction of pancreatic and biliary anastomoses may arise due to the small size of the undilated ducts and jejunal oedema. The parenchyma of the pancreatic remnant is also frequently oedematous if there has been undue delay between the injury and the operation, and the pancreatic duct may be small or obscured if posterior within the gland (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Invagination of the end of the pancreas into a Roux-en-Y jejunal loop has been the most widely used pancreatic-enteric anastomosis. Pancreatogastrostomy can be used in this situation with minimal morbidity (Krige and Thomson 2016). Biliary-enteric continuity is commonly restored by means of a side-to-side hepaticojejunostomy, using the high bile duct reconstruction technique with preplaced sutures. In desperate situations with a minute common bile duct, the gall bladder can be used for the anastomosis after ligating the bile duct below the cystic duct insertion (Krige and Thomson 2016).

Damage control surgery is advised in patients with haemodynamic instability despite full resuscitation, clinical or proven coagulopathy, hypothermia, associated complex and other major multiple visceral injuries,

severe metabolic acidosis and an intra-operative blood transfusion that has exceeded 10 units of packed red blood cells (Rotondo, Schwab et al. 1993, Krige, Kotze et al. 2016).

1.10 Postoperative Care

The principles of postoperative care in patients undergoing resection for complex pancreatic injuries are similar to those in patients with other major abdominal injuries (Krige 1995, Krige, Beningfield et al. 2005, Krige 2006). Attention is paid to ventilatory status, fluid balance, renal function, intestinal ileus and nasogastric tube losses. Meticulous charting of drain content and volume is important. Prolonged ileus and pancreatic complications may preclude normal oral intake in severely injured patients. The principles of nutritional support in the critically ill are generally extrapolated to those who require critical care after pancreatic trauma. A fine bore silastic nasojejunal tube with a weighted tip placed distal to the injury or anastomosis at the initial operation in complex pancreatic injuries allows the option of early postoperative enteral feeding rather than total parenteral nutrition. A submucosal needle technique catheter jejunostomy can be considered in selected cases. The enteral feeding route is cheaper with less morbidity and provides more efficient nitrogen utilization and improved restoration of immune competence.

1.11 Complications

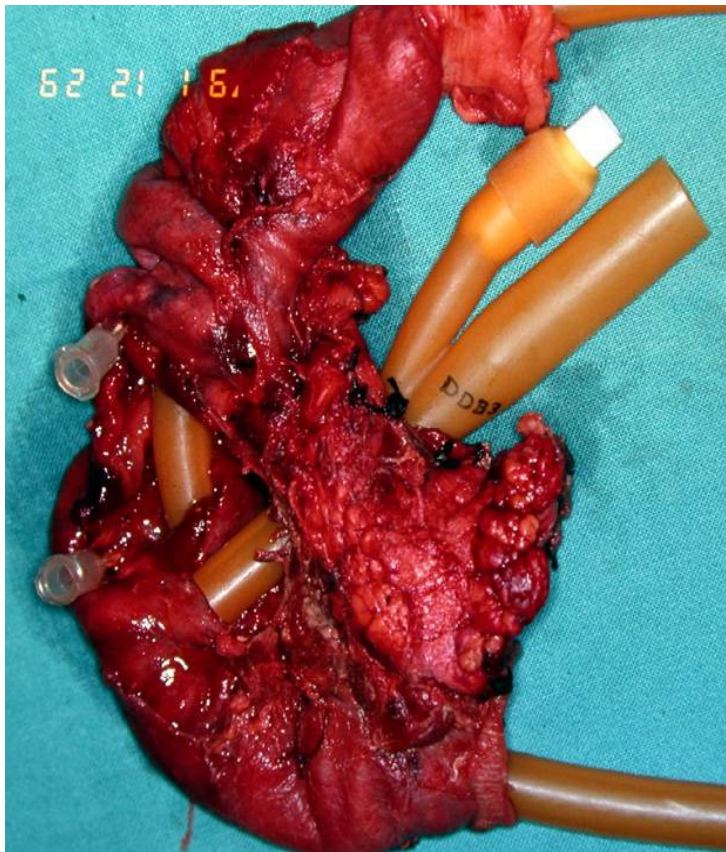
Peripancreatic, subhepatic and subphrenic fluid collections are commonly seen on US or CT after pancreatic trauma (Kao, Bulger et al. 2003, Lin, Chen et al. 2004). An infected collection should be suspected in any patient

with abdominal tenderness, a sustained systemic inflammatory response or persistent organ failure. When confirmed on cross sectional imaging, aspiration for culture and amylase content is mandatory with catheter drainage used in larger accessible unilocular collections. Antimicrobial therapy should be commenced to cover the full bacterial spectrum until definitive culture results become available. Pancreatic necrosis generally requires repeated debridements using transgastric endoscopic ultrasound, percutaneous or surgical access techniques. Secondary haemorrhage from inflammatory autodigestion of surrounding vessels is an uncommon but serious complication which can usually be controlled by angiographic embolization. Operative exposure and packing with abdominal swabs may be life-saving if embolization fails (Krige 1995, Krige, Beningfield et al. 2005).

A pancreatic fistula is the most common pancreas-related complication and occurs in 10-20% of major injuries to the pancreas either after operative drainage or resection (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Most fistulae are minor and resolve spontaneously within 1 or 2 weeks of injury, provided adequate external drainage has been established. High-output fistulae (>700 ml/day) usually indicate a major pancreatic duct disruption. A sinogram may be useful to define the site of a persistent fistula, as well as aiding in the planning of further treatment. Nutritional support is standard management, but the role of somatostatin and octreotide is unproven. The most important role of ERCP in pancreatic

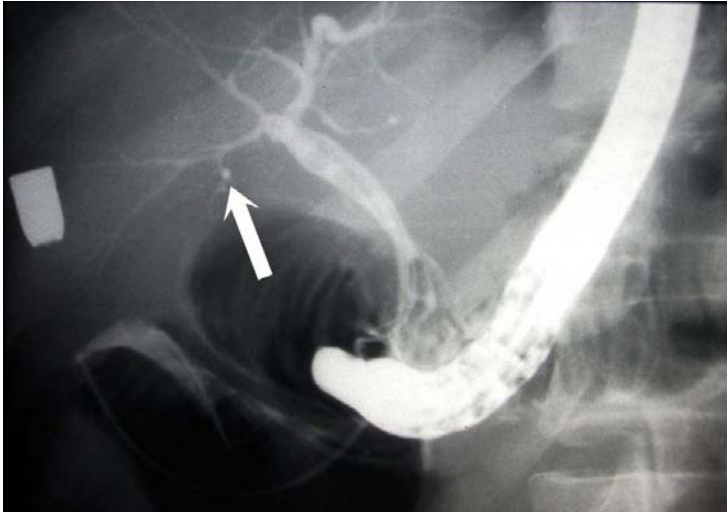
trauma currently is to provide endoscopic intervention with transpapillary stenting for persistent pancreatic fistulae (Figures .6, 7, 8) (Thomson, Krige et al. 2014). The first step if there is failure of resolution after 14 days is endoscopic pancreatography and transpapillary stent insertion. A persistent pancreatic fistula despite prolonged endoscopic stent drainage requires operative intervention with a distal pancreatic resection for leaks in the pancreatic tail or a Roux-en-Y cystjejunostomy for proximal leaks (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006).

Figure 6



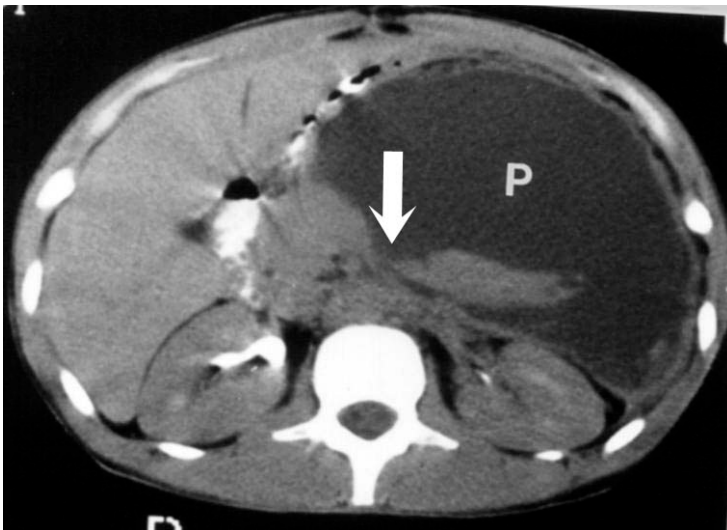
PD specimen showing disruption of the ampulla (arrow)

Figure 7



ERC after Whipple's resection and Imanaga reconstruction showing small associated intrahepatic bile leak (arrow) due to bullet injury

Figure 8



CT scan of pancreatic pseudocyst (P) surrounding pancreatic tail (T) following blunt abdominal injury showing pancreatic fracture (arrow) over vertebral column

Pseudocysts after abdominal trauma may be the end result of a pancreatic fistula or may occur as a result of undetected pancreatic duct disruption and may present weeks or months after the original pancreatic injury (Lewis, Krige et al. 1993, Beckingham and Krige 2001). The surgical strategy in the

management of traumatic pseudocysts will depend on the site and nature of the duct injury, the maturity of the cyst wall and the clinical urgency (Beckingham, Krige et al. 1997). If the pseudocyst is symptomatic or enlarging in size, MRCP or ERCP provide accurate anatomical delineation of the duct injury. If there is minimal communication with a side-duct or if the leak involves the distal duct, percutaneous or endoscopic ultrasound-guided aspiration should be attempted (Lewis, Krige et al. 1993). Pseudocysts with proximal major duct injury should preferably be drained by endoscopic ultrasound-guided either transgastric or transduodenal (Funnell, Bornman et al. 1994, Beckingham, Krige et al. 1997, Beckingham, Krige et al. 1999, Thomson, Krige et al. 2014). If endoscopic drainage is not feasible or unsuccessful, internal surgical drainage by cystgastrostomy, cystduodenostomy or cystjejunostomy is required (Lewis, Krige et al. 1993).

1.12 Conclusion

Injuries to the pancreas are uncommon. The prognosis is determined by the cause, site and grade of the injury, the magnitude of associated injuries and the degree of physiological insult (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Penetrating injuries are more likely to result in exploration and intraoperative detection whereas blunt injuries are more likely to be occult, isolated and investigated with cross sectional imaging. Whatever the cause, delay in diagnosis of main pancreatic injury leads to significant morbidity (Krige 1995, Krige 2004, Krige, Beningfield et al. 2005, Krige 2006). Good quality imaging is the key to establishing the diagnosis in blunt trauma. Most pancreatic injuries detected at surgery for

penetrating trauma are minor and can be treated conservatively by external drainage (Chrysos, Athanasakis et al. 2002). The commonest major blunt injury is a prevertebral laceration of the proximal body or neck of the pancreas which requires a left pancreatectomy (Jurkovich and Carrico 1990, Chrysos, Athanasakis et al. 2002). Major fractures to the right of the portal vein with an intact bile duct are similarly best treated by an extended left pancreatic resection. PD is reserved for severely destructive injuries to the head of pancreas and/or duodenum in which salvage or reconstruction is not feasible (Krige, Nicol et al. 2014). All procedures should include effective drainage of the pancreatic injury.

The modern trend of increasingly conservative surgery for most pancreatic injuries avoids the need for complex resections, elaborate enteric anastomoses or obligatory intra-operative pancreatography and represents a rationalization of previously advocated recommendations allowing preservation of pancreatic tissue without increasing morbidity (Krige and Thomson 2011). It is important to stress that overlooking or neglect of a major duct injury may lead to serious complications including fistulae, pseudocyst formation, sepsis, pancreatitis, and bleeding (Krige and Thomson 2011). In grade 4 and 5 pancreatic injuries early mortality is due to uncontrolled or massive bleeding from associated vascular or visceral injuries (Jurkovich and Carrico 1990), whereas late mortality is a consequence of infection and multiple organ failure. Although morbidity is high after a pancreatic injury, most complications can be resolved by careful

assessment of the injury and appropriate minimally invasive intervention
(Krige and Thomson 2011).

CHAPTER 2

Introduction and rationale for the thesis

The complexity and consequences of major pancreatic injuries are often underestimated. There is now increasing recognition that severe combined injuries involving the pancreatic head, duodenum and bile duct in haemodynamically unstable patients who have associated collateral organ damage are among the most exacting hepatopancreatobiliary injuries to manage and which tax the skill and the ingenuity of even the most experienced trauma and pancreatic surgeons (Ho, Patel et al. 2017). Both the unique anatomic features and the complex physiology of the pancreas have an important influence on the site and outcome of major injuries while the close proximity of large vascular structures and surrounding viscera compounds the complexity of injury management (Chrysos, Athanasakis et al. 2002). Severe blunt and penetrating abdominal trauma invariably damages adjacent organs, including liver, spleen, duodenum and colon. In contrast, isolated pancreatic injuries, though uncommon, pose specific problems in diagnosis and management due to initial containment and the lack of overt clinical signs (Subramanian, Dente et al. 2007).

The unforgiving nature of complex pancreatic injuries results in substantial morbidity rates with in-hospital mortality invariably related to the cumulative effects of the associated injured organs (Mayer, Tomczak et al. 2002, Heuer, Hussmann et al. 2011). Prognosis is influenced by the cause and

complexity of the pancreatic injury, the amount of blood lost, the duration of shock, the speed of resuscitation and the quality and type of surgical intervention (Kao, Bulger et al. 2003, Lopez, Benjamin et al. 2005, Scollay, Yip et al. 2006, Wang, Li et al. 2007). Most early deaths are due to either exsanguination or refractory coagulopathy or the consequences of massive blood transfusions after associated vascular or adjacent solid organ injuries (Thompson, Shalhub et al. 2013, Ragulin-Coyne, Witkowski et al. 2014, van der Wilden, Yeh et al. 2014). Neglect of a main pancreatic duct injury invariably leads to major complications that include pseudocysts, fistulae, sepsis and secondary haemorrhage (Wang, Li et al. 2007). Two-thirds of patients who survive more than 48 hours have major complications as a result of the pancreatic and associated injuries (Chinnery, Krige et al. 2012). One third of patients who die later, do so because of intra-abdominal or systemic septic complications or multi-organ failure (Sharpe, Magnotti et al. 2012).

Urgent intervention and resection of the pancreatic head and reconstruction in severely injured patients with complex pancreatic injuries, aggravated by hypothermia, coagulopathy and acidosis has, in the past, resulted in prohibitive mortality rates (Asensio, Demetriades et al. 1999). Often life-threatening associated collateral injuries, especially those involving adjacent large splanchnic veins including inferior vena cava, portal and superior mesenteric veins take precedence in management (Seamon, Pieri et al. 2007). In addition, there may be technical difficulties when resecting

and reconstructing complex pancreatic injuries which require special surgical skills and expertise (Krige 2016). Unstable patients may require initial damage control before later definitive surgery. Successful treatment of complex injuries of the head of the pancreas depends largely on initial correct assessment and appropriate treatment. The management of these severe proximal pancreatic injuries remains one of the most difficult challenges in abdominal trauma surgery, and there is now consensus that optimal results are most likely to be obtained by an experienced multidisciplinary team (Krige, Kotze et al. 2016).

The relative paucity of detailed publications on pancreatic trauma has impaired the development of clear guidelines on the optimal management of severe pancreatic injuries (O'Reilly, Bouamra et al. 2015). The currently available literature consists mainly of small single centre series which focus mainly on outcome after operative intervention without providing detailed strategic management. A number of earlier studies investigating prognosis and factors influencing survival have produced disparate and incongruent results while the introduction of newer technology and modern surgical strategies have rendered many previously established and orthodox conclusions based on obsolete or outdated techniques invalid. The situation has further become increasingly complex in the era of evolving non-operative management of pancreatic trauma (Pata, Casella et al. 2009, Duchesne, Kimonis et al. 2010).

Most reported large series are from the USA and South Africa which report a high proportion of penetrating pancreatic injuries, mainly from low velocity civilian gunshot wounds (Feliciano, Martin et al. 1987, Chinnery, Krige et al. 2012). The findings of these studies may therefore not reflect or be directly applicable to countries which have different trauma patterns such as the United Kingdom, Canada, Australia, New Zealand and much of Europe where road traffic accidents predominate. This geographical variation in aetiology and differences in investigative approaches result in considerable disparity in the reported severity and spectrum of pancreatic injuries (Krige 2006). Comparisons between various methods of treatment are also difficult to analyse accurately because pancreatic injuries are infrequent, the levels of care at individual centres may differ depending on the facilities and the experience of available staff and consequently there are wide variations in the reported morbidity and mortality rates.

These discrepancies are influenced by cohort bias due to small sample sizes and underpowered studies from some centres which lack structured injury treatment protocols and standardised management planning, compared to high-volume trauma centres that have established protocols and prospective documentation of peri-operative outcomes. Most published studies include all patients with pancreatic injuries without distinguishing between blunt and penetrating pancreatic injuries, which invariably skews interpretation and outcome. Other reports do not consistently divide complications into those that are specifically related to the consequences of

the pancreatic injury. Further limitations of the veracity of current information are that most published data are retrospective observational cohort studies which lack both validity and credibility.

Published results are variable and conflicting because of small sample sizes, referral bias, dissimilar study endpoints and differences in patient selection. While mortality is an objective and finite endpoint, the different grades of severity of postoperative morbidity are poorly defined and less easily quantifiable. In addition, the wide spectrum of the different variables in pancreatic injuries complicate the formulation of a prognostic model. Most previous studies have used subjective criteria to assess postoperative complications, which have hampered accurate comparative studies. Morbidity rates differ substantially within these series and reflect intrinsic biases of smaller hospitals compared to high volume tertiary referral centres as data generated from these reports are influenced by both referral and ascertainment bias.

An evaluation of previous studies shows flaws in data analysis due to the heterogeneity of the patient population included in the studies and a lack of standardization which has resulted in inconsistent data. These limitations are further compounded by a lack of prospective studies with standard protocols which questions both the validity and reliability of the data. This has restricted widespread incorporation of recommendations into routine clinical practice.

An important aspect in the treatment of complex pancreatic trauma has been the role of damage control surgery but currently this is an under-researched and poorly investigated area with inadequate analytic data. Both the early use of damage-control surgery and the need for pancreatic and duodenal resection are important considerations when treating complex combined pancreaticoduodenal injuries (CPDIs), but have not been applied consistently in high-risk situations (van der Wilden, Yeh et al. 2014). The reasons for the lack of clear guidelines for CPDIs and the paucity of reliable and robust data are manifold. Synchronous combined duodenal damage seldom occurs in tandem with injuries to the head of the pancreas (O'Reilly, Bouamra et al. 2015). The relative infrequency of this type of injury suggests that most surgeons will have had minimal operative exposure and limited personal experience when dealing with complex CPDIs. These deficiencies are compounded by the lack of data and clarity in surgical publications, which do not provide an authoritative or comprehensive analysis of the problem. In addition, the lack of a practical and universally relevant classification that can be applied to accurately predict the outcomes of CPDIs has hampered progress. In the absence of accurate contemporary data, persisting historical perceptions may conclude that patients with complex pancreatic injuries do worse because of a self-fulfilling prophecy of expected poor outcome and thus inevitably high mortality rates.

The absence of large contemporary focused and specific prospective pancreatic trauma registries has resulted in a paucity of robust and reliable

data. The datasets in many of the articles on pancreatic trauma have been collected retrospectively and for this reason there is significant potential for observer and selection bias in the coding and categorization of patients and complications. The incidence of pancreas-specific complications may be underestimated or incorrectly coded if data are not directly aligned with recognized standardized International Pancreatic Study Group definitions. Many general trauma databases lack strength, rigor and the necessary granular patient detail to provide in depth analyses of specific issues. This lack of information on key variables substantially weakens data collection, analysis and ultimately conclusions.

In order to address the above crucial shortcomings in the assessment and analysis of pancreatic injuries due to the lack of robust data and deficient surgical strategies, this thesis focused on priority topics and resolving existing unanswered and under-researched questions in the management of complex pancreatic injuries. Each of the following twelve clinical studies in this thesis evaluated a specific aspect of pancreatic trauma based on the detailed analysis of prospective granular data from a large cohort of patients treated in an academic surgery and trauma centre with considerable experience in civilian operative trauma care and where standard and uniform protocols were applied. The literature review component of this work evaluated existing pancreatic injury publications and critically appraised their concept, design, content and conclusions. A summary and key findings of each of the 12 clinical studies is presented below.

2.1 Study 1: Development and validation of a pancreatic injury mortality score (PIMS)

Krige JE, Spence RT, Navsaria PH, Nicol AJ. Development and validation of a pancreatic injury mortality score (PIMS) based on 473 consecutive patients treated at a level 1 trauma center. Pancreatology.2017 Apr 17.pii: S1424-3903(17)30075-3. doi: 10.1016/j.pan.2017.04.009. [Epub ahead of print] PMID: 28596059

The objective of this study was to develop for the first time a pancreatic injury mortality score (PIMS) to predict the likelihood of death in patients who had sustained a major pancreatic injury. We hypothesized that incorporating readily available and clinically relevant data which have a substantial influence on survival in an outcome prediction model would show improved predictive accuracy. In this context, we used prospectively collected data from a large cohort of consecutive patients and applied multivariate analysis and internal validation using robust and reliable methodology with objective and reproducible end-points to create a simple but comprehensive survival prediction model for individual patients after a major pancreatic injury.

The study used data from a prospective database of 473 patients treated for pancreatic injuries between January 1990 and December 2015. Two thirds of the patients were assigned to the derivation cohort and one third to the validation cohort. Clinical correlates of in-hospital death were identified and considered in stepwise logistic regression analyses that identified the factors included in the risk index. Five variables, age >55, shock on

admission, a vascular injury, number of associated injuries and pancreatic AAST correlated with in-hospital death and were used to calculate PIMS. The final score ROC in the derivation dataset was 0.84 (95% CI 0.79 – 0.89) and in the validation dataset was 0.91 (95% CI 0.84 – 0.97), which were comparable ($p= 0.1$). Finally, cut-off scores were used to generate three risk groups and the rate of mortality within the low (PIMS 0-4), medium (PIMS 5-9), and high risk (PIMS 10–20) groups were not significantly different. The scoring system was tested in a validation cohort and showed good calibration and discrimination for in-hospital mortality.

This study derived and validated the PIMS, a novel organ-specific risk prediction score calculated from five variables for in-hospital mortality following major pancreatic trauma. PIMS is simple, quick and easily understandable, increases clinical risk prediction for patients with complex pancreatic trauma and can be used as a benchmark for survival. The PIMS is a comprehensive and validated tool which accurately predicts post-operative mortality progressively across its range of scores based on easily accessible data points. In the trauma environment PIMS is able to provide prognostic information and at an institutional or national level, this score will allow comparison and hence benchmarking of the quality of care provided for this complex patient population.

This study has several substantial strengths. This is the largest study based on prospective data validating the risk for mortality and the PIMS thus generated has a number of advantages including parsimony, comprising

only 5 variables. An important feature is that the primary endpoint of in-hospital mortality is a robust and immutable variable which dispenses with the need and the deficiencies of long-term follow-up. The mortality data generated from this single centre based study is factual and indisputable and avoids the potential bias of underreporting negative events which may occur in multicentre registry-based databases. This model exploits variables readily available to trauma surgeons and has the potential to be effective as a real-time score to predict outcome and to benchmark quality of surgical intervention in the treatment of complex injuries and ultimately to aid in *post hoc* analysis of trauma research and comparative audit.

2.2 Study 2: Prognostic factors, morbidity and mortality in pancreatic trauma

Krige JE, Kotze UK, Setshedi M, Nicol AJ, Navsaria PH. Prognostic factors, morbidity and mortality in pancreatic trauma: a critical appraisal of 432 consecutive patients treated at a Level 1 Trauma Centre. Injury. 2015;46:830-836.

Previous reports have emphasized that outcome is influenced primarily by the cause and complexity of the pancreatic injury, the number and severity of associated vascular and visceral injuries, the duration of shock, the quality and nature of surgical intervention and secondarily by complications related to the pancreatic duct injury, pancreatic enzyme leakage and intra-abdominal sepsis (Smego, Richardson et al. 1985, Krige 1995, Kao, Bulger et al. 2003, Hwang and Choi 2008). There is, however, a paucity of publications which provide a detailed analysis of prognostic factors in

severe pancreatic injuries. This study assessed predictive factors for morbidity and mortality in major pancreatic injuries in a large cohort of consecutive patients using robust and reliable methodology and objective and reproducible end-points.

The records of 432 consecutive patients treated for pancreatic injuries between January 1982 and December 2012 were reviewed. Primary endpoints were postoperative morbidity and death. Bivariate and multivariate logistic regression analyses were used to assess significant predictors of morbidity and mortality. Overall mortality in 432 patients was 15.7% and morbidity 66%. Bivariate logistic regression analysis showed that 9 factors, age, RTS, presence of shock, need for a transfusion, volume of blood transfused, damage control surgery, AAST grade of pancreatic injury, an associated vascular injury and a repeat laparotomy were significant predictors of morbidity. In the final multivariate logistic regression analysis model however only 2 variables, AAST grade of pancreatic injury and a repeat laparotomy were significant predictors of morbidity. When factors associated with mortality were considered, logistic regression analysis found that 11 variables, age, RTS, the presence of shock, patients who required a major blood transfusion, the median number of units transfused, the need for a damage control laparotomy, AAST grade 3,4,5 pancreatic injuries, associated vascular injuries, the number of associated injuries, postoperative complications and days in ICU were significant. However in the final stepwise multivariate logistic regression analysis model only 5 variables, age, shock, median number of units transfused and the presence

of associated complications were significant factors associated with mortality (Krige, Kotze et al. 2015). This study is the most comprehensive single centre series yet to use bivariate and multivariate logistic regression analyses to examine the factors predicting complications and death in consecutive patients undergoing surgery for pancreatic trauma.

2.3 Study 3: Emergency pancreatoduodenectomy for complex pancreatic injuries

Krige JE, Nicol AJ, Navsaria PH. Emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum. HPB (Oxford). 2014;16:1043-1049.

Overall morbidity rates for maximal pancreatoduodenal injuries are substantial and mortality is directly proportional to the number of injuries sustained and is highest in the elderly and those who are haemodynamically unstable (Scollay, Yip et al. 2006). In a small cohort of severely injured patients a pancreatoduodenectomy may be the only option to salvage an otherwise irretrievable situation (Krige and Thomson 2011). Most authors concur that a pancreatoduodenectomy for trauma is seldom necessary and is reserved for maximal injuries involving the head of the pancreas and duodenum in which repair is not feasible and where the decision to do a pancreatoduodenectomy is unavoidable (Asensio, Petrone et al. 2003, Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014).

However, the answers to several issues regarding the role of pancreatoduodenectomy for major pancreatic injuries are unresolved.

These questions include: (i) establishing the mortality for emergency Whipple resection using modern pancreatic and biliary operative techniques; (ii) whether a pylorus-preserving pancreatoduodenectomy is technically feasible and appropriate in acute trauma and (iii) determining whether there is a beneficial role for pancreatogastrostomy in selected patients in reconstruction after an emergency Whipple resection. No publications have specifically assessed the results of emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum when performed by or under the supervision of experienced HPB surgeons. This study critically evaluated the outcome after pancreatoduodenectomy for Grade 5 injuries pancreatic injuries in a cohort of consecutive patients treated at a level I trauma centre using established HPB techniques of resection and reconstruction adapted for the trauma situation.

Prospectively recorded data of patients who underwent a pancreatoduodenectomy for trauma at the Level I Trauma Centre during a 22-year period were analysed. Nineteen of 426 patients with pancreatic injuries underwent a pancreatoduodenectomy (gunshot $n = 12$, blunt trauma $n = 6$ and stab wound $n = 1$). Nine patients had associated inferior vena cava or portal vein injuries. Five patients had an initial damage control procedure and underwent a definitive operation at a median of 15 hours (range 11–92 hours) later when stable. Twelve patients underwent a pylorus-preserving pancreatoduodenectomy and seven had a standard

Whipple resection. Three patients with APACHE II scores of 15, 18, 18 died post-operatively of multi-organ failure. All 16 survivors developed post-operative complications which included Dindo-Clavien grade I (n = 1), grade II (n = 7), grade IIIa (n = 2), grade IVa (n = 6) complications. Factors complicating surgery were shock on admission, number of associated injuries, coagulopathy, hypothermia, gross bowel oedema and traumatic pancreatitis.

This study showed that a pancreateoduodenectomy is a life-saving procedure in the small cohort of stable patients with non-reconstructable pancreatic head injuries and that a pylorus-preserving pancreateoduodenectomy is technically feasible and safe in the trauma situation. A pancreatogastrostomy is an option when a conventional pancreatojejunostomy is difficult as a result of an oedematous jejunum. While an emergency pancreateoduodenectomy has significant morbidity and appreciable mortality due to complicating factors, associated injuries and shock, a resection may be the only option in complex injuries with ampullary destruction or a devitalized duodenum. The current data show that these are patients with complex problems associated with significant post-operative morbidity and should be managed collaboratively by both trauma and HPB surgical teams as the procedure is technically demanding and crucial procedural decisions must be made during resection and reconstruction.

2.4 Study 4: Surgical management of combined pancreatoduodenal injuries

Krige JE, Kotze UK, Setshedi M, Nicol AJ, Navsaria PH. Surgical management and outcomes of combined pancreatoduodenal injuries: 75 consecutive cases analyzed. J Am Coll Surg. 2016;222:737-749.

Severe combined pancreatoduodenal injuries (CPDI) are complex and result in significant morbidity and mortality even when treated in well-resourced high-volume trauma referral centers (Krige 1997, Krige, Beningfield et al. 2005). There are no contemporary data on the role of either primary or secondary resections after DCL for severe CPDI. The 5 most crucial factors influencing management and outcome are grade of pancreatic head damage, degree of ischaemia and viability of the duodenum, extent of ampullary damage, presence of visceral vascular injuries, and magnitude of associated organ injuries. These issues determine both the scale of intervention and ultimate survival.

This study addressed 3 of the major unresolved issues in severe CPDIs, namely, survival after initial damage-control surgery, outcomes after pancreatoduodenectomy, and evaluation of predictive factors for morbidity and mortality in a large cohort of consecutive patients using a CPDI grading score. We hypothesized that bivariate analyses would accurately identify factors influencing morbidity and mortality. In addition, the study sought to define specific criteria for the selection of the type of surgery for complex combined injuries using robust and reliable methodology and objective and

reproducible end points. Survival in CPDI after initial damage-control laparotomy (DCL) and pancreatoduodenectomy was evaluated in a large cohort treated in a Level I trauma center.

The records from a prospective database of 453 consecutive patients treated for pancreatic injuries between January 1990 and April 2015 were reviewed to identify those with CPDI. Primary and secondary end points assessed were death and morbidity. Seventy-five patients with CPDI, underwent 161 operations (range 1 to 9 operations). Twenty-nine patients with complex CPDI underwent a DCL and 46 had definitive treatment during the initial operation. Nineteen had a pancreatoduodenectomy, either during the initial operation (n=13) or after the DCL (n=6). Postoperative complications occurred in 63 (84%) patients. Twenty one (28%) patients died, including 15 (43%) of 35 patients with associated vascular injuries. Sixteen (84%) of the 19 patients who had a pancreatoduodenectomy survived. Significantly more complications related to bleeding, disseminated intravascular coagulation, and hypovolemic shock occurred in those patients who eventually died and significantly more abdominal sepsis and fistulas occurred in patients who survived. Mortality was related to associated vascular injuries overall ($p < 0.01$), major visceral venous injuries ($p < 0.011$), and the combination of vascular plus the total number of associated organs injured ($p < 0.046$). Despite using DCL in CPDIs, morbidity (84%) and mortality (28%) remain substantial. Careful selection of patients undergoing pancreatoduodenectomy resulted in 84% survival.

Associated vascular injuries, major visceral venous injuries, and combined vascular and associated organs injured influenced outcomes and mortality.

This study shows that only one-sixth of patients who had sustained pancreatic injuries overall had synchronous duodenal injuries, and although most CPDIs had associated intraabdominal injuries, importantly, almost half also had major vascular injuries with significant portend. Unlike previous reports on pancreatoduodenal injuries, one quarter of patients in this study underwent a pancreatoduodenectomy and 40% had an initial DCL. A feature in this study was the use of a composite grading system for CPDIs. Additional salient findings in this article are the impact of associated life-threatening visceral vascular injuries on survival and the outcome of simplified duodenal repair and avoidance of previously recommended protective bypass surgery to redirect gastric content into the jejunum. This study demonstrated a paradigm shift in the overall management of complex CPDIs and emphasized that no single operation is appropriate for all pancreaticoduodenal injuries. Pancreatoduodenectomy should be reserved for a select group of patients who have complex CPDIs in whom repair is not feasible and who are haemodynamically stable. In the small cohort of patients who require initial damage control, both the pancreatoduodenectomy and the reconstruction should be delayed until the subsequent definitive operation.

2.5 Study 5: Management of pancreatic injuries during damage control surgery

Krige JE, Kotze UK, Setshedi M, Nicol AJ, Navsaria PH. Management of pancreatic injuries during damage control surgery: an observational outcomes analysis of 79 patients treated at an academic Level 1 trauma centre. Eur J Trauma Emerg Surg. 2017 Jun;43(3):411-420.

Since the initial publication by Stone et al (Stone, Fabian et al. 1981) and the subsequent seminal description by Rotondo et al (Rotondo, Schwab et al. 1993), damage-control methodology has transformed the way trauma surgery is implemented. The concept is now widely accepted as an essential strategy in the management of complex trauma aggravated by coagulopathy, hypothermia and acidosis (Shapiro, Jenkins et al. 2000). Despite these advances mortality rates in patients who have life-threatening pancreatic trauma combined with injuries to contiguous organs including liver, bile ducts, duodenum and vena cava, superior mesenteric and portal veins remain substantial (Chrysos, Athanasakis et al. 2002, Recinos, DuBose et al. 2009). A severe pancreatic injury compounded by visceral and vascular injuries exponentially increases the complexity of operative intervention (Krige, Beningfield et al. 2005).

There are no clear guidelines on the management of a pancreatic injury during damage control surgery. Equally, few published series have specifically addressed outcome of damage control surgery in patients with an associated pancreatic injury. This study evaluated the role of damage

control surgery to determine which factors influenced mortality in a large cohort of patients who sustained pancreatic injuries and underwent DCS at a major trauma centre using a previously defined protocol.

Consecutive patients with pancreatic injuries who underwent DCS between 1995 and 2014 were identified in the prospective database. Seventy-nine patients with pancreatic injuries had DCS. Fifty-nine (74.7%) patients had AAST grade 3, 4 or 5 pancreatic injuries. The 79 patients had a total of 327 associated injuries (mean: 3 per patient, range 0-6) and underwent a total of 187 (range 1-7) operations. Vascular injuries (60/327, 18.3%) occurred in 41 patients. Twenty seven (34.2%) patients died without having a second operation. The remaining 52 patients had two or more laparotomies (range 2-7). Overall 28 (35%) patients underwent a pancreatic resection either during DCS (n=18) or subsequently as a secondary procedure (n=10) including a Whipple (n=6) when stable. Overall 43 (54.4%) patients died. Mortality was related to associated vascular injuries overall, major visceral venous injuries and combined vascular and total number of associated organs injured. Despite the magnitude of their combined injuries and the degree of physiological insult, DCS salvaged 45% of critically injured patients who later underwent definitive pancreatic surgery.

2.6 Study 6: Damage control laparotomy and delayed pancreatoduodenectomy for complex combined pancreatoduodenal and venous injuries

Krige JE, Navsaria PH, Nicol AJ. Damage control laparotomy and delayed pancreatoduodenectomy for complex combined pancreatoduodenal and venous injuries. Eur J Trauma Emerg Surg. 2016;42:225-230.

In the small cohort of patients who have maximal injuries of the pancreatoduodenal complex and in whom there is no other rational surgical option for survival, a salvage pancreatoduodenectomy may be necessary (Koniaris, Mandal et al. 2000, Krige, Nicol et al. 2014, van der Wilden, Yeh et al. 2014). However, surgical intervention of such magnitude in those who are severely injured can only be contemplated in hemodynamically stable patients. The concept of damage control surgery (DCS) is now an essential element in the management of severely injured patients who are hemodynamically unstable and has dramatically improved outcome. However, there is a lack of accurate and robust data assessing the role of DCS in patients who have combined severe pancreatic and vascular injuries. To date there has been no detailed or comprehensive evaluation of the efficacy of an initial damage control laparotomy followed by a proximal pancreatic resection in this high risk group of patients, nor has there been a critical analysis of the timing of the pancreatoduodenectomy. In order to address this deficiency, this study evaluated patient outcome after initial DCS and subsequent pancreatoduodenectomy and reconstruction with particular appraisal of the advantages of delaying resection in unstable

patients with associated major vascular injuries to assess optimal operative sequencing.

During the 20-year study period, 312 patients were treated for pancreatic injuries of whom 14 underwent a pancreaticoduodenectomy. Six of the 14 patients were *in extremis* with exsanguinating venous bleeding and non-reconstructable AAST grade 5 pancreaticoduodenal injuries and underwent a damage control laparotomy followed by delayed pancreaticoduodenectomy and reconstruction when stable. The mean operating room time was 113 minutes, range 90-140 m vs 335 minutes, range 260-395 minutes ($p < 0.01$). During the second laparotomy 5 patients had a pylorus preserving pancreaticoduodenectomy and one a standard Whipple resection. Four of the six patients survived. Two patients died in hospital, one of MOF and coagulopathy and the other of intra-abdominal sepsis and multi-organ failure. Median duration of intensive care was 6 days, (range 1-20 days) and median duration of hospital stay was 29 days, (range 1-94 days).

The effective treatment of complex pancreatic injuries associated with vascular damage continues to be a major challenge for surgeons dealing with abdominal trauma. Careful patient selection is crucial for survival and prolonged surgical procedures consciously avoided. It is essential to appreciate that a damage control approach can be used in smaller hospitals where experience with complex pancreatic and vascular injuries may be limited or where the necessary resources are not available. After control of bleeding and contamination the patient should be transferred to a major

trauma centre where both trauma and HPB surgeons experienced in the management of proximal pancreatic resections and reconstruction are available.

2.7 Study 7: Benchmarking postoperative complications after complex pancreatic injuries using the Accordion classification

Krige JE, Jonas E, Thomson SR, Kotze UK, Setshedi M, Nicol AJ, Navsaria PH. Management of complex pancreatic injuries: benchmarking postoperative complications using the Accordion classification. World J Gastrointest Surg.2017;9(3):82-91.

Major pancreatic resections are technically complex procedures, especially so when performed as an emergency in severely injured patients who also have multiple other injuries (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). There are wide variations in the reported overall postoperative morbidity rates after pancreatic injuries due to non-standardised analyses and a lack of comprehensive datasets which specifically document outcome after resection of complex pancreatic injuries (Scollay, Yip et al. 2006, Antonacci, Di Saverio et al. 2011, Sharpe, Magnotti et al. 2012). The absence of an appropriate and defined methodology to measure and register peri-operative outcome, precludes the generation of validated outcome data, fundamental to accurate benchmarking of surgical performance and internal quality control (Yoon, Chalasani et al. 2013). Both the number and severity of postoperative complications are recognised key short-term surrogate markers of the

quality of operative intervention and surgical outcome(Martin, Brennan et al. 2002). The 6-scale Accordion Severity Grading System (ASGS) which discriminates post-operative complication severity following elective surgery on the basis of escalating interventional criteria, is now widely accepted as a credible, scoring system which is easy to apply and is reproducible with minimal inter-observer variability (Strasberg, Linehan et al. 2009).The aim of this study was use ASGS metrics to assess the usefulness of the scoring system to benchmark the spectrum and severity of complications after pancreatic resection for trauma.

Between 1990 and 2015 one hundred and thirty patients with AAST grade 3, 4 or 5 pancreatic injuries underwent resection (pancreatoduodenectomy n=20, distal pancreatectomy n=110), including 30 who had an initial damage control laparotomy (DCL) and later definitive surgery. AAST injury grades, type of pancreatic resection, need for DCL and incidence and ASGS severity of complications were assessed. Uni- and multivariate logistic regression analysis was applied. Overall 238 complications occurred in 95 (73%) patients of which 73% were ASGS grades 3-6. Nineteen patients (14.6%) died. Patients more likely to have complications after pancreatic resection were older, had a revised trauma score (RTS) <7.8, were shocked on admission, had grade 5 injuries of the head and neck of the pancreas with associated vascular and duodenal injuries, required a DCL, received a larger blood transfusion, had a pancreatoduodenectomy (PD) and repeat laparotomies. Applying univariate logistic regression

analysis, mechanism of injury, RTS <7.8, shock on admission, DCL, increasing AAST grade and type of pancreatic resection were significant variables for complications. Multivariate logistic regression analysis however showed that only age and type of pancreatic resection (PD) were significant. The detailed outcome analysis provided may serve as a reference for future institutional comparisons(Krige, Jonas et al. 2017).

2.8 Study 8: Morbidity and mortality after distal pancreatectomy for trauma

Krige JE, Kotze UK, Nicol AJ, Navsaria PH. Morbidity and mortality after distal pancreatectomy for trauma: a critical appraisal of 107 consecutive patients undergoing resection at a Level 1 Trauma Centre. Injury. 2014;45:1401-1408.

Although several substantial reports (Kao, Bulger et al. 2003, Heuer, Hussmann et al. 2011, Sharpe, Magnotti et al. 2012) have detailed aspects of the management of pancreatic injuries, few series have specifically assessed complications and outcome after distal pancreatectomy for trauma (Wind, Tiret et al. 1999, Malgras, Douard et al. 2011). While mortality is an objective and finite endpoint, different grades of severity of postoperative morbidity are poorly defined and less easily quantifiable (DeOliveira, Winter et al. 2006). Most previous studies have used subjective criteria to assess postoperative complications, which have hampered accurate comparative studies. Morbidity rates differ substantially within these series and reflect intrinsic biases of smaller hospitals compared to high volume tertiary referral centres as data generated from these reports

are influenced by both referral and ascertainment bias. This study critically evaluated morbidity and mortality after distal pancreatectomy for major pancreatic injuries and assessed the severity of pancreas-specific postoperative complications using objective, reliable, and reproducible internationally accepted graded classification systems (Moore, Cogbill et al. 1990, Clavien, Barkun et al. 2009).

The records of 107 consecutive patients who underwent a distal pancreatectomy were reviewed. Primary endpoints were postoperative morbidity and death. Complications were graded according to the Clavien-Dindo severity classification and the International Study Group of Pancreatic Surgery (ISGPS) definitions. 107 patients underwent distal pancreatectomy. Overall mortality was 12%, 16% for gunshot injuries, 8% for blunt trauma and 0% in patients who had stab wounds. Eighty patients had a post-operative complication. A pancreatic leak (n=26) was the most common pancreatic related complication. Median postoperative stay in 28 patients with no or grade I complications was 9 days; in 11 patients with grade II complications was 18 days; in 14 grade IIIa, 31 days; in 19 grade IIIb, 38 days; in 8 grade IVa, 33 days in 14 grade IVb, and in 13 grade V the duration of postoperative stay was 14 ± 39.4 days. Overall mortality for distal pancreatectomy was 12%. Pancreatic leak was a common cause of morbidity. Length of hospitalisation increased with increasing Clavien-Dindo severity grading. There was a significant difference in the duration of

hospitalization in patients with no or grade I complications compared to those with grade II-IV injuries ($p < 0.05$).

This study shows that although mortality after distal pancreatectomy for trauma is substantial, most deaths are unrelated to the pancreatic injury and are due to associated injuries. The foremost risk factors for death were shock on admission to hospital, a major vascular injury and three or more associated adjacent organ injuries. The study demonstrated that mortality was highest in patients who had sustained a gunshot injury and this cohort required significantly more associated damage control operations and repeat laparotomies than blunt or stab injuries of the pancreas. Postoperative morbidity in this study was considerable and an increasing complication severity grade, when measured by the Clavien-Dindo method, led to the need for escalating intervention and prolonged hospitalization.

2.9 Study 9: Endoscopic and operative treatment of delayed complications after pancreatic trauma

Krige JE, Kotze UK, Navsaria PH, Nicol AJ. Endoscopic and operative treatment of delayed complications after pancreatic trauma: An analysis of 27 civilians treated in an academic Level 1 Trauma Centre. Pancreatology. 2015;15:563-569.

While the management of acute pancreatic injuries is well documented, only limited data are available detailing the consequences of delayed complications following a severe pancreatic injury. Endoscopic intervention has no role in severely injured patients with acute pancreatic trauma but may be useful in haemodynamically stable patients who present later with

complications related to the pancreatic trauma. On the basis of our previously published clinical experience we hypothesized that delayed local pancreatic complications that occur after a major pancreatic injury are likely due to main pancreatic duct damage and could thus theoretically be managed effectively by non-operative endotherapeutic methods such as pancreatic duct stenting or pseudocyst drainage (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994, Farrell, Krige et al. 1996, Apostolou, Krige et al. 2006, Krige, Kotze et al. 2011, Thomson, Krige et al. 2014). To test this hypothesis the present study critically evaluated the efficacy of endotherapeutic pancreatic duct stenting and transmural cyst drainage in the management of delayed complications after a major pancreatic injury in a cohort of consecutive patients using robust and reliable methodology with objective and reproducible end-points.

The degree of the pancreatic duct injury was graded using a new duct injury grading system and endoscopic therapeutic outcome assessed according to the grade of injury. During the period under review, 432 consecutive patients were treated for pancreatic injuries of whom 27 (20 men, 7 women, median age 31, range 15-68 years) presented with delayed complications related to the initial pancreatic injury. Sixteen patients had non-resolving symptomatic pancreatic pseudocysts, 10 had persistent pancreatic fistulae and 1 had a symptomatic duct stricture. Fourteen patients with grade 2a, 3a, 3b or 4c main pancreatic duct injuries were successfully treated endoscopically with either pancreatic duct stenting or pseudocyst drainage

while 13 patients with grade 4a or 4b duct injuries who had complete duct division with a disconnected duct syndrome failed endoscopic management and required surgical intervention. The 27 patients underwent a total of 49 endoscopic procedures (47 elective, 2 emergency) of whom 4 developed complications related to the endoscopic treatment. All 4 resolved, 2 after urgent endoscopic re-intervention.

Endotherapy for established pancreatic complications after trauma is generally safe with a low incidence of adverse events and is likely to be effective in half of those with persistent pseudocysts or leaks. All the patients in this study who had either grade 2a, 3a, 3b or 4c pancreatic ductal injuries resolved after endoscopic intervention and those with grade 4a or 4b ductal injuries uniformly required surgery. In this analysis the new proposed Cape Town pancreatic ductal injury grading classification showed a close correlation with outcome after endoscopic and operative intervention.

2.10 Study 10: Isolated pancreatic injuries treated at a Level 1 Trauma Centre.

Krige JE, Kotze UK, Nicol AJ, Navsaria PH. Isolated pancreatic injuries: An analysis of 49 consecutive patients treated at a Level 1 Trauma Centre. J Visc Surg. 2015;152:349-355.

A feature of previous publications assessing pancreatic injuries is the frequency of associated collateral visceral and vascular injuries which profoundly influence outcome and hamper accurate comparative studies

(Kao, Bulger et al. 2003, Hwang and Choi 2008, Krige, Kotze et al. 2014). A further limitation of previous reports is the relatively small number of patients included and the absence of a detailed and precise subgroup analysis of isolated pancreatic injuries. Based on our previously published clinical experience (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012) we hypothesized that much of the morbidity and mortality that occurs as a consequence of a major pancreatic injury is due to collateral damage to adjacent vital organs and in their absence, isolated pancreatic injuries should have a significantly lower complication and death rate. To test this hypothesis the present study used a large, high-quality surgical outcomes database in a cohort of consecutive patients using robust and reliable methodology with objective and reproducible end-points to assess outcome and injury-specific factors associated with morbidity and mortality after an isolated pancreatic injury (IPI).

Four hundred and forty eight consecutive patients were treated between 1990 and 2014 for pancreatic injuries of whom 49 had an IPI. Thirty four (70%) patients underwent urgent surgery, 20 of whom had a distal pancreatectomy and 14 had external drainage of the pancreatic injury. Fifteen (30%) patients presented with a non-resolving pancreatic pseudocyst or fistula; five had grade 4A or 4B ductal injuries and underwent surgery, 10 with 3A and 3B ductal injuries were successfully managed endoscopically. Fifty five percent had post-operative morbidity. Two patients (4%) died of non-pancreatic-related causes. While overall mortality

is low after an IPI, morbidity is high. Two-thirds of patients required operative intervention and one-third were treated endoscopically. The degree of pancreatic ductal injury determined whether endoscopic intervention was effective.

In this analysis, isolated pancreatic injuries in the absence of other major extra-abdominal injuries had a good outcome with low mortality rates. Two-thirds of patients with isolated pancreatic injuries required operative intervention. One third of patients who were stable after abdominal trauma without clinical evidence of shock, peritonitis or an abdominal injury requiring operative intervention were managed conservatively but in retrospect clearly had an underlying but occult pancreatic injury and presented subsequently with a pseudocyst. With careful intra-operative evaluation of the injury, most pancreatic injuries can be managed by either distal resection or drainage without the need for complex enteric diversions or pancreatoenteric anastomoses as a primary procedure during the acute injury phase.

2.11 Study 11: An analysis of predictors of morbidity after stab wounds of the pancreas

Krige JE, Kotze UK, Sayed R, Navsaria PH, Nicol AJ. An analysis of predictors of morbidity after stab wounds of the pancreas in 78 consecutive injuries. Ann R Coll Surg Engl. 2014;96:427-433.

The absence of a universally acceptable classification has prevented accurate comparisons between series (Chrysos, Athanasakis et al. 2002).

Because pancreatic injuries are uncommon and most series have small numbers, some studies include all patients with blunt and penetrating pancreatic injuries (Kao, Bulger et al. 2003, Scollay, Yip et al. 2006), while others combine gunshot and stab wounds of the pancreas (Ivatury, Nallathambi et al. 1990, Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001). Several substantial reports detailing pancreatic injuries have been published in the past, including from our own institution (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012), but none have explicitly evaluated the consequences of stab wounds of the pancreas (Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001). This study therefore examined the factors associated with morbidity and mortality of stab wounds of the pancreas in a high volume academic trauma referral centre.

A retrospective univariate cohort analysis was done of 78 (74 men) patients, median age 26 years (range 16–62) with stab wounds of the pancreas between 1982 and 2011. Median RTS was 7.8 (range 2.0–7.8). Injuries involved head/uncinate process (n=16), neck (n=2), body (n=36) and tail (n=24) of the pancreas. All 78 patients underwent a laparotomy. Sixty-five patients had AAST grade I or II injuries and 13 had grade III, IV or V pancreatic injuries. Eight (10.3%) of 78 patients had an initial damage control operation. Sixty nine (84.6%) patients had drainage of the pancreas only, six had a distal pancreatectomy and one had a Whipple resection. Most pancreas-related complications occurred in patients with AAST grade

III injuries; 8 patients (10.2 per cent) developed a pancreatic fistula. Four (5.1%) patients died. Grade of pancreatic injury (AAST grade I–II vs grade III–V injuries; $p < 0.001$), RTS ($p < 0.007$, OR 5.01, 95% CI 1.46–17.19), presence of shock on admission ($p = 0.022$, OR 3.31, 95% CI 1.16–9.42), need for a blood transfusion ($p < 0.001$, OR 6.46, 95% CI 2.40–17.40) or repeat laparotomy ($p < 0.001$) had a significant influence on the development of general complications.

This analysis showed that although mortality was low after pancreatic stab wounds, morbidity was high. Significant predictors of morbidity in this study were an increasing AAST grade of pancreatic injury, a high revised trauma scale, shock on admission to hospital, the need for a blood transfusion and a repeat laparotomy. The majority of patients in this study had grade I or II pancreatic injuries with neither substantial tissue loss nor a main duct injury and after control of bleeding were effectively treated with external drainage alone. More advanced grade injuries of the body and tail were managed by resection (Krige, Kotze et al. 2014).

2.12 Study 12: Pancreatoduodenectomy for trauma: applying novel reconstruction techniques

Krige JE, Thomson SR. Pancreatoduodenectomy for trauma: applying novel reconstruction techniques. Surgical Techniques Development. 2016. DOI: <http://dx.doi.org/10.4081/std.2016.6293>

Pancreatoduodenectomy and subsequent reconstruction after complicated pancreatic injuries in severely injured patients has in the past resulted in

prohibitive mortality rates. No publications have specifically assessed the technical aspects of reconstruction after emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum. This study evaluated the outcome of pancreatic, biliary and gastric reconstruction methods after pancreatoduodenectomy for major pancreatic injuries in a cohort of consecutive patients treated at a level I academic trauma centre.

Prospectively recorded data including reconstructive techniques used in patients who underwent a PD for trauma were analysed. Twenty patients underwent a PD. Six had an initial damage control procedure. Thirteen had a pylorus-preserving PD and 7 a standard Whipple resection because injury to the pylorus precluded a pylorus-preserving resection. Twelve patients had a pancreatojejunostomy and 8 a pancreatogastrostomy, 3 of whom had a duodenojejunal hepaticojejunal sequence of anastomoses to allow endoscopic biliary stent retrieval. Pancreatic and biliary reconstructions performed under adverse conditions after a trauma PD required a variety of technical modifications. The pylorus does not have to be sacrificed and posterior gastric implantation is a safe option for an oedematous pancreas.

This analysis describes for the first time how techniques for pancreatic, biliary and gastric anastomoses need to be modified for reconstruction after a pancreatoduodenectomy for trauma. This study confirms that delayed resection and reconstruction after damage control is feasible with a reasonable prospect of survival. This study has demonstrated that a

pylorus-preserving pancreatoduodenectomy is feasible in selected patients and that pylorogastric resection is only necessary when dictated by the extent of injury. A practical argument has been advanced that a pancreatogastrostomy may be a safer option than a pancreatojejunostomy when conventional anastomoses are high-risk due to oedematous tissues. These techniques do not need to be used in all pancreatoduodenal injuries requiring resection, but should be applied and adapted to the severity of the situation. The data emphasize that these are complex cases with significant postoperative morbidity and are best managed collaboratively by trauma and HPB surgical teams.

CHAPTER 3

Methodology

Included in this methodology section is (i) the management protocol for the treatment of pancreatic injuries, (ii) the format of the data collection, (iii) the method of data analysis, (iv) the statistical methodology and (v) a description of the process applied for the focussed literature review.

3.1 Management protocol for pancreatic injuries

All patients in this study were admitted to Groote Schuur Hospital, a government-funded, tertiary high-volume, integrated academic surgery referral level-1 Trauma Centre serving a population of 3 million people in the greater Cape Town area and with an annual operative trauma volume averaging 12,000 patients (Nicol, Knowlton et al. 2014). Groote Schuur Hospital is the chief academic teaching and training hospital of the University of Cape Town and one of the largest trauma referral hospitals in the world (Nicol, Knowlton et al. 2014). All patients documented in this study were treated either in the Trauma Centre or in the Hepatopancreatobiliary and Surgical Gastroenterology Units at Groote Schuur Hospital. Initial resuscitation of all injured patients was implemented using Advanced Trauma Life Support (ATLS) guidelines (Kortbeek, Al Turki et al. 2008). Rapid pre-operative evaluation included relevant physical examination, endotracheal intubation when necessary, insertion of resuscitation lines, selected focussed abdominal trauma and cardiac

sonography and chest radiographs. The protocol for evaluation and resuscitation of major abdominal trauma is presented in Table 1. An urgent laparotomy was performed in patients who had clinical evidence of acute major intra-abdominal bleeding or peritonitis. From 1995 onwards haemodynamically unstable patients who had major associated organ and visceral vascular injuries and trigger criteria had initial damage control surgery (DCS) before later definitive intervention.

Table 1 Protocol for resuscitation and evaluation of major abdominal trauma

1. **Resuscitation:**

- Airway patency (intubate)
- Breathing assistance (ventilate)
- Circulatory support
- Central line for venous access
- Crossmatch blood
- Intravenous fluids
 - Rapid crystalloid infusion
- Foley catheter
- Nasogastric tube
- Monitor vital signs
 - Pulse oximeter
 - ECG
 - B.P.

2. **Evaluation:**

History:

- Car accident, fall, assault, stab, gunshot
- Substantial trauma to abdomen or lower chest

Examination:

- Head, neck, chest, abdomen, pelvis, limbs

Abdomen:

- Skin bruising, ecchymoses
- Distension (blood, gas, urine)
- Tenderness, guarding, rigidity (gut perforation or bleeding)
- Lateral lower rib fractures (spleen, liver injury)
- Pelvic fractures (bladder or urethral injury)
- Blood at urethral meatus (urethral injury)

3. **Investigations:**

Haematology:

- Haemoglobin, WCC, INR

Biochemistry:

- Electrolytes, urea, creatinine, amylase
- Blood gases

X-ray

- Chest x-ray:
 - pneumothorax, rib fracture, free air under diaphragm
- Abdominal x-ray:
 - Rib, pelvic fractures, psoas shadow

Ultrasound

CT

3.2 Operative management of pancreatic and duodenal injuries

The emergency laparotomy used a midline incision to provide access to the abdomen. Priority was given to control of bleeding and containment of bowel contamination. If clues of a pancreatic injury which included a lesser sac fluid collection, retroperitoneal bile-staining or crepitus, fat necrosis, or a haematoma overlying the pancreas were present the pancreas and the integrity of the main pancreatic duct was evaluated. The anterior surface of the pancreas was examined by entering the lesser sac through the gastrocolic ligament and the posterior aspect was assessed when necessary by dividing the peritoneum along the inferior border to allow elevation of the pancreas. The duodenum was exposed using an extended Kocher manoeuvre. The ligament of Treitz was divided to assess the fourth part of the duodenum. When indicated, the ascending colon and small bowel were mobilized to fully assess the third part of the duodenum. If required, an operative cholangiogram was done using a 25-gauge butterfly needle in the common bile duct and 10 ml full-strength iodinated contrast injected under fluoroscopic control to assess the integrity of the ampulla. If a duodenal injury was co-incidentally present, a 5Fr paediatric feeding tube was used for operative pancreatography by cannulating the ampulla of Vater. In complex injuries intra-operative ultrasound was used to evaluate pancreatic duct integrity.

3.3 Operative management of pancreatic injuries

Operative management of pancreatic and associated duodenal injuries was based on the haemodynamic stability of the patient, the magnitude and

extent of associated injuries and the location and severity grades of both the pancreatic and duodenal injuries. Minor lacerations of the pancreas without visible duct damage (grade 1 and 2) and injuries of the head of the pancreas without devitalization of pancreatic tissue (grade 3) were managed by closed external suction drainage. Duodenal injuries were treated with debridement of the edges and a single layer primary repair (grade 1 and 2), or with resection of ischaemic tissue and a primary end-to-end anastomosis (grade 3) with intraluminal tube drainage. A feeding jejunostomy was fashioned when there was involvement of greater than 50% of the duodenal circumference and a primary repair or resection and anastomosis was undertaken.

Major lacerations of the neck, body or tail of the pancreas (AAST grade III or IV) with visible or likely duct injury were treated by distal pancreatectomy. In these patients the pancreas was transected at or proximal to the injury site using a diathermy or scalpel, followed by identification of the main pancreatic duct which was ligated at the resection margin with a transfixing 4-0 PDS suture. The anterior and posterior edges of the resection margin were apposed using interrupted 4-0 PDS sutures on an atraumatic needle to achieve haemostasis and minimize fistula formation. All pancreatic injuries were drained using closed silastic suction drains. A pancreatoduodenectomy was restricted to patients who had non-reconstructable injuries due to destruction of the head of the pancreas, duodenum and ampulla (AAST grade 4 and 5) and was done as a primary

procedure during the initial operation if the patient was stable or as a secondary staged procedure after DCS.

3.4 Damage control laparotomy

From 1995 onwards unstable patients who had major associated organ and visceral vascular injuries and trigger criteria had an initial damage control procedure before definitive intervention. The trigger criteria used to initiate and implement a damage control laparotomy in critically injured patients were a severe metabolic acidosis indicated by a pH <7.2, hypothermia with a core temperature <35°C, coagulopathy as evidenced by the onset of non-mechanical bleeding or patients who required a transfusion of more than 10 units of packed red blood cells (Nicol, Navsaria et al. 2010).

The principles applied during DCS were an urgent laparotomy via a long mid-line incision and urgent control of intra-abdominal bleeding. The simplest means possible were used to staunch bleeding and control contamination. These included supracoeliac aortic cross-clamping, packing, suture or ligation, closure of visceral perforations by ligation, bowel stapling to prevent contamination of the peritoneal cavity and rapid volume replacement to correct acidosis, coagulopathy and hypothermia. When necessary, the duodenum was rapidly kocherised using sharp and blunt finger dissection and rotated medially to expose the IVC, renal vessels and aorta. When deemed appropriate, the Cattell-Braasch manoeuvre was used to expose the third part of the duodenum and the superior mesenteric vein and artery. Once haemostasis was complete, temporary closure of the

abdominal wound was achieved using a modified sandwich-vacuum pack technique to avoid abdominal compartment syndrome (Navsaria, Bunting et al. 2003).

After the damage control operation, patients were transferred to the intensive care unit on ventilator support for secondary resuscitation. Haemodynamic objectives were assessed by the patient's response to pulmonary artery wedge pressure levels. Once predetermined endpoints of effective resuscitation were achieved with restoration of normal physiology and haemostasis (correction of acidosis, coagulopathy and hypothermia) and when inotrope support was no longer necessary, the patient was returned to the operating room for definitive treatment of the pancreatic injury.

3.5 Operative technique of pancreatic reconstruction after pancreatoduodenectomy

A pylorus-preserving pancreatoduodenectomy (PPPD) was undertaken in all patients in whom the injury had not irretrievably damaged the pylorus (Krige, Nicol et al. 2014). In those requiring a gastric resection due to an injury to the antrum, a classic Whipple resection was done. After the pancreatoduodenectomy the pancreatic remnant was mobilised for 2.5cm from the splenic and portal vein confluence to facilitate the pancreatic anastomosis. An end-to-side pancreatojejunostomy was constructed by placing the inferior row of interrupted 3/0 PDS sutures to include the edge of the pancreas and incorporate capsule and parenchyma as well as full

thickness jejunal wall. In those in whom the pancreatic duct could be identified, the anastomosis was stented internally with an 8 cm 5Fr silastic paediatric feeding tube cut to size. Four cm of stent were inserted into the pancreatic duct and the remaining 4 cm placed into the adjacent jejunum. The anterior layer pancreatic sutures were individually inserted first and then sequentially into the jejunal wall to complete the anastomosis. In patients in whom the jejunum was grossly oedematous after prolonged resuscitation and unsuitable for an anastomosis, the pancreatic stump was drained into the stomach. A 3cm oblique gastrostomy was made in the posterior wall of the stomach before placing interrupted 3/0 PDS sutures first through the edge of the superior surface of the pancreas, incorporating capsule and parenchyma, and then through the full thickness of the superior edge of the gastrostomy. The anastomosis was completed by suturing the posterior margin of the pancreas to the inferior margin of the gastrostomy in a similar manner.

3.6 Operative technique of biliary reconstruction

The biliary anastomosis was a modification of the standard method used for bile duct reconstruction after iatrogenic injuries (Terblanche, Worthley et al. 1990). The duct was spatulated to increase anastomotic size using an anterior vertical incision positioned to avoid the 3 and 9 o'clock bile duct arteries. All biliary anastomoses were stented with an 8 cm long 5Fr silastic paediatric feeding tube. In situations where the bile duct measured less than 3mm in width and gross oedema jeopardised the bile duct to jejunum anastomosis, the gall bladder was preserved and used as the conduit for

the biliary-enteric anastomosis. In high-risk stented biliary anastomoses a modified Imanaga reconstruction technique was used in which the duodenojejunosomy was created end-to-side as the most proximal jejunal anastomosis to allow post-operative ERCP and biliary stent retrieval.

3.7 Perioperative management

Perioperative management for all patients was according to the pancreatic resection protocol. All patients' drain amylase levels and output volumes were measured postoperatively. Drains were left *in situ* while drain amylase levels were elevated or volume measured over 30 ml per day. No dietary restrictions were imposed and oral food intake was continued while the fistula drained. ERCP with pancreatic duct sphincterotomy was used in patients who had pancreatic fistulas which persisted for more than 2 weeks (Thomson, Krige et al. 2014).

3.8 Management of postoperative intra-abdominal, pancreatic and duodenal complications

Postoperative intra-abdominal collections were drained with 5 Fr percutaneous catheters using ultrasound or CT guided placement. Endoscopic 7 Fr pancreatic duct stents were used for persistent pancreatic fistulas (Thomson, Krige et al. 2014) and an endoscopically placed covered self-expanding metal duodenal stent was used for prolonged large volume drainage of lateral duodenal fistulas (Chinnery, Bernon et al. 2011).

3.8.1 Endoscopic management of pancreatic pseudocysts

The diagnosis of a pseudocyst or pancreatic duct fistula was based on review of the original clinical and operative findings, drain fluid amylase or

lipase levels and ultrasound, CT scan, MRI, MRCP, ERP and EUS findings. The site of the pancreatic duct fistula (head, neck, body or tail) was noted and the size of the pseudocyst was measured in cm in two dimensions and pseudocyst location, relationship and proximity to stomach and duodenal wall recorded. The degree and extent of the main pancreatic duct injury was assessed using the Cape Town pancreatographic grading system for pancreatic injuries, modified from the original classification by Takishima et al. (Takishima, Hirata et al. 2000)

Patients who developed a delayed pancreatic complication as a consequence of an initial pancreatic injury were referred to the Surgical Gastroenterology and HPB unit for treatment. The diagnosis of a pancreatic duct fistula or stricture or pseudocyst was based on review of the original operative and clinical findings, fluid amylase levels, ultrasound and CT scan findings. The site of the pancreatic duct fistula (head, neck, body or tail) was noted on MRCP and ERP. The number and size of the pseudocyst(s) was measured in cm in 2 dimensions and location, relationship and proximity to stomach and duodenal wall recorded. The degree and extent of the main pancreatic duct injury was assessed using the Cape Town pancreatographic grading system for pancreatic injuries modified from the original classification by Takishima et al.

3.8.2 ERP technique

ERP was performed in a dedicated ERCP endoscopy suite and supervised by hepatobiliary surgeons experienced in interventional endoscopy

(Thomson, Krige et al. 2014). Blood was taken for coagulation screen before the procedure and patients were fasted overnight. Intravenous ampicillin and gentamycin were administered for antibiotic prophylaxis. Endoscopic retrograde cholangiopancreatography (ERCP) was performed using a side-viewing duodenoscope (TJF 145 or TJF 160, Olympus Optical Co. Ltd., Tokyo, Japan) under conscious sedation with intravenous midazolam and pethidine. The pancreatic duct was selectively cannulated under direct endoscopic vision via the ampulla. A pancreatogram was obtained to define the site and extent of the ductal injury. This information was recorded and used to determine the therapeutic strategy of either endoscopic transpapillary sphincterotomy with or without pancreatic duct stenting, or transmural pseudocyst drainage or surgery (Thomson, Krige et al. 2014). When endoscopic stenting or pseudocyst drainage was not feasible technically or if the pseudocyst recurred after initial endoscopic management, patients were referred for surgery.

3.8.3 Transmural pseudocyst drainage

The pseudocyst was confirmed to be in close proximity to the gastric or duodenal wall by first evaluating a recent computed tomogram (CT). Endoscopic drainage was performed using a side-viewing duodenoscope. The pseudocyst was identified as a distinct intraluminal bulge in the posterior wall of the stomach or the first part of the duodenum. A needle knife papillotome was passed through a 10-Fr coaxial catheter to puncture the cyst wall at the site of maximal prominence using blended diathermy. The co-axial catheter and a 0.89 mm x 450 cm guide wire (Jagwire[®],

Boston Scientific Corporation, Natick, MA 01760-1537, USA) were advanced into the cavity to secure the tract and maintain endoscopic access. The incision in the mucosa and the deeper layers was extended to approximately 10mm in size using a needle-knife or standard papillotome. In patients who had a thick pseudocyst wall or those with evidence of infection in the pseudocyst, one or two 7Fr or 10Fr double pigtail stents were placed across the cystenteric tract to ensure patency and adequate pseudocyst drainage (Lewis, Krige et al. 1993, Beckingham, Krige et al. 1997). Antibiotic therapy was given for 48 h after drainage and repeat imaging was done during the same hospital admission to gauge response and assess adequacy of drainage.

3.8.4 Transpapillary drainage

Pancreatic duct cannulation was attempted first using a floppy tip guide-wire. If duct access was not achieved, a small volume of contrast was injected via the catheter to identify and define the main pancreatic duct. After successful deep cannulation, more contrast was injected to confirm either pancreatic duct integrity or a stricture or disruption of the duct. Pancreatic duct disruption was regarded as complete if the main duct upstream to the stricture or disruption could not be filled with contrast or was considered to be partial when contrast entered and opacified the main duct upstream from the point of disruption. Duct stenting was done using a 0.89 mm hydrophilic guide wire (Jagwire[®], Boston Scientific Corporation) positioned in the main pancreatic duct and a 7-Fr transpapillary pancreatic stent was advanced over the guidewire into the pancreatic duct.

3.9 Definitions

In patients undergoing an emergency laparotomy the pancreatic injury was assessed and graded according to the Pancreas Organ Injury Scale of the American Association for the Surgery of Trauma. In patients with combined injuries of both pancreas and duodenum, the severity of each injury was graded independently according to the Organ Injury Scaling (OIS) of the American Association for the Surgery of Trauma (AAST) (Moore, Cogbill et al. 1990). A new composite grading system was used to score combined pancreatoduodenal injuries (Krige, Kotze et al. 2016). The grade selected was the more severe injury grade assigned to either pancreas or duodenum. Hypovolaemic shock was defined as a systolic blood pressure less <90mm Hg measured pre- or intra-operatively. Acidosis was defined as a pH <7.3; hypothermia was defined as a temperature <35°C; coagulopathy was defined as an INR >1.5 (Nicol, Navsaria et al. 2010). The Denver multiple organ failure scoring system criteria were used to define organ dysfunction and multiple organ failure (Vogel, Liao et al. 2014). Infectious complications were defined in accordance with the Society of Critical Care Medicine guidelines (Dellinger, Levy et al. 2008). Septic shock was defined according to standard criteria recommended in the Society of Critical Care and Medicine consensus statement (Bone, Balk et al. 1992). Abscesses were defined as purulent fluid collections that required surgical or percutaneous ultrasound-guided catheter drainage. Mortality was defined as any cause of death occurring in hospital after a pancreatic injury.

3.10 Classification of surgical complications

Morbidity was documented as either systemic, intra-abdominal or specific complications directly related to the pancreatic injury. Postoperative complications were classified according to the Dindo-Clavien grading system (Clavien, Barkun et al. 2009) in the initial studies. Subsequently the upgraded Accordion classification was used. In this classification grade 1 and 2 complications were regarded as minor, grade 3 as moderate, 4 as serious and grade 5 complications as life-threatening. Grade 6 complications resulted in the death of the patient and included death from any cause within 30 days of surgery (Strasberg, Linehan et al. 2009) . The overall complication rate was reported as the number of patients with at least one complication. In patients with several complications, the highest graded Accordion complication was used for analysis of the complication severity. Pancreatic fistulas were evaluated according to the International Study Group of Pancreatic Fistula classification (Bassi, Dervenis et al. 2005). To avoid ambiguity and maintain objectivity, pancreatic fistula results were scored and classified using the internet based calculator which applies the ISGPS definition (<http://pancreasclub.com/calculator/>).

3.11 Data collection

Guidelines of good clinical practice enumerated in the Declaration of Helsinki of 1964 and the revision in Edinburgh in 2000 as well as STROBE guidelines for observational studies were followed. Data collection, extraction methodology and analysis were approved by the Human Research Ethics Committee.

The medical records including operative, intensive care, radiology and endoscopy reports were reviewed and the data were abstracted by a specially trained nurse reviewer and recorded using a standardised data form after affirmation by a senior study surgeon. Details of the methodology used to record the variables for each patient have been published. The variables recorded for each patient included demographic data, mechanism of injury, trauma scores, presence of shock on admission, anatomic location and grade of the pancreatic injury, associated intra- and extra-abdominal injuries, injury to operation interval, operative findings and surgical procedure used, blood loss, intra-operative blood transfusion, duration of hospital stay, presence and type of pancreas-related and other complications, radiological and US-guided aspiration or drainage of collections, ERP and pancreatic duct stenting, surgical re-intervention and mortality. (Appendix A)

Patients who developed a delayed pancreatic complication as a consequence of an initial pancreatic injury were referred to the Surgical Gastroenterology and HPB unit for treatment. The diagnosis of a pancreatic duct fistula or stricture or pseudocyst was based on review of the original operative and clinical findings, fluid amylase levels, ultrasound and CT scan findings. The site of the pancreatic duct fistula (head, neck, body or tail) was noted on MRCP and ERP. The number and size of the pseudocyst(s) was measured in cm in 2 dimensions and location, relationship and proximity to stomach and duodenal wall recorded. The degree and extent

of the main pancreatic duct injury was graded using the Cape Town pancreatographic grading system for pancreatic injuries (Krige, Kotze et al. 2015) modified from the original classification by Takishima et al (Takishima, Hirata et al. 2000)

3.12 Data analysis

Descriptive statistics reporting medians with ranges, and frequency distributions, were used to characterize each cohort. Between-group comparisons were made using the Student t-test, the Wilcoxon sum rank test, the ANOVA and the non-parametric Kruskal-Wallis test for normal and non-normally distributed data respectively. The Pearson's χ^2 or Fisher's exact tests were used for analysis of categorical variables, and odds ratios (ORs) with 95 per cent confidence intervals (CI) were calculated. Univariate and then forward stepwise multivariate logistic regression analyses were done to identify factors which could be associated with complications or death. A p value of <0.05 was considered statistically significant. Multicollinearity was tested using the variance inflation factor (VIF) and the Hosmer-Lemeshow statistic was used to test goodness of fit of the model. The data were analysed using Stata software version 11 (StataCorp LP, College Station, Texas, USA).

For the statistical analyses in the PIMS study data were analysed according to methods used by Lee *et al.* to derive and validate the revised cardiac risk score (Lee, Marcantonio et al. 1999). Two thirds of the patients in the pancreatic database were assigned to the derivation cohort which was used

to develop the PIMS. One third of the patients were assigned to the validation cohort. Clinical correlates of in-hospital death were identified with a χ^2 test for categorical variables and a t test or Wilcoxon test for continuous variables. Variables with a univariate correlation with a P value 0.10 were considered in stepwise logistic regression analyses that identified the factors included in the risk index, with a cutoff P value of 0.05. In order to derive a simple and user-friendly model, two versions of the PIMS were compared: one in which the weights were derived from the original logistic regression analysis (original model) and one in which all variables were assigned weights that were rounded off to derive a user-friendly score (simple model). The performance and discriminative ability of the constructed models to predict mortality was assessed using receiver operating characteristic (ROC) analysis. The prediction accuracy was quantified using the concordance index (C-index). The derived scoring algorithm was applied to the validation dataset and logistic regression was repeated using PIMS to predict in-hospital mortality. An ROC analysis was used to compare the discriminatory performance of PIMS in the derivation and validation datasets. Cut-off values for the PIMS were used to define 3 risk groups in the derivation dataset: low, medium and high risk of death. These cut-off values were applied to the validation dataset and the mortality rate within each group was compared ($p < 0.05$).

3.13 Literature review methodology

3.13.1 Rationale

Currently, there is no detailed published consensus providing guidelines on the type of surgical intervention required in patients with complex pancreatic injuries. Herein, the thesis critically reviews the current literature regarding the complex decision-making process deciding on the type of surgery required in high grade pancreatic injuries.

3.13.2 Identifying relevant citations

With the assistance of a medical librarian, the Core Standard Ideal (COSI) model 72 was used to develop a search strategy to identify publications on pancreatic injuries and related interventions including damage control surgery in civilian trauma patients. The following electronic bibliographic databases were searched from their earliest available dates without language, publication date or other restrictions: Ovid, MEDLINE and EMBASE, PubMed, Web of Science, Scopus and the six databases contained within the Cochrane Library. Additional citations were located by searching reference lists of included citations. In order to further increase the sensitivity and coverage of the search, the grey literature was searched for additional indications not reported in the peer-reviewed literature. This involved searching relevant organisational websites (AAST, American College of Surgeons, American Trauma Society, Australasian Trauma Society, British Trauma Society, CAGS, Critical Care Society, EAST, National Trauma Research Institute and <http://www.trauma.org>), Google Scholar and two clinical trial registries (<http://www.clinicaltrials.gov> and

<http://www.controlled-trials.com>) using various combinations of the following key terms: pancreas, trauma, injury, damage control surgery, indication, outcome, complications, morbidity, mortality, survival and prognosis.

CHAPTER 4

Prognostic factors in pancreatic trauma: an appraisal of published data

Prognostic studies have assumed an increasingly important role in the assessment, management and analysis of complex trauma. Reliable and validated scoring systems contribute to the development of improved definitions and enhanced enrolment criteria thereby strengthening severity classifications and risk stratification. Despite a plethora of publications on pancreatic trauma, there is, however, no consensus regarding the specific risk factors which predict morbidity and mortality after a major pancreatic injury. Published results are variable and conflicting because of small sample sizes, referral bias, dissimilar study endpoints and differences in patient selection. In addition, the wide spectrum of different variables encountered in pancreatic injuries complicate the formulation of a prognostic model. Reported mortality rates for pancreatic injuries vary widely and range from 12 to 46%(Chinnery, Krige et al. 2012). Previous reports have emphasized that outcome is influenced primarily by the cause and complexity of the initial pancreatic injury, the number and severity of associated vascular and visceral injuries, the duration of shock, the quality and nature of surgical intervention and secondarily by complications related to the degree of pancreatic duct injury and the extent of intra-abdominal sepsis. Most early deaths are due either to exsanguination or to the consequences of massive blood transfusions after associated visceral

vascular injuries or damage to adjacent solid organs (Krige, Beningfield et al. 2005, Wang, Li et al. 2007, Heuer, Hussmann et al. 2011). Two-thirds of patients who survive more than 48 hours have major complications as a consequence of the pancreatic and associated injuries (Sharpe, Magnotti et al. 2012). One third of patients who die later do so because of intra-abdominal or systemic septic complications or multi-organ failure (Kao, Bulger et al. 2003, Hwang and Choi 2008).

Several models have been proposed to help predict morbidity and mortality in general for particular cohorts of surgical patients (Haskins, Maluso et al. 2017). The American Society of Anesthesiologists classification was developed to predict perioperative mortality for patients undergoing all types of elective surgery (Owens, Felts et al. 1978). The Goldman Index and the Revised Cardiac Index are used predict the risk of cardiac complications and cardiac mortality in patients undergoing non-cardiac surgery (Goldman 2010) while the Acute Physiology and Chronic Health Evaluation (APACHE) II score was developed for risk stratification of patients admitted to the intensive care unit and (Giangiuliani, Mancini et al. 1989) has since been used in trauma surgery and general surgery. The recently developed ACS-NSQIP surgical risk calculator is based on 21 patient variables derived from the NSQIP database (Bilimoria, Liu et al. 2013). There is however a paucity of publications which provide a detailed analysis of prognostic factors specifically in severe pancreatic injuries. The complex nature of current morbidity and mortality predictor models do not lend themselves to the

practical clinical application in patients with major pancreatic injuries. All these models have intrinsic limitations due to subjective variables or lack of general applicability and cannot be extrapolated to patients with complex pancreatic injuries.

In the first major study designed to establish predictors of morbidity and mortality in pancreatic trauma and to delineate possible critical factors, Heitsch et al. from Louisville, Kentucky, analyzed 100 patients with pancreatic injuries (Heitsch, Knutson et al. 1976). Sixteen patients with penetrating injury died within the first 24 hours, 14 of whom died intra-operatively due to major hepatic and/or retroperitoneal venous injuries. Eighty-four patients survived long enough to permit a detailed evaluation of treatment. There was no statistically significant relationship between mode ($p=0.3$) or anatomic area ($p=0.5$) of injury and death. However, death was more common in the presence of a main pancreatic duct injury ($p<0.01$). Pancreatic resection in patients who had a distal main pancreatic ductal injuries compared to drainage alone resulted in significantly lower morbidity and mortality rates ($p<0.05$). Seventeen (20%) of the 84 patients evaluated died. The overall mortality rate was 33% and the pancreatic related mortality rate was 17% (14 patients). Two of 23 patients with blunt injury (9%) and 12 of 61 (20%) patients with penetrating injuries died. Gram-negative sepsis (82%) was the most common cause of death ($p<0.01$), and sepsis correlated with the presence of a pancreatic duct ($p<0.01$) and bowel ($p<0.001$) injury.

In a subsequent study from Louisville which assessed determinants of outcome in pancreatic trauma, Smego et al. evaluated 72 consecutive patients and reported an overall mortality of 29% (Smego, Richardson et al. 1985). The mortality rate from pancreatic causes was 3%. The treatment protocol in these 72 patients categorized injuries into one of four grades: grade I, pancreatic contusion or minor haematoma with an intact capsule and no parenchymal injury; grade II, parenchymal injury without major ductal injury; grade III, parenchymal disruption with presumed ductal injury; and grade IV, severe crush injury. All grade I and most grade II injuries were treated by drainage alone; the grade III and IV injuries were treated by pancreatic resection. Fifty-seven patients survived longer than 24 hours. In the 23 grade I patients there were only minimal pancreatic complications and no deaths. In the 18 patients with parenchymal injuries (grade II), only one death occurred due to an inaccurate estimation of the degree of injury and delay in proper treatment. Sixteen patients with grade III and IV injuries were treated by resection with only one death, although the complications rose with increasing severity of the pancreatic injury. The mortality rate from pancreatic causes was 3% (2/57), a reduction from 19% in a previous report from their unit. This study stressed the value of recognition of a major ductal injury and supported a treatment protocol in which clinical decisions were based on the severity of the pancreatic injury. The authors concluded that recognition of a major ductal injury was crucial and that grade III and IV injuries required treatment by distal resection.

Similarly, Bradley et al contended that mortality and morbidity increased when there was a delay in the detection of a pancreatic ductal injury (Bradley, Young et al. 1998). These authors conducted a retrospective chart review of documented blunt pancreatic injuries from six USA hospitals. A significant correlation between pancreas-specific morbidity and injury to the main pancreatic duct was noted. Patients requiring delayed surgical intervention after an unsuccessful period of observation demonstrated notably higher pancreas-specific mortality and morbidity rates, principally because of the incidence of unrecognized main pancreatic duct injuries. Although detection of main pancreatic duct injuries by computed tomography was unhelpful, endoscopic pancreatography was accurate in each of the five cases this investigation was used. The authors concluded that the principal cause of pancreas-specific morbidity after blunt pancreatic trauma is an injury to the main pancreatic duct. Parenchymal pancreatic injuries not involving the ductal system seldom result in pancreas-specific morbidity or death. Delay in recognizing a main pancreatic duct injury leads to increased mortality and morbidity rates. Computed tomography is unreliable in diagnosing a main pancreatic duct injury and should not be used to guide therapy. The authors suggest that initial selection of patients with isolated blunt pancreatic injuries for observation or surgery can be based on the determination of main pancreatic duct integrity.

In a retrospective review of 55 patients with pancreatoduodenal injuries treated at a level I Trauma Centre between 1989 and 2008 in Bologna, Italy,

Antonacci evaluated factors predictive of mortality (Antonacci, Di Saverio et al. 2011). In their study 85.3% of the patients had blunt abdominal trauma, while 14.9% had penetrating injuries. 78.1% of the patients were treated with external drainage and/or simple suture; distal pancreatectomy was performed in 9% of cases and duodenal resection with anastomosis (3.7%) and diversion procedures (3.7%) were performed in an equal number of patients. Age, American Association for the Surgery of Trauma (AAST) grade, organ involved, haemodynamic status, intraoperative cardiac arrest, and operative time remained strongly predictive of mortality on multivariate analysis. The AAST grade represented, on multivariate analysis, the only independent prognostic factor predictive of overall morbidity. The authors concluded that optimal management and better outcome of pancreatoduodenal injuries seemed to be associated with shorter operative time, and with simple and fast damage control surgery, in contrast to definitive surgical procedures.

In a study from Korea, Hwang and Choi performed a retrospective review on 75 consecutive patients with pancreatic injuries admitted to the Masan Samsung Hospital and who subsequently underwent a laparotomy between January 2000 to December 2005 (Hwang and Choi 2008). Overall mortality and morbidity rates were 13.3% and 49.3%, respectively. Multivariate regression analysis showed that more than a 12 unit blood transfusion and an initial base deficit of less than -11 mM/L were the most important predictors of mortality ($p < 0.05$) while the most important predictors of

morbidity were surgical complexity and an initial base deficit of less than - 5.8 mM/L ($p < 0.01$).

In a retrospective review of 193 patients with a pancreatic injury admitted to a Level I Trauma Centre in Seattle, Kao et al reported a 12% mortality rate (Kao, Bulger et al. 2003). In this study the authors sought to validate the American Association for the Surgery of Trauma organ injury grading system for pancreatic injuries by defining its relationship to subsequent morbidity and to characterize the independent predictors of postoperative complications. The authors undertook a retrospective review of all patients with a pancreatic injury, confirmed by laparotomy, admitted to their Level I trauma centre from 1986 and 1999. Overall morbidity in the series was 50%, with a 22% prevalence of pancreas-related complications. Multivariate analysis found that the grade of pancreatic injury was an independent predictor of both pancreatic complications (OR, 4.4; 95% CI, 1.9-10) and mortality (OR, 2.6; 95% CI, 1.2-5.8). As anticipated, pancreatic and ICU complications were associated with longer hospital stays. The authors concluded that the American Association for the Surgery of Trauma Organ Injury Score predicted the development of complications and mortality after pancreatic injury and identified patients who require extensive resources and may benefit from transfer to a Level I trauma centre.

In the United Kingdom, a high proportion of injuries are due to blunt trauma, which differs markedly from USA and South African series. Two analyses from national trauma databases in the United Kingdom, the Scottish

Trauma Audit Group (STAG) and the Trauma Audit and Research Network (TARN) have provided important information on pancreatic trauma. The STAG database is a national audit across Scotland setup with the aim of improving quality of care, long-term outcome and overall patient experience. Data are prospectively recorded by medical and administrative staff before retrospective data cleaning by local audit coordinators. Inclusion criteria are patients over 13 years of age who have an inpatient stay of at least 3 days, or who die during their hospital admission, or are transferred to another STAG hospital or regional centre. In the STAG study data on a total of 52,676 patients were recorded prospectively between 1992 and 2002 on the STAG database (Scollay, Yip et al. 2006).

The Trauma Audit and Research Network (TARN) database is a collaboration of hospitals from England, Wales and Northern Ireland and is the largest trauma database in Europe, with more than 350,000 records. Overall, 1,155 (0.32%) of the 356,534 trauma cases on the TARN database sustained blunt or penetrating pancreatoduodenal (PD) trauma between 1989 and 2013 which represents 4.7% of the 24,595 cases with abdominal trauma. A total of 901 patients (78.0%) sustained blunt PD trauma and 254 (22.0%) sustained penetrating PD trauma (O'Reilly, Bouamra et al. 2015). Of the 901 with blunt trauma, 529 patients (58.7%) had pancreatic trauma, 309 (34.3%) sustained duodenal trauma, and 63 (7.0%) had an injury to both the pancreas and duodenum. Of the 254 with penetrating trauma, 119 patients (46.9%) had pancreatic injuries, 122 (48.0%) duodenal trauma, and

13 (5.1%) had an injury to both the pancreas and duodenum. These different proportions based on type of injury pattern were statistically significant ($p < 0.001$). The mortality rate for blunt PD trauma was 17.6% and was 12.2% for penetrating PD trauma. Variables predicting mortality after pancreatic trauma were increasing age, Injury Severity Score and haemodynamic compromise (O'Reilly, Bouamra et al. 2015).

The preceding studies are dominated by blunt pancreatic injuries. There is only one major study which has focused exclusively on outcome after gunshot wounds of the pancreas. In a study of 219 civilian pancreatic gunshot injuries by Chinnery, Krige and colleagues from the Cape Town HPB unit, age, shock on admission, need for damage control surgery, a high grade AAST pancreatic injury and associated vascular injuries were associated with mortality on multivariate analysis (Chinnery, Krige et al. 2012). In this study, 219 of 408 patients with pancreatic injuries had gunshot injuries to the pancreas. Eighty patients had proximal pancreatic injuries involving head or uncinate process, 75 had an injury to the body of the pancreas and 64 injuries involved the tail. One hundred and eleven patients had AAST grade I or II pancreatic injuries, and 108 patients grade III, IV or V pancreatic injuries. Two hundred and eighteen patients had a total of 733 associated intra-abdominal injuries, which included 91 vascular injuries. Duodenal injury was associated with increased morbidity (OR 2.61, 1.23 to 5.55; $p = 0.011$), but none of the injury locations was associated with increased mortality. One hundred and twenty patients (54%) had three or more associated intra-abdominal injuries.

In this study fifty-nine patients (27%) had 91 associated vascular injuries which correlated significantly with morbidity ($p < 0.001$) and mortality ($p < 0.001$). The 219 patients underwent a total of 239 laparotomies for the treatment of pancreatic injuries. One hundred and sixty-nine patients (77.2%) had drainage of the pancreas after haemostasis as a primary (157) or secondary (12) procedure. Fifty-nine patients (26.9%) had a distal pancreatectomy and 11 (5.0%) a pancreaticoduodenectomy. Forty-three (19.6%) of the 219 patients had initial damage control surgery for complex pancreatic and associated injuries of whom 24 died. One hundred and fifty patients (68%) had a total of 407 complications. The site of the pancreatic injury (proximal *versus* distal) was not significant with regard to development of general complications ($p = 0.374$). The grade of pancreatic injury, however, had a significant impact on the development of general complications (AAST grade I–II *versus* grade III–V injuries; $p < 0.001$).

Assessing the factors associated with morbidity, univariable analysis showed that age, RTS, presence of shock, the need for transfusion and volume of blood transfused, damage control surgery, grade of pancreatic injury, repeat laparotomy, second pancreatic surgery, associated duodenal or vascular injury, ICU admission and time in ICU were significant predictors of morbidity. In the final multivariable logistic regression analysis model four variables were significant predictors of morbidity: age (OR 2.36, CI 1.09 to 5.11; $p = 0.029$), AAST grade of pancreatic injury (grades I–II *versus* III–V, OR 0.30, CI 0.13 to 0.69; $p = 0.005$), associated vascular injury (OR 3.59, CI

1.10 to 11.68; $p=0.033$) and the need for repeat laparotomy (OR 7.01, CI 1.69 to 29.08; $p=0.007$).

Forty-six of the 219 patients died. Assessing the predictors of mortality, univariable analysis showed that age, RTS, presence of shock, need for a major transfusion and volume transfused, need for DCS, severe grade of pancreatic injury and proximal pancreatic injuries, associated colonic, duodenal and vascular injuries, postoperative complications, ICU admission and time in ICU were significantly associated with death. However, in the final stepwise multivariable logistic regression analysis model only five variables were significant predictors of death: age (OR 4.42, CI 1.60 to 12.20; $p=0.004$), shock (OR 6.38, CI 2.07 to 19.60; $p<0.001$), need for DCS (OR 3.19, CI 1.22 to 8.35; $p=0.018$), severe AAST grade injuries (grades I–II *versus* III–V, OR 0.34, CI 0.13 to 0.88; $p=0.027$) and associated vascular injuries (OR 8.17, CI 2.75 to 24.25; $p<0.001$).

In a further study from the Cape Town HPB group, Krige and colleagues assessed outcome and factors associated with morbidity and mortality in patients who had sustained blunt pancreatic injuries. In this study 110 patients (92 men, 18 women; mean age 30 years, range 13-68 years) were treated between March 1981 and June 2009 (Krige, Kotze et al. 2011). Forty-six patients had American Association for the Surgery of Trauma (AAST) grade 1 or 2 pancreatic injuries and 64 had AAST grade 3, 4 or 5 pancreatic injuries. The overall complication rate was 74.5% and the mortality rate 16.4%. Only 2 of the 18 deaths were attributable to the

pancreatic injury. Shock on presentation was highly predictive of death; 17 of 39 patients with shock died, compared with 1 of 71 patients who were not shocked ($p < 0.0001$). Fourteen of 46 patients with grade 1 and 2 pancreatic injuries died compared with 4 of 64 patients with grades 3, 4 and 5 injuries ($p < 0.001$). Mortality increased exponentially as the number of associated injuries increased. Two of 57 patients with injury to the pancreas only or one associated injury died, compared with 16 of 53 with two or more associated injuries ($p < 0.0013$).

This study demonstrated a significant correlation between the AAST grade of injury and pancreas-specific morbidity and between shock on admission, the number of associated injuries and death, in patients with blunt pancreatic injuries. Although morbidity and mortality rates after blunt pancreatic trauma are high, death was usually the result of major associated injuries and not related to the pancreatic injury. In this study the overall incidence of complications related to the injury and subsequent operation was high. A total of 158 complications occurred in 82 patients (74.5%). All 36 patients with injuries to the head and neck of the pancreas developed complications, 13 of which were pancreas specific. Of the 74 patients with injuries involving body and tail of the pancreas, 58 were complicated, of which 24 were related to the pancreas. The presence of shock on admission did not predict the development of subsequent complications as 10 of 39 shocked patients developed a complication compared to 15 of 71 patients without shock ($p=0.638$). There was no

correlation in this study between the AAST grade of injury and pancreas-related morbidity.

Eighteen patients (16.4%) died as a result of the injuries sustained. Shock on presentation was highly predictive of death. Seventeen of the 39 patients who had a systolic BP of <90mmHg on admission to hospital subsequently died compared to 1 of the 71 patients who were not shocked ($p<0.0001$). Ten of the 31 patients with grade 1 pancreatic injuries died, 4 of 15 with grade 2 injuries, 3 of 45 with grade 3, none with grade 4 and one with grade 5 injuries. Surprisingly, 14 of 46 patients with grade 1 and 2 pancreatic injuries died compared to 4 of 64 patients with grade 3, 4 and 5 injuries ($p<0.001$). Five of the 36 patients with injuries involving the head and neck of the pancreas died compared to 13 of the 74 patients with injuries involving body and tail of the pancreas. This difference was not significant ($p=0.68$). None of the 36 patients with an isolated pancreatic injury died. Detailed analysis showed that mortality increased exponentially as the number of associated injuries increased. Two of 57 patients with pancreas only or one associated injury died compared to 16 of 53 with 2 or more associated injuries ($p<0.0013$). Nearly 40% of patients with 4 or more associated injuries died. In these situations the cause of death invariably was due to the combined sequelae of severe head, spinal and multiple limb injuries.

Despite a plethora of papers on pancreatic trauma, few have access to dedicated prospective pancreas-specific trauma databases while others

lack the granular detail necessary to generate reliable data and obtain valid conclusions. Because pancreatic injuries are uncommon, much of the data on prognostic factors is based on retrospective analyses utilising small number of patients. The Cape Town HPB pancreatic trauma database is currently the largest and most active database worldwide. Applying this database in a subsequent much larger study from Cape Town and using logistic regression analysis, Krige and colleagues evaluated prognostic factors, 30-day morbidity and mortality and pancreas-specific complications in patients who had sustained pancreatic injuries (Krige, Spence et al. 2017). The primary endpoints in this study of 432 consecutive patients were postoperative morbidity and death.

Bivariate and multivariate logistic regression analyses were used to assess significant predictors of morbidity and mortality. Overall mortality was 15.7% and morbidity 66%. Bivariate logistic regression analysis showed that nine factors, age, RTS, presence of shock, need for a transfusion, volume of blood transfused, damage control surgery, AAST grade of pancreatic injury, an associated vascular injury and a repeat laparotomy were significant predictors of morbidity. In the final multivariate logistic regression analysis model only 2 variables were significant predictors of morbidity: the AAST grade of pancreatic injury $p = 0.003$ [OR 2.7, CI 1.4-5.4], and the need for a repeat laparotomy $p = 0.001$ [OR 8.8, CI 2.4-32.6]. When factors associated with mortality were considered, logistic regression analysis found that 11 variables, age, RTS, the presence of shock, patients who required a major blood transfusion, the median number of units transfused, the need for a

damage control laparotomy, AAST grade 3, 4, 5 pancreatic injuries, associated vascular injuries, the number of associated injuries, postoperative complications and days in ICU were significant. However in the final stepwise multivariate logistic regression analysis model only 5 variables were significant factors associated with mortality: age: $p=0.001$ [OR 0.9, CI 0.8-0.9], RTS: $p=0.006$ [OR 2.2, CI 1.2-3.9], shock: $p=0.043$ [OR 4.2, CI 1.0-16.7], the median number of units transfused: $p=0.03$ [OR 0.9, CI 0.9-1.0] and the presence of associated complications $p=0.001$ [OR 12.2, CI 2.7-54.7].

A major factor limiting the use of predictive factors in pancreatic injuries are the unwieldy formulae generated and complicated *post hoc* variables which are not practical in the emergency situation or utilitarian when applied in comparative analyses. To overcome these deficiencies, Krige and colleagues developed in a novel study from Cape Town a pancreatic injury mortality score (PIMS) to identify patients at greatest risk of in-hospital mortality after a major pancreatic injury. The study used data from a prospective database of 473 patients treated for pancreatic injuries between January 1990 and December 2015. Two thirds of the patients were assigned to a derivation cohort and one third to a validation cohort. Clinical correlates of in-hospital death were identified and considered in stepwise logistic regression analyses that identified the factors included in the risk index. Five variables, age >55, shock on admission, a vascular injury, number of associated injuries and pancreatic AAST correlated with in-

hospital death and were used to calculate PIMS. The final score ROC in the derivation dataset was 0.84 (95% CI 0.79 – 0.89) and in the validation dataset was 0.91 (95% CI 0.84 – 0.97), which were comparable ($p= 0.1$). Finally, cut-off scores were used to generate three risk groups and the rate of mortality within the low (PIMS 0-4), medium (PIMS 5-9), and high risk (PIMS 10–20) groups were not significantly different. The scoring system was tested in a validation cohort and showed good calibration and discrimination for in-hospital mortality.

The PIMS which was developed is simple, quick and easily understandable, increases clinical risk prediction for patients with complex pancreatic and can be used as a benchmark for survival. The model exploits variables readily available to trauma surgeons and has the potential to be useful as a real-time score to predict outcome and to benchmark quality of surgical intervention in the treatment of complex injuries and to aid in the post hoc analysis of trauma research and comparative audit. The goal of PIMS risk stratification is the opportunity to further improve patient outcome after complex injuries and surgical intervention.

The above studies have several significant limitations. Much of the data were generated from and reflect the outcome in a select group of patients treated in high volume well-resourced trauma centres. It is thus evident that the data and conclusions which are derived from specialist referral centres may differ substantially from the results emanating from smaller institutions which have limited trauma management facilities or resource constraints

and use different treatment strategies which consequently have differing outcomes. It should be stressed that the analysis and interpretation of these data pertain in particular to pancreatic injuries treated in an urban civilian population.

CHAPTER 5

Pancreatoduodenectomy for trauma

Severe injuries of the head of the pancreas in haemodynamically unstable patients who may also have associated adjacent solid organ, bowel and vascular injuries are complex to manage and tax the skill and ingenuity of even the most experienced trauma and pancreatic surgeons (Krige and Thomson 2011, Krige, Nicol et al. 2017). Overall morbidity rates for grade 4 and 5 pancreatoduodenal injuries are substantial and mortality is directly proportional to the number of injuries sustained and is highest in the elderly and in those who are haemodynamically unstable (Scollay, Yip et al. 2006). Previous reports have indicated that outcome in such injuries is determined by the complexity and grade of the pancreatic injury, the number, extent, and magnitude of associated injuries, the amount of blood loss and the duration of shock, the rapidity and efficacy of resuscitation, and the speed and quality of surgical intervention (Mayer, Tomczak et al. 2002, Krige, Beningfield et al. 2005, Sharpe, Magnotti et al. 2012). Early mortality is due either to uncontrolled venous bleeding or major adjacent organ injuries (Chrysos, Athanasakis et al. 2002, Subramanian, Dente et al. 2007) while late mortality is generally a consequence of infection or multiple organ failure (Kao, Bulger et al. 2003, Wang, Li et al. 2007, Hwang and Choi 2008).

In patients with severe injuries of the head of the pancreas in whom the ampulla has been avulsed and the duodenum rendered ischaemic, lesser procedures with preservation of the pancreatic head will not be possible and the only recourse ultimately will be resection of both the head of the pancreas and the duodenum. However, the mortality rate of a pancreatoduodenectomy in severely injured and unstable patients is prohibitive, and those patients who survive invariably have a high postoperative complication rate (Asensio, Petrone et al. 2003, Seamon, Pieri et al. 2007). When faced with a devitalized head of the pancreas and duodenum, an avulsed ampulla or a near-complete traumatic resection, a surgeon may have no choice but to proceed and complete the resection, provided the patient is haemodynamically stable and the necessary surgical expertise and facilities for advanced post-operative intensive care are available (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014).

A pancreatoduodenectomy for trauma is regarded as the most daunting of all pancreatic resections because the full extent of the injury and the need for resection may only become apparent during the index laparotomy and the ensuing procedure is performed under the most difficult circumstances with severe operative constraints. Optimal management of the associated collateral damage is crucial to ensure survival in this group of severely injured patients and, in particular, injuries to adjacent large visceral splanchnic veins are frequently immediately life-threatening and require priority intervention (Asensio, Petrone et al. 2003). Urgent vascular access

to a lacerated retropancreatic portal or superior mesenteric vein in an exsanguinating patient is often problematic and accelerated exposure and rapid control is necessary (Wang, Li et al. 2007). In gunshot injuries and other complex penetrating injuries of the pancreatic head, assessment of the extent of the pancreatic injury and the need for definitive resection requires mature judgement and skilled evaluation and in these situations intra-operative appraisal by an HPB surgeon may provide invaluable assistance to the trauma surgeon. The decision to proceed with a pancreatoduodenectomy may be obvious and inevitable, especially if severe blunt injury to the epigastrium has resulted in a destroyed head and a fractured neck of pancreas with a near complete *de facto* resection (Krige 1997). However, in some circumstances detailed evaluation of the extent of the injury by an expert will conclude that a lesser procedure is appropriate without resorting to a pancreatoduodenectomy.

Pancreatoduodenal injuries mandating a pancreatoduodenectomy are uncommon. Glancy reviewed 1,407 patients with pancreatic injuries and found only one patient requiring this procedure for an incidence of 0.07% (Glancy 1989). Most authors agree that a pancreatoduodenectomy for trauma is seldom necessary and should be reserved for the select small group of patients with severe injuries of the head of pancreas and duodenum in whom lesser procedures with preservation of pancreas and duodenum is not possible (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). In most studies the indications for a

pancreatoduodenectomy are present in only 2-3% of patients with pancreatic injuries (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). Pancreatoduodenectomy is reserved for patients with ductal disruption in the head of the pancreas with associated injuries to the duodenum and common bile duct, significant injury to the ampulla of Vater, or uncontrolled haemorrhage from the head of the pancreas. On rare occasions, pancreatoduodenectomy may be necessary to manage bleeding from the retropancreatic portal vein. Although the operation can be performed with a high rate of success in injured patients who are stable, the global 30% mortality rate suggests that the procedure should be used judiciously.

No “hard” indications for performing such a complex procedure have yet been established. Subramanian et al., in a review of pancreatic trauma, described the indications for pancreatoduodenectomy to include extensive trauma to the head of the pancreas, severe combined pancreatoduodenal injury, or destruction of the ampulla of Vater (Subramanian, Dente et al. 2007). In the study by Asensio et al. the indications for pancreatoduodenectomy in three-fourths of the patients were massive uncontrollable retropancreatic haemorrhage from associated vascular injuries and massive non-reconstructable injuries to both the pancreas and duodenum (Asensio, Petrone et al. 2003). McKone proposed several specific indications for pancreatoduodenectomy for trauma. These indications are: 1) extensive devitalization of the head of the pancreas and

duodenum in whom there is no prospect of a repair; 2) ductal disruption in the pancreatic head with AAST grade 5 injuries of the duodenum and distal common bile duct; 3) injury to the ampulla of Vater, with disruption of the main pancreatic duct from the duodenum (McKone, Bursch et al. 1988). While other authors (van der Wilden, Yeh et al. 2014) have optimistically suggested that lesser procedures may be applicable for grade V injuries, this is clearly not an option in patients who have a disrupted and devitalised duodenum and pancreas.

The conduct and execution of an emergency pancreatoduodenectomy for trauma differs substantially from the elective operation (Krige 1997, Krige, Beningfield et al. 2005). There is general agreement that patients who have a major pancreatic injury with associated major visceral injuries, who are haemodynamically unstable despite vigorous resuscitation and are coagulopathic, acidotic and hypothermic and have received a massive intra-operative blood transfusion should have an abbreviated laparotomy with a damage control procedure and subsequent re-exploration, resection and reconstruction only when stable (Chrysos, Athanasakis et al. 2002, Wang, Li et al. 2007, Ball 2014, Roberts, Bobrovitz et al. 2016). While some authors recommend that a pancreatoduodenectomy for trauma should be always performed as a two-stage procedure, this is not always necessary as has been demonstrated in an analysis of patients who had a pancreatoduodenectomy for trauma by the Cape Town group (Krige, Nicol et al. 2014).

Resection of the pancreatic head in severely injured patients with complex pancreatic injuries aggravated by hypothermia, coagulopathy and acidosis has in the past resulted in prohibitive mortality rates (Asensio, Petrone et al. 2003). Often life-threatening associated collateral injuries, especially those involving adjacent large splanchnic veins including inferior vena cava, portal and superior mesenteric veins take precedence in management (Wang, Li et al. 2007). In addition, there are technical difficulties resecting and reconstructing complex pancreatic injuries which require special surgical skills and expertise (Oreskovich and Carrico 1984). The answers to several issues regarding the need for a pancreaticoduodenal resection to deal with major pancreatic injuries have not been adequately addressed and remain unresolved. These vexing questions include:

(i) what is the mortality of an emergency pancreaticoduodenectomy when undertaken by an experienced pancreatic surgeon using modern pancreatic and biliary operative techniques?

(ii) is a pylorus-preserving pancreaticoduodenectomy technically feasible and appropriate in acute pancreatic trauma rather than the traditional Whipple operation which has been used in most previous reports for pancreaticoduodenectomy for trauma?

(iii) is there a beneficial role for a pancreaticogastrostomy in selected patients in reconstruction after an emergency pancreaticoduodenectomy when the standard pancreaticojejunostomy cannot be undertaken safely because of adverse anatomical circumstances?

Although several substantial international reviews (Chrysos, Athanasakis et al. 2002, Subramanian, Dente et al. 2007) as well as original data from Cape Town (Krige, Nicol et al. 2014, Krige, Kotze et al. 2016) have detailed aspects of the management of pancreatic injuries, no publications have specifically assessed the results of proximal pancreatic resection and reconstruction in severely injured patients performed by or under the supervision of experienced HPB surgeons using established pancreatobiliary operative techniques adapted for trauma. In this cohort of patients reconstruction is frequently technically difficult as the ducts are non-dilated and the surrounding organs damaged or oedematous which necessitates modification of conventional biliary and pancreatic anastomoses (Krige 2006).

The reputation of an emergency pancreatoduodenectomy is tarnished by high reported mortality rates. In an analysis of 61 publications which reported 220 pancreatoduodenectomies for trauma, Krige *et al* found an overall mortality of 34% (Krige 1997). A review of the literature up to 1999 by Asensio and colleagues recorded 245 pancreatoduodenectomies for trauma. Between 1964 and 2016 the details of 339 pancreatoduodenectomies for trauma have been published with an overall mortality of 30.1% (Table 1). Substantial experience from even the largest trauma centres in the world is scant. Only seven series have treated ten or more patients with pancreatoduodenectomy for trauma. The largest series describing the use of pancreatoduodenectomy for trauma include those by

Yellin and Rossof, Balasegaram, Oreskovich and Carrico, Jones, Feliciano and colleagues, Ivatury and associates, and Stone and co-workers. Each reported between 7 and 13 cases. Oreskovich and Carrico reported the only series dealing exclusively with the use of pancreatoduodenectomy for complex pancreatoduodenal injuries consisting of 10 patients. In 2003 Asensio and colleagues from the University of Southern California published the details of 18 patients who had a pancreatoduodenectomy for trauma with a mortality rate of 33%. Thompson and colleagues reported 15 patients who had pancreatoduodenectomies for trauma with a mortality rate of 13%. In a USA national collective study by van der Wilden 39 patients had pancreatoduodenectomies for trauma with a mortality rate of 33%. The largest single centre series is from Cape Town with 19 patients and a mortality rate of 15.7%

Table 1 Pancreaticoduodenectomy for trauma

Author	Number of Patients	Number of Deaths	Mortality %
Thal (Thal and Wilson 1964)	2	1	50
Walters (Walters, Gaspard et al. 1966)	1	0	0
Thompson (Thompson and Hinshaw 1966)	2	1	50
Salyer (Salyer and McClelland 1967)	1	0	0
Sawyers et al (Sawyers, Carlisle et al. 1967)	1	0	0
Wilson (Wilson, Tagett et al. 1967)	2	0	0
Brawley (Brawley, Cameron et al. 1968)	3	0	0
Werschky (Werschky and Jordan 1968)	1	1	100
Pantazelos (Pantazelos, Kerhulas et al. 1969)	1	1	100
Halgrimson (Halgrimson, Trimble et al. 1969)	3	0	0
Foley (Foley, Gaines et al. 1969)	3	0	0
Gibbs (Gibbs, Crow et al. 1970)	1	0	0
Bach (Bach and Frey 1971)	3	0	0
Nance (Nance and DeLoach 1971)	5	2	40
Smith (Smith, Woolverton et al. 1971)	5	2	40
Salam (Salam, Warren et al. 1972)	4	1	25
White (White and Benfield 1972)	5	0	0

Anderson (Anderson, Weisz et al. 1973)	2	1	50
Owens (Owens and Wolfman 1973)	3	1	33.3
Steele (Steele, Sheldon et al. 1973)	3	3	100
Sturm (Sturm, Quattlebaum et al. 1973)	5	2	40
Yellin (Yellin and Rosoff 1975)	10	6	60
Anane-Sefah (Anane-Sefah, Norton et al. 1975)	6	0	0
Chambers (Chambers 1975)	1	0	0
Heitsch (Heitsch, Knutson et al. 1976)	2	2	100
Lowe (Lowe, Saletta et al. 1977)	6	0	0
Karl (Karl and Chandler 1977)	1	1	100
Hagan (Hagan, Urdaneta et al. 1978)	2	2	100
Graham (Graham, Mattox et al. 1979)	6	3	50
Balasegaram (Balasegaram 1979)	8	5	62.5
Majeski (Majeski and Tyler 1980)	1	0	0
Stone (Stone, Fabian et al. 1981)	3	3	100
Cogbill (Cogbill, Moore et al. 1982)	1	0	0
Levison (Levison, Petersen et al. 1984)	1	1	100
Berni (Berni, Bandyk et al. 1982)	8	0	0
Henarejos (Henarejos, Cohen et al. 1983)	1	0	0
Oreskovich (Oreskovich and Carrico 1984)	10	0	0
Moore (Moore and Moore 1984)	1	0	0
Sims (Sims, Mandal et al. 1984)	2	0	0
Adkins (Adkins and Keyser 1985)	5	1	20
Donohue (Donohue, Crass et al. 1985)	1	1	100
Jones(Jones and Shires 1965, Jones 1978, Jones 1985).	12	7	58.3
Ivatury (Ivatury, Nallathambi et al. 1985)	7	3	42.8
Smego (Smego, Richardson et al. 1985)	1	0	0
Wynn (Wynn, Hill et al. 1985)	3	2	66.6
Nowak (Nowak, Baringer et al. 1986)	1	1	100
Walker (Walker 1986)	1	0	0
Feliciano (Feliciano, Martin et al. 1987)	13	6	46.1
Melissas (Melissas, Baart et al. 1987)	1	0	0
Leppaniemi (Leppaniemi, Haapiainen et al. 1988)	3	1	33.3
McKone (McKone, Bursch et al. 1988)l	5	0	0
Eastlick (Eastlick, Fogler et al. 1990)	1	0	0
Fabian (Fabian, Kudsk et al. 1990)	1	1	100
Heimansohn (Heimansohn, Canal et al. 1990)	6	0	0
Gentilello (Gentilello, Cortes et al. 1991)	3	1	33.3
Ivatury (Ivatury, Nallathambi et al. 1990)	6	2	33.3
Carrillo (Carrillo, Fogler et al. 1993)	7	2	28.5
Delcore (Delcore, Stauffer et al. 1994)	4	0	0
Degiannis (Degiannis, Levy et al. 1996)	3	2	66.6
Smith (Smith, Stanley et al. 1996)	1	1	100
Mistry (Mistry and Durham 1996)	1	0	0
Young (Young, Meredith et al. 1998)	2	0	0
Asensio (Asensio, Demetriades et al. 1999)	10	5	50

Kurusu (Kurusu, Kobayashi et al. 1999)	1	0	0
Koniaris (Koniaris, Mandal et al. 2000)	1	0	0
El-Boghdadly (el-Boghdadly, al-Yousef et al. 2000)	2	2	100
Vasquez (Vasquez, Coimbra et al. 2001)	2	0	0
De Kerpel (De Kerpel, Hendrickx et al. 2002)	1	0	0
Asensio (Asensio, Petrone et al. 2003)	18	6	33.3
Kao (Kao, Bulger et al. 2003)	4	1	25
Sekino (Sekino, Kobayashi et al. 2004)	1	0	0
Lin (Lin, Chen et al. 2004)	2	1	50
Yong (Yong, Concejero et al. 2008)	1	0	0
Gupta (Gupta, Wig et al. 2008)	5	1	20
Hwang (Hwang and Choi 2008)	1	0	0
Seamon (Seamon, Kim et al. 2009)	3	0	0
Thomas (Thomas, Madanur et al. 2009)	1	1	100
Tan (Tan, Chan et al. 2009)	1	1	100
Thompson (Thompson, Shalhub et al. 2013)	15	2	13.3
Van der Wilden (van der Wilden, Yeh et al. 2014)	39	13	33.3
Gulla (Gulla, Tan et al. 2014)	7	0	0
Krige (Krige, Kotze et al. 2016)	19	3	15.7
Total	348	106	30.5%

Although pancreatoduodenectomy as a single-stage procedure was first reported by Whipple et al. in 1935 for an elective resection of a periampullary carcinoma, three decades elapsed before this procedure was first reported in trauma patients (Whipple, Parsons et al. 1935). The first pancreatoduodenectomy for trauma was reported by Howell and colleagues in 1962 in a patient with a gunshot injury to the head of the pancreas, but without success and the patient died (Howell 1961). Later, in 1964, Thal and Wilson reported the first pancreatoduodenectomy for blunt trauma to the pancreas (Thal and Wilson 1964). In 1969 Halgrimson et al reported their experience from Vietnam of two patients, operated on a delayed basis, who survived (Halgrimson, Trimble et al. 1969). Foley et al in 1969 described indications for pancreatoduodenectomy based on three blunt

trauma patients (Foley, Gaines et al. 1969). Numerous subsequent reports have been published, but have all been limited by small sample sizes, ranging between three and ten patients per study. The largest single study on pancreatoduodenectomy to date consists of 20 patients from Cape Town (Krige, Kotze et al. 2016). The majority of patients sustained a penetrating injury, they were predominantly male, and mortality ranged from 20 to 100 %. In a review of all pancreatoduodenectomies described in the literature (245 cases) until 1999, the pooled mortality rate was 31% (Asensio, Petrone et al. 2003).

In the largest collective multicentre national study, van der Wilden and colleagues from Harvard Medical School in Boston used the USA National Trauma Data Bank (NTDB) to compare the outcome of a pancreatoduodenectomy performed for severe injuries of the pancreatic head to patients with similar injuries who did not undergo a pancreatoduodenectomy (van der Wilden, Yeh et al. 2014). The NTDB contains information on trauma patients which has been submitted voluntarily by trauma centres in the United States. Designed and maintained by the American College of Surgeons Committee on Trauma, the data base has been operational since 1997. Currently, the data set includes more than 5 million cases from more than 900 trauma centres of all levels of designation. In their study the authors used NTDB version 7.2 and focused on the Research Data Sets for 2008, 2009, and 2010. The authors excluded patients who underwent a delayed pancreatoduodenectomy which

was arbitrarily defined as more than 4 days. The pancreatoduodenectomy group (n = 39) was compared to patients with severe combined pancreatoduodenal injuries (grade 4 or 5) who did not undergo a pancreatoduodenectomy (non-pancreatoduodenectomy group, n = 38). Patients who died in the emergency department or did not undergo a laparotomy were excluded. The primary outcome of the study was death. Secondary outcomes were intensive care unit length of stay, hospital length of stay, and total ventilator days. A multivariate model was used to determine predictors of in-hospital mortality within each group and in the overall cohort. The authors found that the non-pancreatoduodenectomy group had a significantly lower systolic blood pressure and Glasgow Coma Scale values at baseline and more severe duodenal, pancreatic, and liver injuries. There were no significant differences in outcomes between the two groups. The Injury Severity Score was the only independent predictor of mortality among pancreatoduodenectomy patients [odds ratio (OR) 1.12, 95 % confidence interval (CI) 1.01–1.24] and in the entire cohort (OR 1.06, 95 % CI 1.01–1.12). The operative technique did not influence any of the outcomes and surprisingly, compared to the non-pancreatoduodenectomy group, the pancreatoduodenectomy cohort did not result in improved outcomes despite a lower physiologic burden among pancreatoduodenectomy patients. In this study, 21 % of patients undergoing pancreatoduodenectomy did not have a grade 4 or 5 injury in either the pancreas or the duodenum, nor did they have significant associated injuries in the abdomen.

Detailed analysis of this retrospective study shows major limitations and a flawed study. Scrutiny shows major anomalies in data accrual and interpretation. Experienced trauma surgeons intuitively recognize that the data analysis of this manuscript does not represent reality. Although the authors used a large database to acquire the largest possible sample size for this procedure, there are limitations with the NTDB that must be clarified. The NTDB is a convenience sample that is not fully representative of all trauma centres in the United States and voluntary submission of data results in selection bias. Additionally, the likelihood of inaccurate diagnostic coding and the limitation of included data variables exists. Unfortunately the NTDB does not include granular detail including operative reports, intra-operative haemodynamic measurements, and surgeon or institutional experience which may influence the decision to perform a pancreatoduodenectomy. In addition, complications are likely to be underreported in this database. Despite all these limitations, the authors argue that the NTDB is a powerful tool and is useful for studying injuries of a low incidence.

The outcome after a trauma pancreatoduodenectomy was analysed by Feliciano and colleagues in an 18-year experience with 129 consecutive patients with combined pancreatoduodenal injuries treated at the Ben Taub General Hospital, a Level I trauma centre affiliated with the Baylor College of Medicine in Houston, Texas, from 1968 to 1985 (Feliciano, Martin et al. 1987). Transections of the pancreatic duct in the head of the pancreas or at

the ampulla of Vater were treated by a pancreatoduodenectomy. More than 88% were men, and the average age was 29 years. The most common mechanism of injury was a penetrating wound (104 of 129 = 80.6%), and gunshot wounds accounted for 78.8% (82 of 104) of these. The head of the pancreas and the second portion of the duodenum were the most frequently injured areas, and multiple duodenal injuries were present in 30 patients. Primary repair or resection of one or both organs coupled with pyloric exclusion and gastrojejunostomy (68 patients) and drainage was used in 79 patients (61.2%) in the entire study and in 59% (36 of 61) of all patients treated since 1976. Simple primary repair of one or both organs and drainage was performed in 31 patients (24%), whereas the remaining 19 patients (14.8%) had pancreatoduodenectomies (13 patients) or no repair before exsanguination (six patients).

A Whipple procedure or a total pancreatoduodenectomy was required in 13 patients, while six patients died in the operating room before any type of repair could be completed. The overall mortality rate was 29.4% (38 of 129), with 55.3% (21 of 38) of patients dying within 48 hours of injury secondary to hypovolaemic shock and transfusion-associated coagulopathies. Six or more intra-abdominal visceral or vascular injuries were present in 15 (71.4%) patients with perioperative deaths. In the four patients who died in the perioperative period since 1981, the average operative blood loss was 32 units. Seventeen patients died (17 of 38 = 44.7%) in the late

postoperative period, with sepsis and/or multiple organ failure (nine patients) and respiratory failure (five patients) accounting for most deaths.

The authors concluded that based on their review of the operative treatment of 129 patients with combined pancreatoduodenal injuries, the following recommendations could be made: when the duodenum is devascularized, the pancreatic duct in the head transected, or the ampulla of Vater is destroyed, either a Roux-en-Y drainage procedure or Whipple procedure should be considered if the patient's condition is stable. If the patient's condition is unstable, a conservative resection, pyloric exclusion with gastrojejunostomy, and drainage should be performed. Unfortunately these conclusions are no longer valid as a Roux-en-Y drainage procedure is inappropriate. The authors suggest that if the patient's condition is unstable, a conservative resection or pyloric exclusion with gastrojejunostomy and drainage should be performed, a notion that is wholly wrong and likely to lead to the death of the patient.

In a subsequent study by Asensio and colleagues from the Los Angeles County/University of Southern California Medical Center¹⁸ patients sustained severe pancreatoduodenal injuries mandating pancreatoduodenectomy between May 1992 to December 2002 (Asensio, Petrone et al. 2003). There were 17 men (94%) and one woman (6%). Seventeen patients (94%) sustained penetrating injuries. Twelve of 18 patients (67%) sustained gunshot wounds, and 5 (28%) stab wounds; the only blunt trauma patient admitted incurred the injury from a motor vehicle

accident. In the emergency department, three patients (17%) required intubation, and one (6%) underwent a thoracotomy, aortic cross-clamping, and open CPR. An additional five patients (28%) required resuscitative operating room thoracotomy of whom one (20%) survived. Eighteen patients sustained severe injuries to the head of the pancreas involving the main pancreatic duct that were deemed unreconstructable; 17 incurred AAST-OIS-pancreas grade V injuries and 1 a grade IV injury. Eighteen patients sustained severe duodenal injuries, all AAST-OIS-duodenum grade V. Ten patients (56%) had multiple duodenal injuries and eight (44%) had isolated injuries. Forty nine patients had associated nonvascular injuries and 16 had associated vascular injuries. All eighteen patients had a standard pancreatoduodenectomy because of unreconstructable injury to the head of the pancreas involving the main pancreatic duct, the intrapancreatic portion of the distal common bile duct, with devitalization and destruction of its blood supply, or combinations of both. All 18 patients also had massive unreconstructable injuries to the duodenum involving the first or second portions, the ampulla of Vater, or multiple injuries to the duodenum with devitalization and destruction of its blood supply or combinations of all of the above. Thirteen of the 18 patients (72%) also had massive uncontrollable retropancreatic haemorrhage from associated vascular injuries to the portal vein, superior mesenteric artery, and superior mesenteric vein; Five patients underwent an initial damage control with staged reconstructive procedures. Twelve of the 18 patients survived for an overall survival rate of 67%. All patients who died required resuscitative

thoracotomy, one in the emergency department and five in the operating room. All patients died secondary to exsanguination.

Complications in this study were separated into general and injury specific. There were 11 general complications, for a mean of 0.9 complications per patient and 15 injury specific complications, for a mean of 1.25 complications per patient. Injury-specific complications included four duodenal or pancreatic fistulas, or both (33%); six intra-abdominal abscesses (50%); two postoperative haemorrhages (17%); two cases of postoperative pancreatitis (17%); and one patient developed a biliary tract stricture (8%). A single patient developed a biliary tract stricture requiring readmission within 3 months and had a successful reconstruction with a hepaticojejunostomy. The mean hospital length of stay was 57 days (range 30 to 514 days).

In a report by McKone from the Department of Surgery, Michigan State University, Grand Rapids, five patients underwent pancreatoduodenectomy for severe combined injury to the pancreas and duodenum between July 1980 to December 1986 (McKone, Bursch et al. 1988). All five patients survived. The average age of the patients was 29 years. Four patients sustained blunt trauma and one sustained penetrating trauma. The average duration of the operation was 5 hours. In addition to the pancreatic and duodenal injuries, an average of two other organs were injured per patient. The average hospital stay was 24 days. Two patients had postoperative complications requiring re-operation. All patients were discharged tolerating

oral feedings without the need for insulin or pancreatic exocrine supplements. The authors concluded that their report confirmed the utility of pancreatoduodenectomy for severe combined pancreatic and duodenal trauma in a community trauma centre.

In a study by Dr Heimansohn and colleagues from the Department of Surgery, Indiana University School of Medicine, Indianapolis, six young men with a mean injury severity score of 15.4 who underwent a pancreatoduodenectomy for trauma were reviewed (Heimansohn, Canal et al. 1990). Four patients sustained penetrating trauma and two patients suffered blunt injuries; each had a pancreatic ductal disruption combined with a significant duodenal injury. Four patients underwent pancreatoduodenectomy primarily, while two patients underwent initial drainage and diverticulization. The four patients who underwent an immediate resection had a mean hospital stay of 28 days (18-42 days) and did not require further surgical intervention. All were alive and well six months to nine years later. The two patients who had drainage and repair of their injuries had a mean hospital stay of 115 days (84-147 days) and required additional laparotomies for pancreatic leaks, enterocutaneous fistulae, or drainage of abscesses. Pancreatoduodenectomy was ultimately performed in each case, and both have survived. The authors concluded that a pancreatoduodenectomy has a role in the management of combined pancreatic and duodenal injuries.

A retrospective review by Thompson and colleagues from Seattle of all patients presenting to a single Level I trauma center who required pancreatoduodenectomy for trauma from 1996 to 2010 was performed (Thompson, Shalhub et al. 2013). During the study period, 56,271 patients were admitted with blunt or penetrating trauma, and 276 patients (0.49%) were admitted with trauma to the pancreaticoduodenal complex. Of this group, 15 patients (median age, 29 years; 93% male; median Injury Severity Score [ISS], 35) underwent pancreatoduodenectomy following blunt (n = 5) or penetrating trauma (n = 10). Twelve patients (80%) underwent damage-control surgery (DCS) with or without the initial stage of Whipple resection as their first operation. Three patients (20%) underwent a complete Whipple procedure, including reconstruction, as their first operation. Overall, 87% of patients (13 of 15) were acidotic, hypothermic, and coagulopathic during their first operation. Average operative time was longer for the completion pancreatoduodenectomy versus DCS (460 [98] minutes vs. 243 [112] minutes). The mean (SD) overall hospital LOS was 21.4 (24) days, and the mean (SD) ICU LOS was 21.4 (27) days. The overall complication rate was 87%, with complications occurring in 13 of the 15 patients. In-hospital mortality was 13% (n = 2).

In this study the authors present both the largest series of patients to date who underwent a DCS or staged Whipple procedure for complex pancreaticoduodenal trauma and the largest series with blunt trauma. Using a staged approach, the authors report the lowest mortality rate for such

injuries in the literature, less than half of that reported in the most recent series (33%). Given the frequent occurrence and recognized detrimental impact of acidosis, hypothermia, and coagulopathy in patients with severe pancreatoduodenal trauma as well as the proven benefits of DCS, the authors proposed that these patients should undergo initial DCS and staged reconstruction.

This study has substantial limitations. The sample is heterogeneous and includes both penetrating and blunt injury patients. One third of patients underwent their initial operation at an outside institution. The author's referral pattern potentially selects for survival. As anticipated, the rarity of such patients resulted in relatively small numbers, making statistical comparisons difficult, given the high potential for Type I and Type II errors. For this reason, the raw data was presented rather than the details and results of statistical analyses. Moreover, there were multiple attending surgeons involved in the initial care of these patients; only three surgeons operated on more than one patient, and each of them operated on only two patients total. In addition, this study spans a 15-year period during which operative and critical care management would have changed significantly, including the use of damage control surgery with or without staged Whipple resection for devastating pancreatoduodenal injuries since 1999. However, these latter facts also make extrapolation regarding outcomes more feasible.

In a report by Oreskovich and Carrico from the Department of Surgery, University of Washington School of Medicine, Harbourview Medical Centre, Seattle, Washington, ten of 117 patients who had sustained a pancreatic injury over a 6 year period, underwent a pancreatoduodenectomy. The mean age of the 10 patients was 27 years and the mean interval from injury to operation was 1.7 hours. Fifty-five percent arrived at the trauma centre in shock.

Unlike previous publications, a novel feature in the study of 19 pancreatoduodenectomies by Krige and colleagues from Cape Town was the ability to do a pylorus-preserving pancreatoduodenectomy in a substantial proportion of injured patients. In six patients who, in addition to maximal injuries to the pancreas, also had severe injuries to adjacent vascular, biliary, enteric, colonic or solid organs and had persistent shock, an initial damage control operation was followed by delayed pancreatoduodenectomy and reconstruction when the patient was stable. This study also used a pancreatogastrostomy in high risk pancreatic anastomoses.

In summary, severe pancreatoduodenal trauma is an uncommon event that creates a difficult scenario for clinicians in the initial evaluation, operative management, and postoperative course. Proceeding with a pancreatoduodenectomy for trauma is seldom necessary and is reserved for maximal injuries involving the head of the pancreas and duodenum in which repair is not feasible and where the decision to do a

pancreatoduodenectomy is unavoidable. Recent studies have shown that a pylorus-preserving pancreatoduodenectomy is technically feasible in the trauma situation. Pancreatogastrostomy is an option when conventional pancreatojejunostomy is difficult due to an oedematous jejunum. Initial damage control with delayed resection and reconstruction is applicable in a select group of patients. The benefits of damage control surgery are appreciable in the literature; similarly, a multistage pancreatoduodenectomy for trauma has been shown to yield more favorable operative conditions for reconstruction. Despite this, current literature indicates that single-stage pancreatoduodenectomy remains the predominate management for patients with devastating pancreaticoduodenal injury. While an emergency pancreatoduodenectomy has significant morbidity and appreciable mortality due to complicating factors, associated injuries and shock, resection may be the only option in complex injuries with ampullary destruction or devitalised duodenum. Experienced surgeons advocate staging the operation, first applying damage-control principles to prevent major haemorrhage and loss of life and returning to the OR after the patient is adequately resuscitated and coagulopathy is corrected. Current data show that these are patients with complex problems associated with significant postoperative morbidity and should be managed collaboratively by both trauma and HPB surgical teams.

CHAPTER 6

Severe combined pancreatic and duodenal injuries

Severe injuries involving both the pancreas and duodenum continue to result in substantial complications, prolonged ICU and hospital stays and overall mortality rates of 31% to 50%, even when treated in well-resourced high volume trauma referral centres (Ragulin-Coyne, Witkowski et al. 2014, O'Reilly, Bouamra et al. 2015). Most deaths occur early and are due to associated injuries and the consequences of uncontrolled blood loss and shock (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). Late deaths are usually due to resistant intra-abdominal sepsis and multisystem organ failure (Tyburski, Dente et al. 2001, Krige, Beningfield et al. 2005). The five most crucial factors influencing management and outcome are (i) the grade of pancreatic head damage, (ii) the degree of ischaemia and viability of the duodenum, (iii) the extent of ampullary damage, (iv) the presence of visceral vascular injuries and (v) the magnitude of associated organ injuries (Krige, Kotze et al. 2016). These fundamental issues determine both the scale of intervention and ultimate survival. Both the early use of damage control surgery and the need for pancreatic and duodenal resection are important considerations when treating complex combined pancreatoduodenal injuries but neither have not been applied consistently in high risk situations (van der Wilden, Yeh et al. 2014).

The optimal surgical management of complex combined pancreatoduodenal injuries is currently characterized by continued controversy and contradiction (Krige, Kotze et al. 2016). The reasons for the lack of clear guidelines and the paucity of reliable and robust data are manifold. Synchronous duodenal damage seldom occurs in tandem with injuries to the head of the pancreas and are therefore uncommon (Krige, Kotze et al. 2016). In the prospective TARN (O'Reilly, Bouamra et al. 2015) and STAG (Scollay, Yip et al. 2006) databases combined pancreatoduodenal injuries occurred in only 0.2% and 0.3% of predominantly blunt abdominal injuries, while a large cohort study from Cape Town reported double the number of combined pancreatoduodenal injuries after abdominal gunshot wounds compared to blunt trauma (Chinnery, Krige et al. 2012).

The relative infrequency of this type of injury suggests that most surgeons will have had minimal operative exposure and limited personal experience when dealing with complex combined pancreatoduodenal injuries (CPDI). These deficiencies are compounded by the lack of data and clarity in surgical publications which consist mostly of small retrospective or outdated series and collective reviews which do not provide an authoritative or comprehensive analysis of the problem. In addition, the lack of a practical and universally relevant classification that can be applied to accurately predict the outcome of combined pancreatoduodenal injuries has further hampered progress. Both the widely used Lucas (Lucas 1977) and AAST (Moore, Cogbill et al. 1990) classifications have flaws which hinder a

detailed comparison of treatment choices in major combined pancreatoduodenal injuries. For example, in the pancreatic injury AAST classification, no provision is made for associated duodenal injuries which may be a critical factor determining the need for a pancreatoduodenectomy (Krige, Beningfield et al. 2005).

The lack of consensus on the current optimal treatment of combined pancreatoduodenal injuries has hindered advances. Three major unresolved issues in severe combined pancreatoduodenal injuries are (i) survival after initial damage control surgery, (ii) outcome following pancreatoduodenectomy, and (iii) evaluation of predictive factors for morbidity and mortality in a large cohort of consecutive patients using a CPDI grading score (Krige, Kotze et al. 2016). Several factors have prevented a detailed and accurate comparative analysis of the treatment options. Historically, morbidity and mortality data reporting combined pancreatoduodenal injuries has varied widely due to selection bias, exclusion of patients with associated vascular injuries and deaths occurring intra-operatively or within the first 24 hours (Kao, Bulger et al. 2003, Recinos, DuBose et al. 2009). The management of complex injuries has also varied widely and remains mired in historical dogma (Krige, Kotze et al. 2016). A wide spectrum of surgical options have been recommended for combined pancreatoduodenal injuries, ranging from conservative to radical and have included simple closure and drainage, debridement and primary repair, resection and end-to-end anastomosis, a selection of duodenal

diversions and pancreatoduodenectomy (Graham, Mattox et al. 1979, Moore and Moore 1984, Feliciano, Martin et al. 1987, Mansour, Moore et al. 1989, Flynn, Cryer et al. 1990). There remains disagreement in the current literature regarding the relative merits of the various options. Earlier studies recommended that additional surgical procedures to bypass and protect the duodenal repair using pyloric exclusion or diverticulization of the duodenum were always necessary in complex injuries. Most authorities now believe this approach has been overused and current data would suggest that complex prolonged supplementary procedures in severely injured patients are inappropriate and are often unnecessary (Lopez, Benjamin et al. 2005, Sharpe, Magnotti et al. 2012).

Although the pancreas and duodenum are intimately connected and function anatomically and physiologically as a unit, most publications analyse pancreatic and duodenal injuries separately without considering combined injuries as a single entity. Published mortality rates for pancreatoduodenal injuries vary widely due to variable referral patterns in the respective datasets, inclusion of differing ratios of blunt-to-penetrating pancreatoduodenal injuries and data dilution by inclusion of low grade injuries treated non-operatively (Table 1).

Table 1 Published morbidity and mortality of pancreatoduodenal injuries

Study	Number of patients	Gunshot Wounds	Blunt	Stab	Whipple	Duodenal complications	Pancreatic complications	Overall morbidity	Mortality
Graham, 1979*	68	50	13	5	5	3 (4.4%)	24 (35.3%)	44 (64.7%)	18 (26.5%)
Moore, 1984	34	18	15	1	1	1 (2.9%)	14 (41.2%)	12 (35.3%)	3 (8.8%)
Feliciano, 1987*	129	89	25	15	10	7 (5.4%)	28 (21.7%)	No data	38 (29.5%)
Mansour, 1989	62	30	25	7	4	1 (1.6%)	22 (35.5%)	No data	12 (19.4%)
Tyburski, 2001	27	23	2	2	5	No data	No data	No data	7 (26%)
Lopez, 2005	33	24	6	3	0	2 (6.1%)	3 (9.1%)	No data	6 (18.2%)
Krige, 2016	75	57	13	5	19	17 (22.6%)	14 (18.7%)	63 (84%)	21 (28%)

**both papers from Ben Taub General Hospital, Houston, Texas and contain overlapping data*

In a report by Graham, Mattox, Vaughan and Jordan from Ben Taub General Hospital, Houston, Texas, 308 pancreatic injuries and 175 duodenal injuries were treated over a nine year period of whom 68 had combined pancreatic and duodenal injuries (Graham, Mattox et al. 1979). Eighteen patients had a primary repair and external drainage while 50 required more extensive procedures which included duodenal diversion and pyloric exclusion (n=32), pancreatoduodenectomy (n=6), and a variety of other procedures (n=12). Operative mortality rate was 26.5%, including five patients who died intraoperatively. Only one death was directly attributable to the pancreatoduodenal injury. The authors concluded that no single procedure was uniformly applicable to all CPDIs and that surgeons treating injuries of this severity should be familiar with a variety of techniques for repair and that treatment should be individualized and preservation of tissue should be attempted where possible. As will be shown subsequently, techniques recommended by these authors such as duodenal diversion and pyloric exclusion are no longer advisable and have been superceded by simpler and more effective alternatives.

In a study by Moore from Denver, Colorado, 34 patients with CPDI were treated operatively (Moore and Moore 1984). Twelve patients had sump drainage and repair while 22 required more extensive procedures including pyloric exclusion with or without pancreatic resection in 14, and pancreatoduodenectomy in one patient. Overall mortality rate was 8.8% with 2 early deaths secondary to associated injuries and 1 late death due to the pancreatoduodenal injury. Complications directly related to the combined injury occurred in 47% of the

patients including a 20% incidence of pancreatic fistulas. The authors concluded that although no single operative procedure could be uniformly used in complex CPDIs, the use of active sump drainage, pyloric exclusion, and early nutritional support via needle catheter jejunostomy was advocated. As in the above criticism of the previous study, pyloric exclusion is now outdated and has been replaced by primary duodenal repair, enteral feeding and external tube drainage.

In a subsequent report from Ben Taub General Hospital by Feliciano, 129 patients with combined pancreatoduodenal injuries were treated, of whom 104 (81%) had penetrating wounds (Feliciano, Martin et al. 1987). Primary repair or resection of one or both organs with pyloric exclusion and gastrojejunostomy (68 patients) and drainage was used in 79 patients (61%). Simple primary repair was used in 31 patients (24%). A Whipple resection or a total pancreatoduodenectomy was required in the 13 patients, while six patients died in the operating room before any type of repair could be completed. Major pancreatoduodenal complications including pancreatic fistulas (26%), intra-abdominal abscess (17%), and duodenal fistulas (7%) occurred in 108 (84%) patients who survived more than 48 hours. The overall mortality rate was 29.4% (38 of 129), with 55.3% (21 of 38) of patients dying within 48 hours of injury secondary to hypovolaemic shock and transfusion-associated coagulopathies. Six or more intra-abdominal visceral or vascular injuries were present in 15 (71.4%) patients with perioperative deaths. Seventeen patients died (17 of 38 = 44.7%) in the late postoperative period, with sepsis and/or multiple organ failure (nine patients) and respiratory failure (five patients)

accounting for most deaths. The authors concluded that the mortality rate of CPDIs would remain high because of collateral injuries to associated organs and vascular structures. The morbidity and late mortality rates due to moderate to severe pancreatoduodenal injuries could be decreased by the addition of pyloric exclusion and gastrojejunostomy to the primary repairs.

In a later 12-year review of 62 patients with CPDI by Mansour and colleagues from Denver, Colorado, grade I and II injuries (39%) were treated with simple repair and drainage, grades III and IV (51%) were managed primarily by pyloric exclusion, while grade V injuries (10%) underwent pancreatoduodenectomy (Mansour, Moore et al. 1989). Pancreatic and duodenal complications developed in 35% and 2% respectively. The overall mortality was 19.4% of whom 83% died within the first 24 hours from exsanguination or severe head injuries. The authors concluded that although no single procedure could be applied uniformly to the CPDIs, active sump drainage of the pancreas, pyloric exclusion of the duodenum, and early nutritional support through needle catheter jejunostomy were considered the mainstay treatment principles.

In a report from the Ryder Trauma Centre in Miami by Lopez, 33 of 240 patients who sustained a pancreatic or duodenal injury had CPDI (Lopez, Benjamin et al. 2005). The majority of patients (82%) had penetrating injuries of whom 72% had sustained gunshot wounds and 45% had an associated major vascular injury. These 33 patients underwent a total of 57 laparotomies with an average of 1.7 operations per patient (range, 1 to 5 operations). Eighty-four per cent of the patients had an associated gastrointestinal injury and 45% had a major vascular injury. Thirteen of the 33 (39%) patients presented *in extremis* and

underwent an abbreviated laparotomy. Overall complication rate was 36% including fistula, abscess, pancreatitis and organ dysfunction with an 18.2% mortality rate. The authors concluded that CPDIs were associated with a variety of other serious injuries, which added to the overall complexity and that an abbreviated laparotomy may be helpful when managing CPDIs in patients who are *in extremis*.

In a study by Antonacci, Di Saverio and Ciaroni from Bologna, Italy, mortality, morbidity, prognostic factors and the value of specific surgical techniques were analysed (Antonacci, Di Saverio et al. 2011). In 55 patients with pancreatoduodenal injuries 68.5% had pancreatic injuries, 20.4% had duodenal injuries and 11.1% had combined pancreatoduodenal injuries; 85.3% had blunt abdominal trauma, while 14.9% had penetrating injuries. The authors treated 78.1% of the patients with external drainage and/or simple suture; distal pancreatectomy was performed in 9% and duodenal resection with anastomosis (3.7%) and diversion procedures (3.7%) were performed in an equal number of patients. Age, American Association for the Surgery of Trauma (AAST) grade, organ involved, haemodynamic status, intraoperative cardiac arrest, and operative time were strongly predictive of mortality on multivariate analysis. The AAST grade represented, on multivariate analysis, the only independent prognostic factor predictive of overall morbidity. The authors concluded that optimal management and better outcome of pancreatoduodenal injuries are associated with shorter operative time and with DCS, in contrast to definitive surgical procedures.

Tyburski and colleagues from Wayne State University School of Medicine, a urban Level I trauma centre in Detroit, did a retrospective review of 167 patients over 7 years from 1989 to 1996 with injuries of the duodenum and pancreas (Tyburski, Dente et al. 2001). Fifty-nine patients (35%) had isolated injury to the duodenum (13 blunt, 46 penetrating), 81 (49%) had isolated pancreatic trauma (18 blunt, 63 penetrating), and 27 (16%) had combined injuries (two blunt, 25 penetrating). The overall mortality rate was 21 per cent and the infectious morbidity rate was 40 per cent. The majority of patients had primary repair and/or drainage as treatment of their injuries. Patients with pancreatic injuries (alone or combined with a duodenal injury) had a much higher infection rate than duodenal injuries. The patients with duodenal injuries had significantly lower penetrating abdominal trauma indices, number of intra-abdominal organ injuries, and incidence of hypothermia. On multivariate analysis independent factors associated with infections included hypothermia and the presence of a pancreatic injury. The authors concluded that although injuries to the pancreas and duodenum often coexist it was the pancreatic injuries that contributed most to infectious morbidity.

Recent expert recommendations have urged a more conservative approach to many intra-abdominal organ injuries, including combined pancreatoduodenal injuries. The current guidelines issued by the Eastern Association for the Surgery of Trauma recommend non-operative management for Grade I and II injuries, and operation including resection or drainage for injuries of Grade III and higher (Ho, Patel et al. 2017). The US Nationwide Inpatient Sample (NIS) was queried for the period from 1998 to 2009 for all patients with pancreatic or

duodenal trauma. The NIS, a part of the Healthcare Cost and Utilization Project (HCUP), is a national, all-payer discharge database containing information on a representative stratified sample of 20% of non-federal US community hospitals in participating states, including academic and specialty hospitals. The NIS weighting strategy facilitates the drawing of population-based estimates at the national level. Elizaveta Ragulin-Coyne and colleagues from the Department of Surgery, Beth Israel Deaconess Medical Center and Harvard Medical School in Boston evaluated the changing patterns of intervention for pancreatoduodenal injuries on a national basis over 12 years (Ragulin-Coyne, Witkowski et al. 2014). In the study the primary outcome measures were rates of surgical interventions in pancreatoduodenal injuries over time. Secondary outcomes included mortality, length of stay and major in-hospital complications, including cardiovascular or deep vein thrombosis, gastrointestinal, pulmonary or urinary complications, infection and myocardial infarction. Analyses included chi-squared tests, Cochran–Armitage trend tests and logistic regression. During the study period, 27,216 nationally weighted patients with pancreatoduodenal injuries were admitted. Nearly three-quarters of this cohort (73.6%) were male. The mean age of the patients was 37.7 years; the mean Elixhauser score was 0.8. The majority of patients were treated at urban (93.1%), large (73.4%) and teaching (74.0%) hospitals. Overall, 1976 patients (36.0%) underwent a primary repair procedure, 2681 (48.9%) underwent distal pancreatectomy, 162 (3.0%) underwent total pancreatectomy, 165 (3.0%) underwent radical pancreatoduodenectomy or radical pancreatectomy, and 499 (9.1%) underwent partial or proximal pancreatectomy. A total of 46.6% of patients had major complications. The most common complications were pulmonary and infectious

complications. Patients who underwent an operation had increasingly higher rates of complications and this was especially significant in those having pancreatic surgery in whom complications increased from 50.2% to 71.8% ($p < 0.0001$). Significant independent predictors of mortality included combined pancreatic and duodenal injuries, penetrating trauma and age > 50 years (Ragulin-Coyne, Witkowski et al. 2014).

Detailed analysis of this study identifies several important limitations. The NIS is an administrative database and lacks important clinical variables, including patient factors such as injury severity score, imaging, laboratory values, operative data (blood loss, transfusions, operative time) and long-term follow-up and readmission information. Major postoperative complications were assessed using a validated set of ICD-9 codes; however, complication rates can be underestimated because individual medical records cannot be reviewed and the NIS does not include complications that occur after the patient discharge. Insufficient coding specifications in the NIS precluded the accurate assessment of the important complications such as bile duct stricture, duct injury, leak or fistula. The database also does not allow assessment of relevant peri-operative variables that influence the surgeon's decision to operate which results in selection bias.

In a large cohort study O'Reilly and colleagues from Manchester assessed the incidence, mechanisms of injury, initial operation rates and outcome of patients who had pancreatoduodenal injuries in the United Kingdom from a large trauma registry over the period 1989-2013 (O'Reilly, Bouamra et al. 2015). The Trauma Audit and Research Network (TARN) database was searched for details of

patients with blunt or penetrating trauma to the pancreas, duodenum or both. Of 356,534 trauma cases, 1,155 (0.32%) had pancreatoduodenal injuries. Blunt trauma was the most common type of injury seen, with a ratio of blunt-to-penetrating PD injury ratio of 3.6:1. Road traffic accidents accounted for 673 cases (58.3%). The median injury severity score (ISS) was 25 (IQR: 14-35) for blunt trauma and 14 (IQR: 9-18) for penetrating trauma. The mortality rate for blunt pancreatoduodenal injuries was 17.6% and 12.2% for penetrating trauma. Mortality was high in the UK but comparison with other surgical series is difficult because of selection bias in the datasets. Variables predicting mortality after pancreatic trauma were increasing age, ISS and haemodynamic compromise. Similar findings have been found by STAG, who identified overall number of injuries, age, male sex, blunt trauma and haemodynamic compromise as independent risk factors for death. The study by Chinnery et al with 219 civilian gunshot injuries of the pancreas from Cape Town found that age, shock on admission, need for damage control surgery, high grade injury and associated vascular injuries were associated with mortality on multivariate analysis (Chinnery, Krige et al. 2012). The authors concluded that patients die mainly from exsanguinating injuries to other pancreatoduodenal injuries organs rather than as a consequence of PD trauma itself (O'Reilly, Bouamra et al. 2015).

Analysis of this study identifies several limitations of this study. In particular the lack of data providing information on the specific management of isolated PD injuries (O'Reilly, Bouamra et al. 2015). The diagnostic accuracy of CT is dependent on the grade of injury and the timing of the imaging and it is uncertain how this has changed over time, especially with the introduction of

modern spiral and multichannel scanners. Low sensitivity for detecting PD injury is present, even using 16 and 64-multidetector CT scanners. These factors will have a substantial impact on patient assessment and intervention.

There are few detailed reports on pancreatoduodenectomy in patients with CPDIs (Table 1). In the seven publications detailing CPDIs in which complete operative data are presented, a pancreatoduodenectomy was done on 48 occasions in a total of 318 patients who had grade 5 CPDIs which is an incidence of 15.1% (range: 0-25%). The incidence of pancreatoduodenectomy depends on the proportion of grade 5 injuries treated and the institutional protocol and experience in complex injuries. There are no clear guidelines on the precise role of pancreatoduodenectomy in patients with CPDI. Most authorities agree that a pancreatoduodenectomy for trauma is seldom necessary and should only be undertaken in stable patients with grade 5 injuries of the head of pancreas and duodenum in whom a repair is not feasible (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). Data show that a severe pancreatic injury compounded by visceral and vascular injuries exponentially increases the complexity and mortality of the operative intervention (Ivatury, Nallathambi et al. 1985). There is consensus that patients with severe CPDIs and haemodynamic instability due to uncontrollable bleeding, hypothermia, acidosis or coagulopathy should have an abbreviated laparotomy with DCS and subsequent re-exploration, resection and reconstruction when stable (Thompson, Shalhub et al. 2013). While this practice is now self-evident, the procedure has not been universally applied. In an analysis of the National Trauma Data Bank pancreatoduodenal injury

register from 2008-2010, 13 (33%) of 39 patients who underwent a trauma Whipple died at a median of 7 days (range 1-180 days). In the majority of cases the Whipple was performed during the index operation and most procedures were done within 6 hours of admission. Similarly, in an analysis of 11,011 patients in the US Nationwide Inpatient Sample (NIS) who required an operation for pancreatic and duodenal injuries over a 12 year period, 48.9% underwent a distal pancreatectomy, 3% had a total pancreatectomy and 3% had a radical pancreatoduodenectomy or a radical pancreatectomy, a notion which is contrary to and deviates markedly from current principles espoused for pancreatic trauma surgery (Ragulin-Coyne, Witkowski et al. 2014). This is in stark contrast to a study from Seattle 12 of 15 patients with severe pancreatoduodenal injuries appropriately underwent DCS with or without the initial stage of a Whipple resection as their first operation. The pancreatoduodenectomy was completed in two stages in eight patients (67%) and in three stages in four patients (33%). Two of the 12 died (17%) of bleeding and MOF (Thompson, Shalhub et al. 2013).

In a study from Cape Town which specifically assessed the role of DCS and pancreatoduodenectomy, the records of patients with CPDI were evaluated to assess optimal surgical intervention (Krige, Kotze et al. 2016). Primary and secondary end points assessed were death and morbidity. Seventy-five patients with CPDI, underwent 161 operations (range 1 to 9 operations). Twenty-nine patients with complex CPDI underwent a DCS and 46 had definitive treatment during the initial operation. Nineteen had a pancreatoduodenectomy, either during the initial operation (n=13) or after the DCS (n=6). Postoperative

complications occurred in 63 (84%) patients. Twenty one (28%) patients died, including 15 (43%) of 35 patients with associated vascular injuries. Sixteen (84%) of the 19 patients who had a pancreatoduodenectomy survived. Significantly more complications related to bleeding, disseminated intravascular coagulation, and hypovolaemic shock occurred in those patients who eventually died and significantly more abdominal sepsis and fistulas occurred in patients who survived. Mortality was related to associated vascular injuries overall ($p<0.01$), major visceral venous injuries ($p<0.011$), and the combination of vascular plus the total number of associated organs injured ($p<0.046$). Despite using DCS in CPDIs, morbidity (84%) and mortality (28%) remain substantial. Careful selection of patients undergoing pancreatoduodenectomy resulted in 84% survival. Associated vascular injuries, major visceral venous injuries, and combined vascular and associated organs injured influenced outcomes and mortality. This study emphasized the lethality of complex pancreatoduodenal injuries when combined with major visceral vascular injuries involving the portal vein, the superior mesenteric vein and the inferior vena cava. Almost half the patients had associated visceral vascular injuries and 45% of the DCS group died without having a second definitive operation.

In previous reports from Cape Town overall mortality rates of 15.7% (Krige, Kotze et al. 2015) for pancreatic injuries and mortality rates of 5.1% (Chinnery, Krige et al. 2012), 16.4% (Krige, Kotze et al. 2011) and 21% (Krige, Kotze et al. 2014) for stab wounds, blunt injuries and gunshot wounds of the pancreas have been documented. In the TARN database, the mortality for blunt PD trauma was 17.6% and was 12.2% for penetrating PD trauma. Variables predicting

mortality after pancreatic trauma were increasing age, ISS, hemodynamic compromise and not having undergone an operation (O'Reilly, Bouamra et al. 2015). However, unlike the Cape Town study, the results and outcome of the TARN database are skewed as the majority of patients had only AAST grade I pancreatic and duodenal injuries and a third of patients had no operation during their hospital admission (O'Reilly, Bouamra et al. 2015). Overall mortality in the Cape Town study was 28% which reflects a selected group of patients with multiple injuries in which one third of deaths were due to exsanguination as a consequence of unsalvageable vascular injuries. The results of the Cape Town study represent the full spectrum of CPDI and include the very worse end of the injury continuum and incorporate patients who arrive in the operating room in extremis, some of whom die soon after initiation of the laparotomy (Krige, Kotze et al. 2016). This study demonstrated that $RTS < 7.8$, shock on presentation, increased composite grade of injury, the need for damage control surgery and the presence of vascular injuries overall and major visceral venous injuries as well as the combination of vascular plus the total number of associated organs injured are inter-related risk factors which influence mortality.

A major difference in this study, compared to other series, is the number of patients who had a pancreatoduodenectomy. Although this study represents the largest current series of patients with CPDI, there are several caveats and limitations that should be considered when interpreting these results. A substantive limitation is that these data were generated from and reflect the outcome of a highly select cohort of patients treated in a large volume well-resourced tertiary referral academic Level I Trauma Centre with a special

interest in HPB trauma and access to experienced pancreatic surgical assistance. Although these data may be similar to other major academic institutions or trauma centres, it is not applicable to community-based hospitals. A strength in this longitudinal cohort study was the detailed prospective documentation of complications and causes of death within 30 days of surgery which provided consistent and objective end-points. The unvalidated composite grading system used in this study demonstrated a difference in complications and mortality between grades 1-2 vs 3-5 which may be an important component for assessing and comparing future reports on complex combined injuries as this feature has been lacking in past publications (Krige, Kotze et al. 2016).

The lack of a unified approach to CPDIs is a reflection of both the wide variety of injuries that may occur, as well as the number of operative procedures currently available. Also, comparisons between various forms of treatment are difficult to interpret because of the infrequency of solitary injuries to these organs, the lack of a uniformly acceptable injury classification and the small number of patients in individual treatment groups. The Cape Town data demonstrate a paradigm shift in the overall management of complex combined pancreatoduodenal injuries and emphasizes that no single operation is appropriate for all pancreatoduodenal injuries (Krige, Kotze et al. 2016). Operative intervention in each patient should ideally be individualized and surgeons need to have a flexible strategy and should be familiar with the full range of surgical techniques required for repair (Krige, Kotze et al. 2016). The data and outcome in this study are in keeping with current concepts in DCS (Roberts, Bobrovitz et al. 2015, Roberts, Bobrovitz et al. 2016) and in line with

guidelines for duodenal injuries (Malhotra, Biffi et al. 2015). The optimal management of grade 1-3 duodenal injuries is primary repair or resection of the damaged segment of duodenum and anastomosis without the need for elaborate bypass procedures or pyloric exclusion to exclude the duodenum and protect the duodenal repair. Once haemostasis has been achieved, most pancreatic head injuries with an intact ampulla and no devitalization can effectively be managed with external sump drainage. If an ensuing pancreatic fistula persists, treatment with endoscopic stenting is safe. Pancreatoduodenectomy should be reserved for a select group of patients who have complex combined pancreatoduodenal injuries in whom repair is not feasible and who are hemodynamically stable. In the small cohort of patients who require initial damage control, both the pancreatoduodenectomy and the reconstruction should be delayed until the subsequent definitive operation. Despite using DCS in CPDIs, morbidity (84%) and mortality (28%) remain substantial. Careful selection of patients undergoing PD resulted in 84% survival. Associated vascular injuries, major visceral venous injuries and combined vascular and associated organs injured influenced outcome and mortality (Krige, Kotze et al. 2016).

CHAPTER 7

Management of pancreatic injuries during damage control surgery

Damage control surgery (DCS) has been one of the major advances in trauma surgery over the past two decades and is now a well-established surgical strategy in the management of the severely injured and shocked patient (Nicol, Navsaria et al. 2010). DCS refers to the conscious decision by the surgeon to minimise operative time in a seriously injured patient when the combined effects of the magnitude of the injury and the markedly altered physiological state of the patient preclude an immediate and safe definitive operative procedure (Nicol, Navsaria et al. 2010). DCS encompasses a change in the surgical mindset with the realisation of the need in the severely injured and shocked patient to halt and then reverse the lethal cascade of events that include hypothermia, acidosis and coagulopathy, a sequence which has been termed the 'lethal triad' (Roberts, Ball et al. 2017). During the initial abbreviated surgical intervention, bleeding is stopped, contamination is controlled and after temporary abdominal wall closure, the patient is transferred to the intensive care unit for 'physiological resuscitation and stabilisation' (Wang, Li et al. 2007). Once specific predetermined physiological end-points have been reached, the patient is returned to theatre to complete the definitive treatment (Loveland and Boffard 2004). It is important to appreciate that the surgical decision to apply DCS is not a 'bailout operation' but the realisation that successful trauma surgery not only requires attention to the injuries sustained but also an acute awareness of the

physiological status of the patient (Nicol, Navsaria et al. 2010). This review evaluates the management of severe pancreatic injuries in the context of DCS.

In essence, damage control surgery should be regarded as a physiological approach to surgery with the objective of gaining time to stabilize the severely injured patient and to optimize their physiological state before definitive repair (Ball 2014). The term 'damage control' is derived from the United States Navy, with reference to a strategy that allows the rapid inspection and urgent temporary repair of a damaged hull during conflict thereby enabling the ship to return safely to port and undergo definitive repair under optimal conditions. The success of the naval strategy led to the use of the term to describe a similar approach in trauma surgery where the emphasis is on rapid assessment and often temporary repair to enable the survival of the patient (Nicol, Navsaria et al. 2010). Rotondo et al. from the University of Pennsylvania used this term in 1993 to describe an abbreviated surgical strategy in the setting of a 'damage control laparotomy (Rotondo, Schwab et al. 1993). The concept was not new, as there had been surgical reports of packing wounds as far back as the American Civil War (Schwab 2004). Pringle subsequently described the technique of packing to control haemorrhage in the early 20th century (Pringle 1908). In the 1970s and later further reports demonstrated the effectiveness of liver packing after trauma, and in 1983 Harlan Stone successfully applied a new approach using an 'abbreviated laparotomy with intra-abdominal packing' in patients with apparent intra-operative coagulopathy (Stone, Strom et al. 1983). This surgical strategy has since evolved beyond the abdomen to include the management of

injuries involving the neck, chest, pelvis and extremities (Roberts, Ball et al. 2017).

Since the initial publication by Stone et al (Stone, Strom et al. 1983) and the subsequent seminal description by Rotondo et al (Rotondo, Schwab et al. 1993), damage-control methodology has transformed the way trauma surgery is implemented. The concept is now widely accepted as an essential strategy in the management of complex trauma aggravated by coagulopathy, hypothermia and acidosis (Roberts, Ball et al. 2017). However, despite these advances, mortality rates in patients who have life-threatening pancreatic trauma combined with injuries to contiguous organs including liver, bile ducts, duodenum and vena cava, superior mesenteric and portal veins remain substantial and approach 50% (Scollay, Yip et al. 2006). A severe pancreatic injury compounded by visceral and vascular injuries exponentially increases the complexity of any operative intervention undertaken (Krige, Kotze et al. 2016).

Modern damage control surgery has become increasingly refined and has now evolved to comprise five stages (Kaafarani and Velmahos 2014). Stage 1 is the specific and conscious decision to initiate DCS in a severely injured and hypotensive patient; stage 2 is instituting the abbreviated initial operation during which bleeding is staunched, bowel contamination is contained and controlled and the procedure concluded with temporary abdominal wall closure; stage 3 is the restoration of disturbed physiology to normality in the intensive care unit; stage 4 is the relook laparotomy and definitive reparative surgery and stage 5 is the final abdominal wall closure. The decision to perform DCS (stage 1) may range from an intuitive and obvious situation such as a high-velocity

gunshot wound of the abdomen to more difficult operative decisions for implementation of DCS as may be encountered in complex liver and pancreatic injuries. Most experts agree that it is vital that the decision to employ DCS is made early in the operative course and not delayed until the patient is hypothermic and coagulopathic with a firmly established 'vicious cycle (Roberts, Ball et al. 2017).

Specific criteria for instituting DCS have been proposed. There is general consensus that DCS should be initiated when the patient's pH is <7.20 , the base excess is worse than -10.5 and the core temperature is less than 35°C (Ball 2014). However, when a major injury in an unstable patient is recognised, the surgeon should not delay until these criteria are reached before implementing DCS (Loveland and Boffard 2004). During the second stage of DCS the surgeon should do the minimum required at the initial operation to rapidly control exsanguination (suture, ligation, temporary vascular shunt or packing) and to prevent spillage of gastro-intestinal content and urine in the abdomen (suture, ligation, stapling or ureterostomy). Prolonged and complex surgical procedures that include resection and anastomosis should be avoided during this stage (Roberts, Bobrovitz et al. 2015). Where primary fascial closure is not possible and abdominal compartment syndrome is a concern, a modified sandwich technique with temporary abdominal wall closure should be used. The optimal temporary abdominal wall closure strategy should protect the bowel, evacuate fluid, provide rapid and easy access to the abdominal cavity, and allow for expansion of abdominal contents to prevent abdominal compartment syndrome (Kobayashi, Kubota et al. 2016)ⁱ. Restoration of normal physiology is

undertaken in the ICU and includes warming the patient, judicious resuscitation with appropriate fluid administration, correction of acidosis and coagulopathy and treatment of infection (Loveland and Boffard 2004). Other critical care management decisions include sedation and ventilation, early enteral nutrition, and maintenance of renal function (Lee and Peitzman 2006). The goal of the second stage of DCS is to facilitate rapid and safe return to theatre (Kobayashi, Kubota et al. 2016)ⁱ. The relook laparotomy should ideally be undertaken between 24 - 48 hours after arrival in the ICU depending on the indication for the original DCS (Nicol, Navsaria et al. 2010). Liver packs should only be removed at 48 hours after the initial operation, as the risk of rebleeding from the liver significantly increases during an early relook at 24 hours. During this stage it is important to conduct a thorough examination for missed injuries and bowel and vascular structures are reconstructed, but high-risk anastomoses are avoided if possible. Final abdominal wall closure (stage 5) is generally performed after definitive surgery has been completed, but in the case of an open abdomen, skin grafting on granulated bowel may be required with later closure of the ventral hernia.

A further logical step in the development of DCS followed when Rotondo and Schwab proposed adding a stage DC 0 or “damage control ground zero” to include those interventions provided within the prehospital and trauma admissions area before operation (Roberts, Ball et al. 2017). A newer notion and the most recent addition to damage control protocols is the combination of DCS with DCR which includes rapid control of bleeding, permissive hypotension, administration of blood products in a ratio similar to whole blood

and minimal crystalloid usage (Duchesne, Kimonis et al. 2010, Roberts, Ball et al. 2017). Although DC intervention is believed to result in improved patient outcomes when appropriately applied compared to definitive surgery, outcomes are difficult to analyze, and therefore limited data exist regarding ultimate effectiveness and safety (Roberts, Bobrovitz et al. 2016).

Although DCS has been applied for two decades, several areas remain unresolved. Despite the intuitive expectation of improved survival rates in critically injured patients following the introduction of DCS, a collective review published in 2000 quoted mortality rates as high as 50% (Shapiro, Jenkins et al. 2000). While patients may survive their initial injuries after DCS there appears to be a 'two-hit phenomenon' during which many of the survivors die later as a result of multi-organ failure and sepsis (Kairinos, Hayes et al. 2010).

Several studies have suggested that damage control surgery has been overutilised or applied inappropriately (Ball 2014, Roberts, Bobrovitz et al. 2016). This is concerning as DCS is reported to have resulted in substantial complications in survivors. A retrospective cohort study reported that one in five patients who had DCS at a high-volume trauma centre between 2004 and 2008 failed to meet at least one of the traditional indications. In this study, only 33% of patients were acidotic, 43% hypothermic and 48% coagulopathic on arrival in the ICU from theatre. Although these patients may have been selected for DCS before they developed the lethal triad, a further retrospective cohort study has suggested that applying DCS to patients who are not in physiological *extremis* could potentially lead to harm.

A Cochrane systematic review on damage control laparotomy in 2010 identified seven observational studies and no randomised controlled trials. No single set of “appropriateness indications” for damage control surgery exists, a large number of heterogeneous, sometimes non-specific, and even contradictory indications for the procedure have been proposed. In addition to the lethal triad (or its component parts), indications based on specific patient injuries, characteristics of the surgeon or healthcare team (e.g. limited surgeon experience with major trauma) and even various trauma care structural or environmental factors (e.g. a non-level I trauma centre with little surgical or intensive perioperative monitoring capabilities) have been suggested (Roberts, Bobrovitz et al. 2015). Indications based on biochemical or laboratory measurements (e.g. pH) or the temperature or fluid resuscitation requirements of the patient (e.g. the number of units of packed red blood cells administered) also have a large number of cut-offs or decision thresholds (Roberts, Bobrovitz et al. 2016). Moreover, while indications have been proposed across all phases of trauma surgical decision-making (prehospital, emergency department and intraoperative), it is not clear when the decision to perform damage control instead of single-stage surgery should best be made, with some authors suggesting that this should occur preoperatively and others intraoperatively. A previous study from the Cape Town found that age, base excess, pH and core temperature were significant pre-operative predictors of death (Timmermans, Nicol et al. 2010). The study recommended that the specific trigger points at which DCS should be implemented were when pH falls below 7.20, the base excess exceeds -10.5 and the core temperature is less than 35⁰C (Timmermans, Nicol et al. 2010).

In addition to general uncertainties about the indications and outcome there has been limited evaluation of damage control surgery in patients with severe pancreatic injuries. In a recent expert appropriateness rating study on indications for use of damage control surgery, there was expert opinion consensus that DCS was useful *inter alia* in patients with combined pancreatoduodenal injuries and intraoperative haemodynamic instability or in patients who had devascularisation or massive destruction of the pancreatic head or pancreatoduodenal complex. While the principles of DCS are well-defined and the procedure forms an integral part of the management of the multiply injured patient, there is limited clinical or published experience when DCS has been applied in the presence of major pancreatic injuries. Despite irrefutable data, some studies provide no evidence of using DCS in patients undergoing major surgery for pancreatic injuries. In an analysis of 11,011 patients recorded in the US Nationwide Inpatient Sample (NIS) over a 12 year period with pancreatic and duodenal injuries who required an operation, in the surgical resection group 48.9% underwent a distal pancreatectomy, 3% had a total pancreatectomy and 3% had a radical pancreatoduodenectomy or a radical pancreatectomy, a notion which deviates markedly from current principles espoused for pancreatic trauma surgery (Ragulin-Coyne, Witkowski et al. 2014).

Neither the optimal timing of DCS nor the timing of reoperation after initial DCS have been standardized in previous publications and both require careful strategic consideration. In addition, there are no clear guidelines on when to do the pancreatoduodenectomy and the optimal reconstruction method after

resection of the pancreatic head. There is consensus that patients with major pancreatic injuries and haemodynamic instability due to uncontrollable bleeding, hypothermia, acidosis or coagulopathy should have an abbreviated laparotomy with DCS and subsequent re-exploration, resection and reconstruction when stable. While this practice should be self evident this is not universally applied. In an analysis of the National Trauma Data Bank pancreatoduodenal injury register from 2008-2010, 13 (33%) of 39 patients who underwent a trauma Whipple died at a median of 7 days (range 1-180 days). In the majority of cases the Whipple was performed during the index operation and most procedures were done within 6 hours of admission. This lack of consensus regarding damage control indications has frequently resulted in the inclusion of heterogeneous populations of patients with unbalanced determinants of outcomes in damage control studies, resulting in difficulties in comparing outcome data in various studies and may contribute to damage control practice variation.

The objectives of this analysis of damage control surgery is to evaluate outcome in civilian trauma patients with pancreatic injuries in a summation of published material (Table 1). Robust data are scant and only two substantial studies, one from the USA and one from Cape Town, have published details of DCS in the context of pancreatic trauma. The total number of patients studied is 131 from 8 papers, six of which are case reports. As in many damage control studies, gunshot injuries of the pancreas dominate (Table 1). Overall 39% of patients had a pancreatic resection, either as a primary event during damage control or subsequently when stable during the relook laparotomy. The majority

of resections were distal pancreatectomies in 25% and a pancreatoduodenectomy in 14% of patients. Morbidity, as anticipated, was substantial and averaged 71% with a wide range, from 0 to 97%. Mortality was 47% with a similar wide range. Analysis suggests that the data are skewed by single case reports and the influence of selection and publication bias and the reluctance to publish high mortality data.

Table 1 Damage Control for pancreatic injuries

Author	No of patients	GSW	Stab	Blunt	Pancreatic Resections	Distal Pancreatectomy	Pancreato-duodenectomy	Morbidity	Mortality
Eastlick 1990 New York, USA	1	1	-	-	1	-	1	0	0
Mistry 1996 St Louis, USA	1	1	-	-	1	-	1	1 (100%)	0
Koniaris 2000 Baltimore, USA	1	1	-	-	1	-	1	0	0
Sekino 2004 Matsumoto, Japan	1	-	-	1	1	-	1	0	0
Gupta 2008 Chandigarh, India	5	1	1	3	4	-	4	4 (80%)	1 (20%)
Yong 2008 Kaohsiung, Taiwan	1	-	-	1	1	-	1	1 (100%)	0
Seamon 2009 Philadelphia, USA	42	28	2	12	14	11	3	10 (24%)	18 (43%)
Krige 2017 Cape Town, RSA	79	62	3	14	28 (35%)	22	6	77 (97%)	43 (55%)
TOTAL	131	94 (72%)	5 (4%)	31 (24%)	51 (39%)	33 (25%)	18 (14%)	93 (71%)	62 (47%)

In the first study, a two-centre, retrospective review from the University of Pennsylvania and Temple University Hospitals, both urban Level I trauma centres in Philadelphia, Seamon et al evaluated 42 patients who had pancreatic injuries and required DCS between 1997 and 2004 (Seamon, Kim et al. 2009). Pancreatic injuries were graded during laparotomy and the operating attending trauma surgeon made the intra-operative management decisions, including the need for DCS. Four study groups were identified and were based on operative management during the initial laparotomy (packing only, packing with drainage, distal pancreatectomy, or pancreatoduodenectomy) and were compared with respect to clinical characteristics and outcomes. Outcomes evaluated included pancreatic complications, hospital length of stay in days, early mortality (<24 h), and in-hospital mortality (Seamon, Kim et al. 2009).

As in most studies detailing pancreatic injuries from the USA, patients were mainly men (90.5%) with penetrating injuries (71.5%). Twenty-eight had gunshot wounds and 2 had stab wounds, while 12 patients had blunt pancreatic injuries. The pancreatic head was the most commonly injured anatomic area (50%), while the pancreatic neck or body (16.7%) and pancreatic tail (33.3%) were injured less often. Pancreatic injuries were moderate to severe (mean grade, 2.6 ± 1.2), and haemorrhagic shock (71.4%) from vascular injuries (59.5%) was common. Forty-one of the 42 patients had associated abdominal injuries. Overall, the mean Injury Severity Score for the 42 patients was 29.1 ± 16.7 . Fourteen of the 42 patients had a pancreatic resection. Of the 12 patients who underwent an initial pancreatic resection (11 distal pancreatectomies, 1 pancreatoduodenectomy), all distal pancreatectomies were

performed during the initial DC laparotomy while the pancreatoduodenectomy reconstruction was delayed until a subsequent laparotomy. Mortality was substantial and 18 (43%) of the 42 patients died (packing only, 70%; packing with drainage, 25%, distal pancreatectomy, 55%).

The authors concluded that the haemodynamic state, concomitant injury, and the anatomic pancreatic injury complex dictated the extent of pancreatic operative intervention during the initial damage control laparotomy. While patients without evidence of acidosis, coagulopathy, or hypothermia underwent distal pancreatic resection, packing combined with adequate pancreatic drainage effectively controlled both haemorrhage and abdominal contamination in patients with either life-threatening physiologic parameters or proximal pancreatic injuries. In their study, increased mortality rates in patients who were packed without drainage during DCS indicated that this method was ineffective and should be abandoned (Seamon, Kim et al. 2009).

The specific limitations in assessing the Seamon et al study are inherent in the retrospective, non-randomised design. Underscoring the scarcity of this injury complex, the modest sample size, despite the inclusion of two busy urban trauma centres, limits the statistical power of the study. Only through a large multi-centre study can specific operative management strategies be compared validly with one another. Furthermore, the decision to employ damage control techniques and choice of operative intervention were both based on the discretion of the operating trauma surgeon and not formalised study protocols (Seamon, Kim et al. 2009).

In the largest cohort study to date from Cape Town the role of damage control surgery was evaluated in 79 patients who sustained pancreatic injuries and underwent DCS between 1995 and 2014 to determine which factors influenced mortality. Fifty-nine (74.7%) patients had AAST grade 3, 4 or 5 pancreatic injuries. The 79 patients had a total of 327 associated injuries (mean: 3 per patient, range 0-6) and underwent a total of 187 (range 1-7) operations. Vascular injuries (60/327, 18.3%) occurred in 41 patients. Twenty-seven (34.2%) patients died without having a second operation. The remaining 52 patients had two or more laparotomies (range 2-7). Overall 28 (35%) patients underwent a pancreatic resection either during DCS (n=18) or subsequently as a secondary procedure (n=10) including a Whipple (n=6) when stable. Overall 43 (54.4%) patients died. Mortality was related to associated vascular injuries overall ($p<0.01$), major visceral venous injuries ($p<0.01$) and combined vascular and total number of associated organs injured ($p<0.04$). Despite the magnitude of their combined injuries and the degree of physiological insult, DCS salvaged 45 % of critically injured patients who later underwent definitive pancreatic surgery. Mortality correlated with associated vascular injuries overall, major visceral venous injuries and the combination of vascular plus the total number of associated organs injured.

This study from Cape Town is distinctive as the largest series documenting damage control laparotomy in a subset of severely injured, exsanguinating patients with a pancreatic injury and multiple other competing injuries. Four-fifths of the patients had sustained abdominal gunshot injuries and three-quarters had AAST grade 3, 4 or 5 pancreatic injuries. This study shows the

lethality of complex injuries of the head and neck of the pancreas when combined with major visceral vascular injuries involving the portal vein, the superior mesenteric vein and the inferior vena cava. More than half the patients had associated visceral vascular injuries and one-third of the total group died without having a second definitive operation. Overall mortality in this study was 54% which reflects a highly selected group of patients with multiple injuries in which one third of deaths were due to exsanguination as a consequence of unsalvageable vascular injuries. The degree of pre-operative shock, the presence of major vascular injuries, the number of associated injuries, and the location and complexity of the pancreatic injury are inter-related risk factors which influence mortality.

The optimal timing of reoperation after initial DCS has not been standardized in previous publications and requires careful strategic consideration. Most major units use a policy that once the predetermined endpoints of effective resuscitation are achieved with restoration of physiological haemostasis including core temperature, normal coagulation and biochemistry, the patient is returned to the operating room for definitive treatment. Premature return to the operating room may result in increased rebleeding and the need for additional operations. Patients who are returned to the operating room within 72 hours have been shown to have improved morbidity and mortality, compared with patients who return later. While there are several small published series confirming the worth of initial damage control surgery in complex pancreatoduodenal injuries, there is no agreement on how to manage severe pancreatic injuries during the damage control phase. In particular, there are no

published data detailing the benefits of instituting an initial damage control operation and delaying the pancreatoduodenectomy and reconstruction in terms of fluid management and blood requirements. Nor are there accurate data on the timing of the relook and reconstruction after ICU resuscitation. Analysis of the existing published data shows that several strategies of dealing with the pancreatic injury during the damage control laparotomy have been proposed and implemented. All these methods involve an initial DCS to achieve control of bleeding and prevention of bowel contamination. The management of the pancreatic injury has differed substantially with either a primary resection and delayed reconstruction or a delayed secondary resection with reconstruction. The first category involves the initial DCS and an immediate pancreatoduodenectomy with stapled closure of the pancreas, bowel and bile duct. Reconstruction is completed in a stable patient 36 hours later. This technique was used by Eastlick and colleagues. In their report the pancreas was not anastomosed during the reconstruction and the patient received permanent exocrine replacement (Eastlick, Fogler et al. 1990). Koniaris (Koniaris, Mandal et al. 2000) reported reconstruction 72 hours later and Yong (Yong, Concejero et al. 2008) reconstruction 96 hours later. In a series from India, Gupta, Wig and Garg undertook reconstruction in 4 patients between 6 and 28 weeks after the initial pancreatoduodenectomy (Gupta, Wig et al. 2008). In a report by Mistry and Durham, DCS was performed with a secondary pancreatoduodenectomy 30 hours later and the final reconstruction delayed until 10 weeks later. Pancreatic drainage was never re-established (Mistry and Durham 1996). In a study by Thompson and colleagues from Seattle 12 of 15 patients with severe pancreatoduodenal injuries underwent DCS with or without

the initial stage of a Whipple resection as their first operation (Thompson, Shalhub et al. 2013). The pancreatoduodenectomy was completed in two stages in eight patients (67%) and in three stages in four patients (33%). Two of the 12 died (17%) of bleeding and MOF. These studies show the usefulness of a staged procedure with initial damage control surgery followed by a delayed secondary pancreatoduodenectomy and reconstruction in critically injured patients with associated major injuries.

A further study from Cape Town evaluated the efficacy of damage control surgery and delayed pancreatoduodenectomy and reconstruction in patients who had combined severe pancreatic head and visceral venous injuries to assess optimal operative sequencing (Krige, Navsaria et al. 2016). During the 20-year study period, 312 patients were treated for pancreatic injuries of whom 14 underwent a pancreatoduodenectomy. Six of the 14 patients were *in extremis* with exsanguinating venous bleeding and non-reconstructable AAST grade 5 pancreatoduodenal injuries and underwent a damage control surgery followed by ICU transfer and physiological stabilisation and subsequent pancreatoduodenectomy and reconstruction when stable. All six patients had associated abdominal injuries with a mean of 3.3 (range 3-6) organs involved. All had non-reconstructable injuries of the head of the pancreas involving the main pancreatic duct, intra-pancreatic distal common bile duct with devitalisation and destruction of the blood supply or combinations of both. In addition all six patients had associated major visceral venous injuries with profuse retropancreatic bleeding due to portal vein, IVC, renal and lumbar vein injuries. Median time in ICU for continued resuscitation and physiological

stabilisation, before returning to the operation room, was 38 hours (range 11- 92 hours). During the second laparotomy five patients had a delayed pylorus preserving pancreatoduodenectomy and one patient who had a pancreatoduodenal injury which involved the pylorus and precluded pylorus preservation underwent a standard Whipple resection. Four of the six patients survived. Two patients died in hospital, one of MOF and coagulopathy and the other of intra-abdominal sepsis and multi-organ failure.

Most experts agree that in a critically injured patient who has received a massive blood transfusion and is haemodynamically unstable, hypothermic, coagulopathic and acidotic, prolonged and complex surgery is ill-advised and unlikely to have a satisfactory outcome. Under these adverse conditions, it is crucial to apply damage control principles and stage the procedure by truncating the initial operation and returning later to complete the resection in a favourable environment and a stable patient. In the USC Medical Centre series reporting 18 patients who had a pancreatoduodenectomy for trauma, 5 (28%) underwent initial damage control and staged reconstructive procedures. However no data or details are provided on the technique or timing of the reconstruction (Asensio, Petrone et al. 2003). In a two-centre retrospective study from Philadelphia and Columbus, Ohio, detailing 42 patients who had sustained pancreatic injuries and had DCS, 3 patients underwent a pancreatoduodenectomy, one during the DCS with delayed reconstruction, and 2 had a delayed pancreatoduodenectomy and reconstruction (Seamon, Kim et al. 2009). In a Seattle study 12 patients had DCS as their initial operation and the pancreatoduodenectomy performed in two stages in 8 patients and in three

stages in four patients. No information is provided regarding the timing of reconstruction (Thompson, Shalhub et al. 2013).

The effective treatment of complex pancreatic injuries associated with vascular damage continues to be a major challenge for surgeons dealing with abdominal trauma. The surgical decision to implement a damage control strategy is not regarded as a 'surgical retreat' but recognition that successful trauma surgery demands attention not only to the extent and magnitude of collective injuries sustained but also requires a careful assessment of the physiological status of the patient. It is important to identify the need for DCS at an early stage. Careful patient selection is crucial for survival and prolonged surgical procedures consciously avoided. The application of damage control has been substantially influenced by the evolution of trauma resuscitation practices and the identification of coagulopathy as a principal cause of death in exsanguinating trauma patients. It is essential to appreciate that a damage control approach can be used in smaller hospitals where experience with complex pancreatic and vascular injuries may be limited or where the necessary resources are not available. After control of bleeding and contamination the patient should be transferred to a major trauma centre where both trauma and HPB surgeons experienced in the management of proximal pancreatic resections and reconstruction are available (Krige, Thomson et al. 2013). The principles of DCS have now been used to reshape the practice of other civilian surgical subspecialties, military surgery, and trauma resuscitation itself (Chovanes, Cannon et al. 2012, Roberts, Ball et al. 2017).

CHAPTER 8

The evolution of the Whipple operation and the application of modifications to achieve optimal reconstruction methods after pancreatic head resection in trauma surgery

Elective resection of the head of the pancreas and the duodenum was first undertaken 119 years ago in Europe. In 1898 Alessandro Codivilla, an Italian surgeon from Modena, was the first surgeon to perform an *en bloc* resection of the pancreatic head, distal stomach, proximal duodenum and distal bile duct. The reconstruction after resection comprised a Roux-en-Y gastrojejunostomy and a cholecystojejunostomy with no anastomosis to the pancreatic remnant. The patient subsequently developed intractable diarrhoea and “died postoperatively of cachexia after 21 days”.

Shortly after Codivilla's procedure, Halsted at Johns Hopkins Hospital in Baltimore performed the first successful resection of an ampullary carcinoma. Using a transduodenal approach, Halsted resected a wedge of duodenum *en bloc* around an ampullary carcinoma including short segments of adjacent pancreatic and common bile ducts. The ducts were re-implanted into the reconstituted duodenum at the site of the primary duodenal closure. The patient survived the operation but died later that year from complications related to local recurrence of her cancer, suggesting that the operation failed to achieve clear margins.

The first successful resection of a peri-ampullary cancer was performed by the German surgeon Walther Kausch in 1909 and described by him in 1912.

Because the patient was severely malnourished and jaundiced, Kausch elected to perform a two stage procedure to minimize the surgical risk. In the first procedure he created a loop cholecystojejunostomy and a Braun anastomosis over Murphy buttons to relieve the jaundice. Two months later, Kausch completed the procedure by performing an *en bloc* distal gastrectomy, proximal duodenectomy, and partial pancreatic head resection followed by a loop gastrojejunostomy and end-to-end pancreatoduodenostomy. The patient lived for 9 months before dying of cholangitis.

Although Alessandro Codivilla in Italy and Walther Kausch in Germany had each performed a partial pancreatoduodenectomy decades before, Whipple's presentation at the American Surgical Association meeting in 1935 of 3 patients who underwent a two-stage operation and his successful performance of a one-stage pancreatoduodenectomy 5 years later established the procedure in mainstream surgery. The details of this seminal surgical development by Whipple, Parsons and Mullins at the Columbia-Presbyterian Medical Center in New York were published in a report entitled "Treatment of Carcinoma of the Ampulla of Vater" in 1935 which described the operative procedure. This two-stage operation for the radical resection of periampullary cancers consisted of an initial cholecystogastrostomy and a posterior loop gastrojejunostomy followed later by a partial duodenectomy, partial pancreatic head resection and pancreatic stump occlusion. This was the first report of a complete excision of the duodenum and the head of the pancreas. The first patient died 30 hours after the operation due to an anastomotic breakdown. The second and third patients lived for 9 and 24 months and died of cholangitis and liver metastases.

In 1940 Whipple performed the first successful single-stage pancreatoduodenectomy for a non-functioning islet cell carcinoma. The resection included the distal stomach, the entire duodenum and the pancreatic head and was reconstructed using a loop gastrojejunostomy and choledochojejunostomy. The patient recovered uneventfully and died 9 years later of metastatic disease

A few weeks later in 1940, Trimble from Johns Hopkins Hospital in Baltimore, unaware of the procedure by Whipple in New York, performed a similar one-stage radical resection. Trimble added a distal gastrectomy to avoid a blow-out of the duodenal stump. Later in 1940 Hunt added a pancreatojejunostomy to prevent a leakage from the pancreatic stump.

Whipple had previously specifically avoided a pancreatic anastomosis and had closed the pancreatic stump to avoid serious anastomosis-related complications. In 1942 he further refined his technique and incorporated an end-to-side pancreatojejunostomy using a duct-to-mucosa technique. Whipple described his procedure as follows:

“(I) At least two days of vitamin K and bile salts therapy; (II) the distal half of the stomach, the entire duodenum, the terminal portion of the common duct and the head of the pancreas were removed en masse; (III) a vertical limb of the jejunum, starting at the duodenojejunal junction, was brought up through a rent in the mesocolon, behind the colon, with the following anastomoses in sequence: (i) a choledochojejunostomy, end-to-end; (ii) an anastomosis between the pancreatic duct and the wall of the jejunal opening the size of the pancreatic duct, followed by the tacking of the stump of the resected pancreas to the wall of the jejunum; (iii) an end-to-side gastrojejunostomy. A sump drain in the bed of the duodenum was used. Silk technic was employed throughout.”

In 1946 Whipple published his 10-year experience of radical excision of the head of pancreas and duodenum in which he proposed several modifications to his original operation and advocated a one-stage procedure. By the end of his career, Whipple had performed 37 pancreatoduodenectomies with a total mortality rate of approximately 33%. Whipple originally used the anastomotic sequence of bile duct, pancreas and then stomach, whereas currently the most widely used method of reconstruction is the sequence of pancreas, bile duct and stomach, also known as Child's operation.

Subsequent improvements in operative technique and perioperative care contributed to making a pancreatoduodenectomy a safe operation that continues to evolve. The "Whipple procedure" which included resection of the gastric antrum remained the standard operative technique for carcinomas of the head of the pancreas until Traverso and Longmire from UCLA in Los Angeles reintroduced the concept of pylorus preservation in 1978 to reduce the incidence of postgastrectomy syndrome and marginal ulceration. Pylorus-preserving pancreatoduodenectomy (PPPD) had originally been described by Kenneth Watson in England in 1944 and consisted of a resection similar to Whipple's original two-stage procedure but with retention of the gastric antrum and a reconstruction that used an end-to-end duodenojejunostomy rather than a loop gastrojejunostomy. Traverso and Longmire's PPPD, which was constructed with an end-to-side duodenojejunostomy, became popular because the procedure was simpler with reduced operative times, and by preserving the distal stomach and the pyloric sphincter, gastrectomy-related complications were perceived to be reduced. There has been controversy which is the

superior operation and studies comparing the two procedures have been inconsistent and contradictory. A systematic review and meta-analysis of randomized, controlled trials comparing PPPD to classical PD which included 27 studies and a total of 2,599 patients suggested that PPPD has less blood loss and a shorter operative time, but the two procedures are otherwise equivalent in terms of mortality, morbidity and survival.

In contrast to the exponential progress in the early 1940s during the development of pancreatic head resections, limited improvement occurred during the next 40 years, and mortality rates of 20 to 40%, morbidity rates between 40 and 60%, and poor 5-year survival rates persisted.

Optimal reconstruction and drainage of the pancreatic stump after a pancreatoduodenectomy is a crucial factor in preventing postoperative complications as a major leak from the pancreatic anastomosis results in substantial morbidity and contributes to prolonged hospitalization and mortality. Post-operative complications included sepsis, intra-abdominal abscesses, delayed gastric emptying, pancreatic and biliary fistulae and bleeding due to false aneurysms of the gastroduodenal artery stump, which were generally attributed to the "Achilles' heel" of the procedure, leakage at the pancreatic anastomosis (Are, Dhir et al. 2011). Several techniques have been described for reconstruction of pancreatic continuity to minimize the risk of a pancreatic fistula. Most surgeons join the pancreatic stump to jejunum using an end-to-side anastomosis over a plastic stent. A pancreatic leak occurs in about 15% of operations; 70% resolve with conservative management, which includes adequate control of the fistula with drains, enteral feeding and antibiotics if

necessary. To decrease pancreatic secretions, octreotide has been recommended, but multi-institutional trials have shown that it is of limited use (Zenilman 2000).

Considerable attention has been focused on decreasing the incidence of pancreatic fistula. These efforts have encompassed technical considerations: modification of the pancreatojejunal anastomosis technique (PJ), reconstruction with pancreatogastrostomy (PG), and placement of pancreatic duct stents. Risk factors for pancreatic fistula included a soft pancreas, a small pancreatic duct, the underlying pathology, reduced regional blood supply, and the surgeon's experience (Fernandez-Cruz, Belli et al. 2011). In the search for a safer method, pancreatogastrostomy has been shown to be a viable alternative. There are two main advantages of pancreatogastrostomy. The anastomosis is easy to perform, especially after preservation of the stomach using the pylorus-preserving pancreatic resection. The close proximity of the pancreatic remnant to the posterior gastric wall allows a wide, tension-free anastomosis with adequate tissue to "telescope" the stump into the stomach. In addition, the acidic environment of the stomach inhibits activation of pancreatic enzymes. Waugh and Clagett first proposed joining the pancreatic remnant to the stomach in 1946 and, to date, data on 841 patients have been reported in the literature. Techniques have varied and Mackie proposed performing a pancreatogastrostomy after a partial gastrectomy to give a direct view and easy access to the intragastric anastomosis while others have advocated the use of an anterior gastrotomy to facilitate the anastomosis. Most surgeons agree that

the anastomosis can be done from outside the posterior gastric wall similar to a standard enteric anastomosis.

A systematic review and meta-analysis of randomized controlled trials (RCTs) by Guerrini et al compared patients with pancreatogastrostomy (PG group) to pancreatojejunostomy (PJ group). The meta-analysis assessed eight RCTs and included 1,211 patients. The analysis showed that the PG group had a significantly lower incidence rate of postoperative pancreatic fistulas [OR 0.64 (95% CI 0.46–0.86), $p=0.003$], intra-abdominal abscesses [OR 0.53 (95% CI 0.33–0.85), $p=0.009$] and length of hospital stay [MD–1.62; (95% CI 2.63–0.61), $p=0.002$] than the PJ group, while biliary fistula, mortality, morbidity, rate of delayed gastric emptying, reoperation, and bleeding did not differ between the two groups. This meta-analysis suggested that the most effective treatment for reconstruction of pancreatic continuity after a pancreateoduodenectomy is a pancreatogastrostomy (Guerrini, Soliani et al. 2016).

The main criticism of these studies has been that the analysis of outcome did not consider the various modifications of the PG or PJ techniques to allow valid comparison as there are several different methods of pancreatojejunostomy reconstruction including a two-layer duct to mucosa anastomosis, single-layer end-to-side anastomosis or an invagination pancreatojejunostomy. The lack of a uniform technique is also found when performing PG as the different techniques include telescoping the pancreas through the gastric stump, an anterior-wall gastrotomy or a duct-to-mucosa anastomosis (Fernandez-Cruz, Belli et al. 2011). The authors concluded that there is no universal consensus indicating that one particular type of pancreatic anastomosis is safer and less likely to

pancreatic leakage than any other. In addition, there was a lack of proper stratification in the studies of the risk of a pancreatic fistula in most RCTs. The authors concluded that further studies were needed to define the optimal technique for pancreatic reconstruction after PD and that future trials should be conducted in high-volume centres by high-volume surgeons, with attention to the definition of a pancreatic fistula. Future trials should employ standardized technical methods and proper pancreatic fistula risk stratification (Tewari, Hazrah et al. 2010).

When choosing between the available methods for reconstruction of pancreatocenteric continuity the outcomes to be considered are the ease of the operation, the incidence of postoperative complications and the long-term effects and consequences. An anastomosis between the pancreas and the stomach is technically easier as the stomach holds sutures better and there is lesser tension on the anastomosis as the pancreas is anatomically closer to stomach compared to the jejunum. In addition, the stomach has a thicker wall, a wider lumen and better blood supply which makes operative handling easier compared to the smaller lumen and less secure blood supply of the jejunum. A pancreatogastrostomy also reduces the number of anastomoses to the jejunum, thereby decreasing the likelihood of loop kinking. While the Canadian authors concluded that pancreatogastrostomy was safer, they cautioned that much of the evidence comes from observational cohort study data (McKay, Mackenzie et al. 2006).

Similarly, Wente and colleagues from Heidelberg in Germany also performed a meta-analysis on 16 articles published until end of March 2006 comparing PJ

and PG after PD. Results of 3 RCTs showed no significant differences between PJ and PG considering overall postoperative complications, pancreatic fistula rates, intra-abdominal fluid collections or mortality. While analysis of 13 non-randomized observational clinical studies showed significant results in favour of pancreatogastrostomy with decreased rates of pancreatic fistula and mortality the authors concluded that both PJ and PG were equally good methods of pancreatic drainage and caution that the observational studies have a publication bias (Wente, Shrikhande et al. 2007).

Both these meta-analyses highlight the particular importance of performing well-designed RCTs and the role of evidence-based medicine in guiding modern surgical practice. This is relevant because technical difficulties resecting and reconstructing complex pancreatic injuries require special surgical skills and expertise and clearly the optimal methods should be used in high risk situations. While most of the comparative data are derived from elective pancreatic resections completed under favourable conditions, few publications have specifically assessed the technical aspects of reconstruction after emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum. In the first study to evaluate this question, Delcore and associates from the University of Kansas Medical Center in Kansas City reviewed the records of all patients undergoing pancreatogastrostomy after pancreatoduodenal resection for trauma (Delcore, Stauffer et al. 1994). Five patients with a mean age of 26 years (range, 20-32 years) and severe penetrating (n=3) or blunt (n=2) traumatic injuries have required pancreatoduodenectomy followed by pancreatogastrostomy (n=4) or pancreatogastrostomy alone (n=1) since 1975.

Their mean Trauma Score was 12 (range, 9-16) and all five patients had soft, previously normal pancreatic glands without induration or ductal dilatation. The mean duration of surgery was 6 hours (range, 5-7 hours), mean blood loss was 7200 mL (range, 1,000-17,500 mL), mean transfusion requirements were 14 units of blood (range, 2-32 units), and mean hospital stay was 37 days (range, 11-90 days). Two patients developed right upper quadrant abscesses that required a second procedure. There were no pancreatic anastomotic leaks, fistulas, or other complications related to the pancreatogastrostomy. All five patients were well without endocrine or exocrine pancreatic insufficiency after a mean follow-up of 4 years (range, 1-9 months). Pancreatogastrostomy following pancreatoduodenectomy for trauma had not been reported prior to this study. The experience by Delcore showed that pancreatogastrostomy was a safe method for reconstruction of the pancreatic remnant after a pancreatoduodenectomy for trauma. These results suggested that pancreatogastrostomy had several advantages over pancreatojejunostomy for restoring pancreato-intestinal continuity in trauma patients.

Support for a pancreatogastrostomy is provided by a study from Durban by Chinnery, Thomson and colleagues in which seven patients who had sustained blunt abdominal trauma with resultant isolated main pancreatic duct injuries which were managed by drainage of the distal pancreas into either stomach (n=5) or jejunum (n=2). One patient developed an amylase-rich low output fistula which resolved with conservative management. The authors argue that in a stable patient with an isolated main pancreatic duct injury drainage of the distal pancreas into stomach or jejunum is a viable option and simpler to

perform than a distal pancreatectomy with splenic preservation. Furthermore, it has the advantage of pancreatic tissue and spleen preservation and a low fistula rate. The authors believe pancreatogastrostomy is the easier to perform and prefer to fashion pancreatogastrostomy in trauma patients because the stomach is close by and requires no specific preparation, the stomach is well vascularised and as such may aid healing, the anastomosis is easily accomplished, and there is one less anastomosis to perform than in a Roux en Y pancreatojejunostomy (Chinnery, Thomson et al. 2008).

The fundamental steps in a pancreatoduodenectomy for trauma have been elucidated in detail by Krige and Thomson (Krige and Thomson 2016). The key technical risk factors, as in elective resections, are the pancreatic and biliary anastomoses. In the largest and most detailed study to evaluate outcome of pancreatic, biliary and gastric reconstruction methods after a pancreatoduodenectomy for severe pancreatic injuries in a cohort of consecutive patients treated at a level I academic trauma centre, Krige and Thomson evaluated the optimal reconstruction methods in 20 patients who had a pancreatoduodenectomy. This analysis describes for the first time how techniques for pancreatic, biliary and gastric anastomoses need to be modified for reconstruction after a pancreatoduodenectomy for trauma. Unlike other reported series, a unique aspect of this study was the capability of doing a pylorus-preserving pancreatoduodenectomy in those injured patients in whom the pylorus was intact. Two immediate advantages of using a pylorus-preserving pancreatoduodenectomy in this study were that retention of the stomach allowed the full posterior gastric wall to be accessible for a

pancreatogastrostomy and the modified Imanaga sequence of reconstruction allowed postoperative endoscopic access through the duodenojejunal anastomosis to the biliary system for retrieval of biliary stents and balloon enhanced cholangiography which was important in patients who had an associated bile leak due to collateral damage to the liver. In this study a pylorus-preserving pancreatoduodenectomy (PPPD) was undertaken in all patients in whom the injury had not irretrievably damaged the pylorus. In those requiring a gastric resection a classic Whipple resection was done. The end-to-side pancreatojejunostomy was constructed and stented internally with a 5Fr silastic paediatric feeding tube cut to size. In patients in whom the jejunum was grossly oedematous after prolonged resuscitation and unsuitable for an anastomosis, the pancreatic remnant was drained into the stomach. In this study 13 patients had a PPPD and seven a standard Whipples resection while eight had a pancreatogastrostomy and in 12 patients an end-to-side pancreatojejunostomy was fashioned (Krige 2016).

An end-to-side hepaticojejunostomy, using the high bile duct reconstruction technique with preplaced sutures is regarded as the gold standard for elective restoration of biliary-enteric continuity. Similar to the gastric and the pancreatic reconstruction, the biliary anastomosis is complex after a pancreatoduodenectomy for trauma because of the unfavourable circumstances. The major risk factors for bile leaks and ultimately biliary strictures are the size of the bile duct and the adequacy of the blood supply of the bile duct. Both these factors are relevant after a pancreatoduodenectomy for trauma. "Skinny" ducts have been shown to result in bile leaks in 4% of

elective pancreatoduodenal reconstructions. In this study the biliary anastomosis was a modification of the standard method used for bile duct reconstruction after iatrogenic injuries. Small size was a universal feature in this study which required a modified approach and biliary stenting. In this study the operative technique of biliary reconstruction spatulated the duct to increase the anastomotic size by using an anteriorvertical incision positioned to avoid damaging the 3 and 9 o'clock bile duct arteries. All biliary anastomoses were stented with a 5Fr silastic paediatric feeding tube. In situations where the bile duct measured less than 3mm in width and gross oedema jeopardised the bile duct to jejunum anastomosis, the gall bladder was preserved and used as the conduit for the biliary-enteric anastomosis. In high-risk stented biliary anastomoses a modified Imanaga reconstruction technique was used in which the duodenojejunostomy was created end-to-side as the most proximal jejunal anastomosis to allow post-operative endoscopic cholangiography and biliary stent retrieval (Krige 2016).

As in elective resections, the pancreatic anastomosis following a pancreatoduodenectomy for trauma is the weakest link and pancreatic anastomotic failure is the most important factor responsible for the substantial postoperative morbidity and mortality. Even under elective circumstances the fistula rate is appreciable and is highest in those with a soft pancreas and a small duct. These risk factors pertain in the trauma situation and are compounded by a pancreas that is damaged and oedematous, as well as an oedematous bowel wall, making the situation even more unfavourable for a successful anastomosis. The elective operative techniques need to be adapted

to the prevailing operative circumstances. In this study the solution to overcoming these considerable technical difficulties was to use a stented single layer interrupted anastomosis with a pancreatic leak rate of 30% in survivors. A pancreatogastrostomy was used in this study when profound shock, prolonged resuscitation and major vascular injuries resulted in an oedematous jejunum which jeopardised the anastomosis. Under these adverse circumstances there are several cogent practical and technical reasons for doing a pancreatogastrostomy in preference to a pancreatojejunostomy. Current evidence suggests that it is technically more important to identify the subgroup of patients who may benefit from a specific technique rather than pursue a universal technique and attempt a “one size fits all” methodology (Krige 2016).

CHAPTER 9

Development and validation of a pancreatic injury mortality score (PIMS) based on 473 consecutive patients treated at a Level 1 Trauma centre

9.1 Introduction

Trauma has become a major burden in global health and is now the leading cause of death worldwide in people less than 40 years old. The pancreas is the least injured of the intra-abdominal solid organs but may result in considerable morbidity and mortality if the injury is incorrectly assessed or inadequately treated (Krige, Kotze et al. 2016, Krige, Kotze et al. 2016). The pancreas is seldom injured in isolation and in-hospital mortality is usually related to the cumulative effect of all the injured organs (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005, Subramanian, Dente et al. 2007). Major pancreatic injuries are often associated with severe vascular injuries with lethal consequences, due to the close proximity of the pancreas to adjacent large visceral vessels (Kao, Bulger et al. 2003, Wang, Li et al. 2007, Heuer, Hussmann et al. 2013). Most early deaths are thus caused by either exsanguination or refractory coagulopathy or the consequences of massive blood transfusions after associated vascular or adjacent solid organ injuries (Sorrentino, Moore et al. 2012). Two-thirds of patients who survive more than 48 hours have major complications as a result of the pancreatic and associated injuries. One third of patients who die later, do so because of intra-

abdominal or systemic septic complications or multi-organ failure (Heuer, Hussmann et al. 2011).

Previous reports have emphasized that outcome is influenced primarily by the cause and complexity of the initial pancreatic injury, the number and severity of associated vascular and visceral injuries, the duration of shock, the quality and nature of surgical intervention and secondarily by complications related to the degree of pancreatic duct injury and the extent of intra-abdominal sepsis (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Wang, Li et al. 2007, Hwang and Choi 2008, Heuer, Hussmann et al. 2011, Chinnery, Krige et al. 2012, Sorrentino, Moore et al. 2012, Heuer, Hussmann et al. 2013). At present there is no consensus regarding the specific risk factors which predict mortality after a major pancreatic injury. Published results are variable and conflicting because of small sample sizes, referral bias, dissimilar study endpoints and differences in patient selection. In addition, the wide spectrum of the different variables in pancreatic injuries complicate the formulation of a prognostic model. To overcome these complexities, a large database is required which includes both the dependent and independent variables for each patient. Our unit has previously reported results of pancreatic injuries and has a large established prospective database of patients with pancreatic injuries containing sufficient detailed granular information to address specific clinical questions (Krige, Kotze et al. 2011, Krige, Nicol et al. 2014, Krige, Kotze et al. 2015, Krige, Kotze et al. 2016, Krige, Navsaria et al. 2016, Krige, Kotze et al. 2017).

The objective of the present study was to develop a pancreatic injury mortality score (PIMS) using readily available and clinically relevant data in order to

predict the likelihood of death in patients who had sustained a major pancreatic injury. We hypothesized that incorporating these data which have a substantial influence on survival in an outcome prediction model would show improved predictive accuracy. In this context, we used prospectively collected data from a large cohort of consecutive patients and applied multivariate analysis and internal validation using robust and reliable methodology with objective and reproducible end-points to create a simple but comprehensive survival prediction model for individual patients after a major pancreatic injury.

9.2 Methods

9.2.1 Study design and patient population

The study process involved data retrieval from an existing faculty approved and registered database, which since inception has prospectively documented the details of all patients who had sustained pancreatic injuries and were treated in the Level 1 Trauma Centre and the Hepatopancreatobiliary and Surgical Gastroenterology units in Groote Schuur Hospital, Cape Town. The analysis included consecutive patients who had a pancreatic injury and were treated between January 1990 and December 2015. The study was approved by the University of Cape Town Ethics and Research Committee.

9.2.2 Data collection

All information abstracted from clinical records was recorded on hard copy using a systematically prepared data form and entered into a Microsoft computer programme after data affirmation and validation by a senior study surgeon. Comprehensive details of database documentation, definitions,

management and the operative strategy for pancreatic injuries including pancreatoduodenectomy, distal resection, combined pancreatoduodenal injuries, damage control and non-resection have been published (Krige, Kotze et al. 2011, Krige, Nicol et al. 2014, Krige, Kotze et al. 2015, Krige, Kotze et al. 2016, Krige, Navsaria et al. 2016, Krige, Kotze et al. 2017). The duration of hospital and ICU stay are given in days. The primary outcome was in-hospital all cause mortality. Mortality was defined as any cause of death in hospital.

9.2.3 Statistical analyses

The data was analysed according to methods used by Thomas Lee *et al.* to derive and validate the revised cardiac risk score (Lee, Marcantonio et al. 1999). Two-thirds of the 473 patients in the pancreatic database were assigned to the derivation cohort (n=315), which was used to develop the PIMS. One third of the patients were assigned to the validation cohort (n=157). Clinical correlates of in-hospital death were identified with a χ^2 test for categorical variables and a t test or Wilcoxon test for continuous variables. Variables with a univariate correlation with a P value 0.10 were considered in stepwise logistic regression analyses that identified the factors included in the risk index, with a cutoff P value of 0.05. In order to derive a simple and user-friendly model, we compared 2 versions of the PIMS: one in which weights were derived from the original logistic regression analysis (original model) and one in which all variables were assigned weights that were rounded off to derive a user-friendly score (simple model). After each variable addition to models, the change of the risk estimates and their associated standard errors were reviewed to screen for collinearity and a Wald test was performed to assess for significant interaction

between variables. The performance and discriminative ability of the constructed models to predict mortality was assessed using receiver operating characteristic (ROC) analysis. The prediction accuracy was quantified using the concordance index (C-index), which is equivalent to the area under the ROC curve and reflects the ability of a model to discriminate participants who develop the event of interest (i.e. death) from those who do not. Values range from 0.5 to 1; a value of 1 is indicative of a model with perfect predictive power. Because ROC analyses did not show an advantage for the index using the exact weights defined by the logistic regression analysis, the index with the simpler algorithm was adopted to derive the new PIMS.

The derived scoring algorithm was then applied to the validation dataset and logistic regression was repeated using PIMS to predict in-hospital mortality. An ROC analysis was used to compare the discriminatory performance of PIMS in the derivation and validation datasets. Furthermore, cut-off values for the PIMS were used to define 3 risk groups in the derivation dataset: low, medium and high risk of death. These cut-off values were applied to the validation dataset and the mortality rate within each group was compared ($p < 0.05$).

9.3 Results

9.3.1 Patient demographics

Four hundred and seventy three consecutive patients (median age 26, range 13–73 years) were treated for pancreatic injuries of whom 432 (91.3%) were men (Table 1). Two hundred and eighty nine patients (61.1%) were stable on

admission with a Revised Trauma Score (RTS) of 7.8. Penetrating injuries accounted for 72.9% of all injuries (Table 1).

9.3.2 Anatomic site and severity of injury

Proximal pancreatic injuries occurred in 160 (33.8%) patients involving the pancreatic head or uncinate process (n=128) or pancreatic neck (n=32). The body and tail of the pancreas were injured in 313 patients (Table 1). American Association for the Study of Trauma (AAST) grade 1 or 2 pancreatic injuries occurred in 243 (51.4%) patients, while 230 injuries were AAST grade 3, 4 or 5.

9.3.3 Associated injuries

Fifty-four patients (11.4%) had an isolated pancreatic injury (Table 1). Of the remaining 419 patients, 244 (51.6%) had one or two associated abdominal organ injuries while 174 (37%) had three or more associated intra-abdominal injuries.

Table 1 Clinical data of 473 patients with pancreatic trauma

	Total n=473	Blunt injuries n=128 27.1%	Gunshot wounds n=258 54.5%	Stab injuries n=87 18.4%
Male	432	109 (85.2%)	243 (94.2%)	80 (92%)
Female	41	19 (14.8%)	15 (5.8%)	7 (8%)
Age				
Median (range)	26 (13-73)	30 (13-73)	26 (14-69)	26 (16-62)
Revised Trauma Score				
< 7.8	184	50 (39.1%)	111 (43%)	23 (26.4%)
7.8	289	78 (60.9%)	147 (57%)	64 (73.6%)
Shock on admission	175	44 (34.4%)	108 (41.9%)	23 (26.4%)
Patients transfused	317	83 (85.2%)	195 (75.6%)	39 (44.8%)
Blood transfusion				
Median units (Range)	7 (1-124)	6 (1-82)	8 (1-124)	7 (1-20)
Damage Control Surgery	84	15 (11.7%)	65 (25.2%)	4 (4.6%)
Pancreatic Injury Site				
Head of pancreas	128	20 (15.6%)	79 (30.6%)	29 (33.3%)
Neck of pancreas	32	21 (16.4%)	9 (3.5%)	2 (2.3%)
Body of pancreas	179	54 (42.2%)	85 (32.9%)	40 (46%)
Tail of pancreas	134	33 (25.8%)	85 (32.9%)	16 (18.4%)
Associated Abdominal Injuries				
Nil (isolated injury)	54	47 (36.7%)	2 (0.8%)	5 (5.7%)
1 or 2 organs injured	244	70 (54.7%)	109 (42.2%)	65 (74.7%)
3 or more injured	175	11 (8.6%)	147 (57%)	17 (19.5%)
Outcome				
Died	72	18 (14.1%)	50 (19.4%)	4 (4.6%)

9.3.4 Surgery and outcome

Overall 149 (31.5%) patients had a primary pancreatic resection, 21 had a pancreatoduodenectomy, 111 a distal pancreatectomy and splenectomy, and 17 a spleen-preserving distal pancreatectomy. Three hundred patients (63.4%) had non-resectional surgical intervention (placement of a pancreatic drain, suture or packing). Eighty-four patients (17.8%) with complex injuries had an initial damage control procedure, most of whom (n=65, 77.4%) had sustained single or multiple GSWs. Sixty-five (77.4%) patients were shocked on admission and vascular injuries were present in 43 (51.2%). Overall 140 patients (29.6%) required a relook laparotomy (median n=1, range 1-11). Seventy-two (15.2%) of the 473 patients died (Table 1). Twenty-one (14.1%) of the 149 patients who had a pancreatic resection died [pancreatoduodenectomy n=4/21, (19%), distal pancreatectomy n=17/128, (13.3%)]

9.3.5 Derivation and validation of the PIMS

The patients in the derivation and validation cohorts were comparable (Table 2). Some differences included that patients in the validation cohort were younger and a greater proportion of patients were shocked on admission, sustained a blunt MVA mechanism of injury and had associated lung or liver injuries. Patients in the derivation dataset on the other hand had a greater proportion of males, with blunt assault or GSWs, and a greater proportion of colon, jejunal, kidney and vascular injuries.

Factors that correlated with in-hospital death in the derivation dataset included age, revised trauma score, shock on arrival, associated colon, duodenal, ileal

and vascular injuries, number of associated injuries, injury to the head of the pancreas and the pancreatic AAST score (Table 2). The result of the final multivariate logistic regression model built to predict in-hospital death in the derivation dataset is shown in Table 3.

Table 2 Comparison of the derivation and validation datasets

	Derivation n (%)	Validation n (%)	Relative risk for death and 95% CIs in derivation cohort	P-Value
Age>55	11 (3.49)	2 (1.27)	5.1 (1.66 - 15.66)	<0.0001
Male sex	290 (92.06)	141 (89.81)	1.3 (0.50 - 3.49)	NS
Median RTS (IQR)	7.8 (7.1 - 7.8)	7.8 (7.1 - 7.8)	0.46 (0.36 - 0.58)	<0.0001
Shock on arrival	121 (38.41)	53 (33.76)	11.25 (5.94 - 21.30)	<0.0001
<i>Mechanism of injury</i>				
Blunt assault	29 (9.21)	14 (8.92)		
Blunt MVA driver	12 (3.81)	4 (2.55)		
Blunt MVA passenger	11 (3.49)	1 (0.64)	0.83 (0.42 - 1.62)	NS
Blunt MVA pedestrian	22 (6.98)	16 (10.19)		
Penetrating GSW	175 (55.56)	83 (52.87)		
Penetrating knife	55 (17.46)	32 (20.38)		
<i>Associated abdominal injuries</i>				
Colon	79 (25.08)	31 (19.75)	2.72 (1.47 - 5.02)	<0.001
Duodenum	60 (19.05)	27 (17.20)	1.85 (0.94 - 3.63)	<0.1
Gallbladder	10 (3.17)	7 (4.46)	2.13 (0.53 - 8.53)	NS
Ileum	14 (4.44)	3 (1.91)	10.24 (3.28 - 31.96)	<0.001
Jejunum	39 (12.38)	17 (10.83)	1.29 (0.56 - 2.99)	NS
Kidney	83 (26.35)	34 (21.66)	0.87 (0.44 - 1.71)	NS
Liver	136 (43.17)	76 (48.41)	1.39 (0.78 - 2.51)	NS
Spleen	78 (24.76)	41 (26.11)	1.08 (0.61 - 1.9)	NS
Stomach	126 (40.0)	64 (40.76)	0.93 (0.56 - 1.56)	NS
Vascular injuries	65 (20.63)	25 (15.92)	6.92 (4.01 - 11.94)	<0.0001
<i>Number of associated abdominal injuries</i>				
None	39 (12.38)	21 (13.38)		
One	82 (26.03)	43 (27.39)	1.29 (1.02 - 1.75)	<0.1

Two	95 (30.16)	43 (27.39)		
Three or more	99 (31.43)	50 (31.85)		
Location of injury				
Tail	96 (30.48)	51 (32.48)	Reference	
Body and tail	26 (8.25)	14 (8.92)	1.17 (0.4 - 3.41)	NS
Body	96 (30.48)	43 (27.39)	1.54 (0.77 - 3.07)	NS
Head	77 (24.44)	37 (23.57)	2.41 (1.23 - (4.77)	<0.001
Neck	20 (6.35)	12 (7.64)	0.85 (0.23 - 3.09)	NS
AAST pancreatic injury scale				
1	87 (27.62)	51 (32.48)	Reference	
2	66 (20.95)	38 (24.2)	1.83 (0.77 - 4.35)	<0.01
3	119 (37.78)	50 (31.85)	2.22 (1.03 - 4.8)	<0.1
4	21 (6.67)	8 (5.1)	5.76 (2.08 - 15.92)	<0.01
5	22 (6.98)	10 (6.37)	11.29 (4.38 - 29.11)	<0.001
Died	54 (17.14)	18 (11.46)		

RTS: Revised Trauma Score

MVA: Motor Vehicle Accident

GSW: Gunshot Wound

AAST: American Association for the Study of Trauma

Table 3 Multivariate model used to derive the PIMS

Multivariate model	Odds ratio	95% CI	P-Value
Age > 55 years	7.24	2.57 - 36.92	0.001
Shock on admission	6.81	4.29 - 17.23	<0.001
Associated vascular injury	2.48	1.24 - 4.96	0.01
Number of associated injuries	1.28	1.01 - 1.62	0.04
AAST pancreatic injury scale	1.49	1.16 - 1.93	0.002

AAST: American Association for the Study of Trauma

The resultant PIMS relies on five variables, namely age greater than 55, presence or absence of shock on admission, presence or absence of a vascular injury, number of associated injuries and the pancreatic AAST. The discriminatory ability of the original model to predict an in-hospital death compared to the simple model was no different ($p= 0.15$) (Figure 1). The simple model with user-friendly weightings was therefore adopted and the scoring rubric for the PIMS is shown in Table 4.

Figure 1 Comparison of the discriminatory ability of the original and simple models to predict an in-hospital death

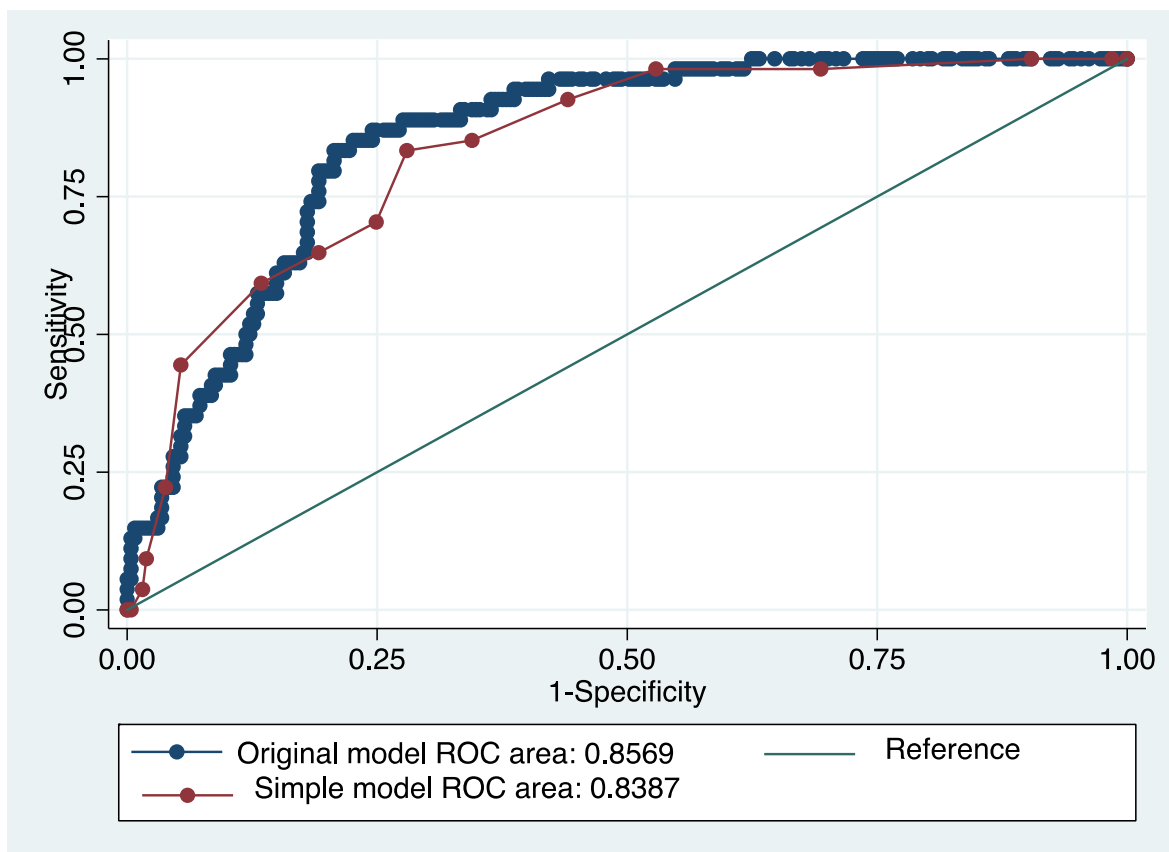


Table 4 Scoring rubric for the Pancreatic Injury Mortality Score (PIMS)

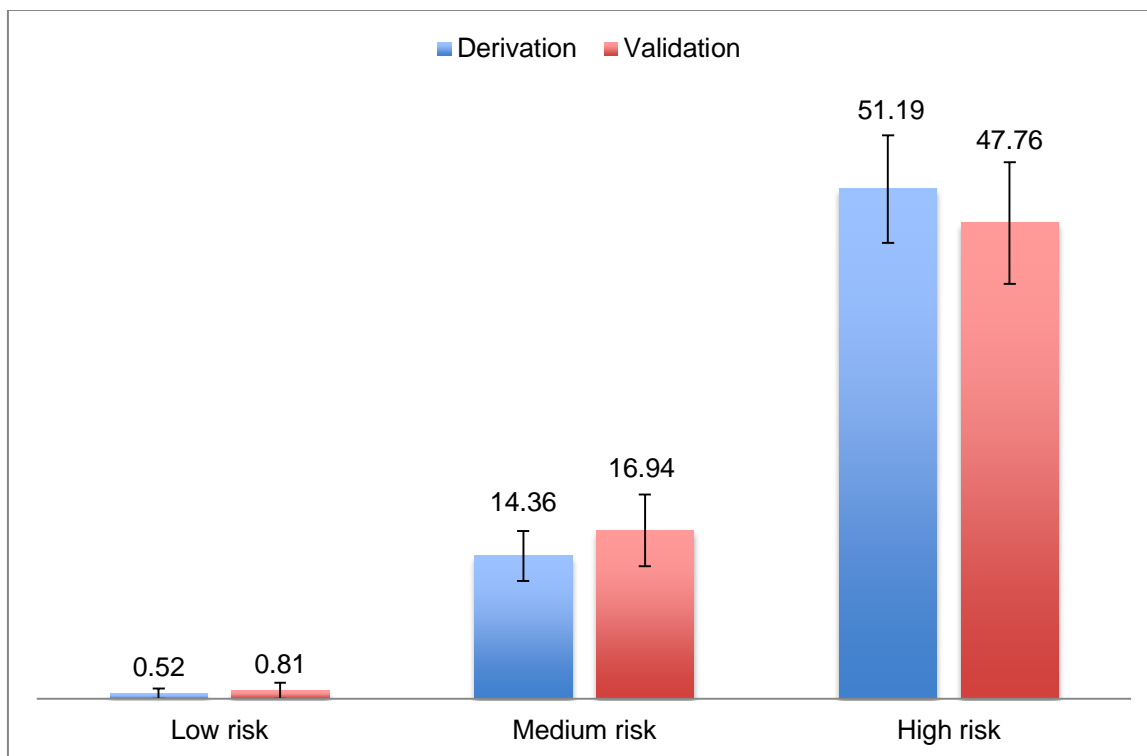
Age>55 years	
Yes	5
No	0
Shocked	
Yes	5
No	0
Major vascular injury	
Yes	2
No	0
Number of associated abdominal injuries	
None	0
One	1
Two	2
3 or more	3
AAST pancreatic injury scale	
I	1
II	2
III	3
IV	4
V	5
Total Score	/20

AAST: American Association for the Study of Trauma

The score ranges from 0 to 20, with higher scores indicating patients at higher risk of in-hospital death after a pancreatic injury. The ROC of the final score in the derivation dataset was 0.84 (95% CI 0.79 – 0.89) and in the validation dataset was 0.91 (95% CI 0.84 – 0.97), which were comparable (p= 0.1). Finally, cut-off scores were used to generate three risk groups and the rate of mortality in the low (PIMS 0-4), medium (PIMS 5-9), and high risk (PIMS 10–20)

groups was 0.52%, 14.36% and 51.19%, and 0.81%, 16.94% and 47.76% in the derivation and validation datasets, respectively. These mortality rates were not significantly different as seen in Figure 2.

Figure 2 Mortality rate by PIMS risk group in the derivation and validation datasets



Because the dataset spans 25 years and management of these injuries may have improved over time, it was necessary to establish whether the date of injury was associated with the primary outcome of death. In order to do this the cohort was divided into injuries which occurred before (n=261) and after (n=212) 1 January 2000. In the univariate screen, this clustering did not have a significant association with in-hospital death ($p=0.39$). Furthermore it was necessary to test the performance of PIMS within these two time periods. The ROC of the PIMS in the time period before 2000 was 0.87 (95% CI 0.82-0.92)

and after 2000 was 0.8 (95%CI 0.72-0.88), which were comparable ($p=0.14$). Date of injury was therefore not associated with in-hospital death and PIMS discriminated equally well before and after the year 2000.

9.4 Discussion

Prognostic studies have an important role in the management and analysis of complex trauma and contribute to the provision of improved definitions of enrolment criteria and a better classification of severity based on prognostic risk thus improving stratification (Gomez, de-la-Cruz et al. 2014). Despite a plethora of papers on pancreatic trauma, few have specifically assessed factors predictive of death. The present study is, to our knowledge, the first to create a user friendly injury score to identify a high risk mortality group of patients with pancreatic trauma. This study identified five variables; age greater than 55 years, the presence of a vascular injury, shock on admission to hospital, the number of associated injuries and the pancreatic AAST score as predictors of mortality in patients with major pancreatic injuries. These variables allowed the development of a PIMS. Cut-off scores were used to calculate low, medium and high-risk mortality categories, which are relevant for internal or external benchmarking and quality improvement audits.

Previous publications indicate that morbidity is increased in patients who have severe pancreatic injuries (AAST grades 3-5), combined with other injuries, a delay of more than 24 hours in establishing the diagnosis and unsatisfactory or ineffective initial treatment (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Wang, Li et al. 2007, Hwang and Choi 2008, Antonacci, Di Saverio et al. 2011). A previous study from our unit of 219 civilian pancreatic gunshot injuries

found that age, shock on admission, need for damage control surgery, a high grade AAST pancreatic injury and associated vascular injuries were associated with mortality on multivariate analysis (Chinnery, Krige et al. 2012). Similar findings were reported in a study using the Scottish Trauma Audit Group (STAG) database in which the overall number of injuries, age, male sex, blunt trauma and haemodynamic compromise were identified as independent risk factors for death (Scollay, Yip et al. 2006). Similarly an increasing age, ISS, haemodynamic compromise and having undergone an operation were variables predicting mortality after pancreatic trauma in an analysis from the Trauma Audit and Research Network (TARN) database in the UK (O'Reilly, Bouamra et al. 2015).

The mortality in this study was 15.2% which is similar to other studies reporting mortality rates ranging from 12% to 33% (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Wang, Li et al. 2007, Hwang and Choi 2008, Antonacci, Di Saverio et al. 2011). Our data concur with the findings of others that the principal cause of early death after major pancreatic trauma is the severity of the primary injury and number of associated solid, visceral and vascular injuries (Kao, Bulger et al. 2003, Scollay, Yip et al. 2006, Wang, Li et al. 2007). As demonstrated in this study, pancreas-related deaths were uncommon, occurred late, and were due to sepsis and multi-organ failure. Previous studies from Cape Town have shown in a stepwise multivariate logistic regression analysis model that 5 variables, age, shock, median number of units transfused and the presence of associated complications were significant factors associated with mortality (Krige, Kotze et al. 2015).

Several previous studies have sought to detect predictors of morbidity and mortality in pancreatic trauma. In the first major study to delineate likely critical factors, Heitsch et al. from Louisville, Kentucky reported a 34% mortality rate in patients with pancreatic trauma and concluded that death was more common in the presence of duct injury ($p < 0.0001$) (Heitsch, Knutson et al. 1976). Pancreatic related mortality rate was 17%. Gram-negative sepsis was the most common cause of death ($p < 0.01$) and sepsis correlated with the presence of pancreatic duct ($p < 0.0001$) and bowel ($p < 0.001$) injury. In a subsequent study from Louisville which assessed determinants of outcome in pancreatic trauma, Smego et al. evaluated 72 consecutive patients and reported an overall mortality of 29% (Smego, Richardson et al. 1985). The mortality rate from pancreatic causes was 3%. The authors concluded that recognition of a major ductal injury was crucial and that grade III and IV injuries required treatment by distal resection. Similarly, Bradley et al contended that mortality and morbidity increased when there was a delay in the detection of a pancreatic ductal injury (Bradley, Young et al. 1998).

In a retrospective review of 55 patients with pancreatoduodenal injuries treated in Bologna, Italy, Antonacci found that age, AAST grade, organ involved, hemodynamic status, intra-operative cardiac arrest and operative time were strongly predictive of mortality on multivariate analysis (Antonacci, Di Saverio et al. 2011). Hwang and Choi from Korea reported an overall mortality rate of 13.3% in 75 patients with pancreatic injuries (Hwang and Choi 2008). Multivariate regression analysis showed that greater than a 12 unit blood transfusion and an initial base deficit of greater than -11 mM/L were significant

predictors of mortality. In a retrospective review of 193 patients with a pancreatic injury admitted to their Level I trauma center in Seattle, Kao et al reported a 12% mortality rate (Kao, Bulger et al. 2003). Multivariate analysis showed that the grade of pancreatic injury was an independent predictor of mortality (odds ratio, 2.6; 95% CI 1.2–5.8) (Kao, Bulger et al. 2003).

The PIMS is proposed as a comprehensive and validated tool to accurately predict post-operative mortality progressively across its range of scores based on easily accessible data points. In the trauma environment PIMS is able to provide prognostic information and at an institutional or national level, this score will allow comparison and hence benchmarking of the quality of care provided for this complex patient population. This study has several substantial strengths. This is the largest study based on prospective data validating the risk for mortality and the PIMS thus generated has a number of advantages including parsimony, comprising only 5 variables. An important feature is that the primary endpoint of in-hospital mortality is a robust and immutable variable which dispenses with the need and the deficiencies of long-term follow-up. The mortality data generated from this single centre based study at one of the busiest academic trauma centres in the world is factual and indisputable and avoids the potential bias of underreporting negative events which may occur in multicentre registry-based databases.

There are a number of limitations to this study. These calculations and the ultimate score were generated from source data obtained from a select group of patients treated in a high volume well resourced tertiary academic Level I Trauma center which has a particular interest in HPB trauma. In this unit senior

multidisciplinary staff are involved in the constant care of patients and the assessment and management of complex pancreatic resections are done under the supervision of experienced HPB surgeons. It is thus evident that these data may differ substantially from the results emanating from smaller institutions which have limited trauma management facilities and may have and use different treatment strategies. The generalizability of the model thus may not fit the profile and outcome in smaller and less well resourced trauma centres. External validation of this newly developed PIMS will be necessary to test its validity in similar international cohorts and as health care delivery and surgical trauma quality improve, further re-evaluation and recalibration of the model may be required. An important point to stress is that the primary aim of this study was to develop a quality comparative assessment score and not a tool for implementation of a management algorithm.

In conclusion, this study has derived and validated the PIMS, a novel organ-specific risk prediction score calculated from five variables for in-hospital mortality following major pancreatic trauma. The PIMS is a simple, quick and easily understandable score that increases clinical risk prediction for patients with complex pancreatic and associated injuries and can be used as a benchmark for survival. This model exploits variables readily available to trauma surgeons and has the potential to be useful as a real-time score to predict outcome and to benchmark quality of surgical intervention in the treatment of complex injuries and to aid in the post hoc analysis of trauma research and comparative audit. The ultimate goal of PIMS risk stratification is the opportunity

to further improve patient outcome after complex injuries and surgical intervention.

CHAPTER 10

Prognostic factors, morbidity and mortality in pancreatic trauma: a critical appraisal of 432 consecutive patients treated at a Level 1 Trauma Center

10.1 Introduction

The pancreas is the least injured of the intra-abdominal solid organs but results in considerable morbidity and mortality rates if the injury is incorrectly assessed or inadequately treated (Krige, Beningfield et al. 2005, Krige, Kotze et al. 2011). Penetrating pancreatic injuries, in particular bullet wounds, are frequently associated with major vascular injuries, often with lethal consequences, due to the close proximity of the head and neck of the pancreas to the adjacent large visceral vessels (Wang, Li et al. 2007, Heuer, Hussmann et al. 2011). Thus most early deaths are due to exsanguination or the consequences of massive blood transfusions after associated injuries to the inferior vena cava, portal, superior mesenteric or splenic veins, aorta or superior mesenteric artery or damage to adjacent vascular solid organs (Krige, Beningfield et al. 2005, Heuer, Hussmann et al. 2011, Chinnery, Krige et al. 2012). Two-thirds of patients who survive more than 48 hours have major complications as a consequence of the pancreatic and associated injuries. One third of patients who die later do so because of intra-abdominal or systemic septic complications or multi-organ failure (Krige, Beningfield et al. 2005, Krige and Thomson 2011).

Previous reports have emphasized that outcome is influenced primarily by the cause and complexity of the pancreatic injury, the number and severity of

associated vascular and visceral injuries, the duration of shock, the quality and nature of surgical intervention and secondarily by complications related to the pancreatic duct injury, pancreatic enzyme leakage and intra-abdominal sepsis (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Baiocchi, Tiberio et al. 2008, Hwang and Choi 2008). There is however a paucity of publications which provide a detailed analysis of prognostic factors in severe pancreatic injuries. The present study assessed predictive factors for morbidity and mortality in major pancreatic injuries in a large cohort of consecutive patients using robust and reliable methodology and objective and reproducible end-points.

10.2 Methods

10.2.1 Study population

The design of the study was a retrospective observational cohort analysis. Both the study and the data extraction methodology and analysis were approved by the University of Cape Town Human Research Ethics Committee. The study process involved data retrieval from an existing faculty approved and registered database which since inception has documented the details of all patients who had sustained pancreatic injuries and were treated in the Level 1 Trauma Centre and the Hepatopancreatobiliary and Surgical Gastroenterology units in Groote Schuur Hospital, Cape Town. The analysis included consecutive patients who had a pancreatic injury and were treated between January 1982 and December 2013.

10.2.2 Data collection

All information abstracted from clinical records was recorded on hard copy using a systematically prepared data form and entered into a Microsoft computer programme after data affirmation and validation by a senior study surgeon. Comprehensive details of the database have been documented and recorded previously (Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Thomson, Krige et al. 2014). The relevant variables recorded for each patient are tabulated in Tables 1, 2, 3. The duration of hospital and ICU stay are given in days.

10.2.3 Definitions

The definitions used in this manuscript which included (i) shock, (ii) pancreatic injury severity grading proposed by the Organ Injury Scaling (OIS) of the American Association for the Surgery of Trauma (AAST) (Moore, Cogbill et al. 1990), (iii) pancreatic fistula classification formulated by the International Study Group for Pancreatic Fistula (Bassi, Dervenis et al. 2005) (iv) infectious complications outlined by the Society of Critical Care Medicine guidelines (Dellinger, Levy et al. 2008) (v) septic shock from the Society of Critical Care and Medicine consensus statement (Bone, Balk et al. 1992) and (vi) surgical complications according to the Clavien-Dindo classification (Clavien, Barkun et al. 2009) have been provided in detail in previous publications (Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014). Mortality was defined as any cause of death in hospital.

10.2.4 Operative management of pancreatic injury

Advanced Trauma Life Support (ATLS) guidelines were used for initial resuscitation. Patients who had an acute abdomen with signs of peritonitis, or evidence of major intra-abdominal bleeding underwent urgent surgery. Operative management of the pancreatic injury was according to the outline of a previous published strategy (Farrell, Krige et al. 1996). This applied protocol simplified the assessment and treatment of the injured pancreas. Minor injuries without an evident ductal injury were drained using closed vacuum drains. Major injuries involving the neck, body or tail of the pancreas with an obvious or likely main pancreatic ductal injury were treated by distal resection (Krige, Kotze et al. 2014). Major ductal injuries of the head of the pancreas were drained. Severe grade V injuries of the head with devitalisation of the duodenum or disruption of the ampulla underwent a Whipple operation. If there was persistent haemodynamic instability, a damage control operation was done followed by later definitive management (Krige, Nicol et al. 2014).

10.2.5 Statistical analyses

Descriptive statistics, that is, medians with ranges, and frequency distributions, were used to characterize the cohort. Between-group comparisons were made using the ANOVA and the non-parametric Kruskal-Wallis test for normal and non-normally distributed data respectively. The Pearson's χ^2 or Fisher's exact tests were used for analysis of categorical variables, and odds ratios (ORs) with 95 per cent confidence intervals (CI) were calculated. Univariate and then forward stepwise multivariate logistic regression analyses were done to identify factors which could be associated with complications or death. A p value of

<0.05 was considered statistically significant. Multicollinearity was tested using the variance inflation factor (VIF) and the Hosmer-Lemeshow statistic was used to test goodness of fit of the model. The data were analysed using Stata software version 11 (StataCorp LP, College Station, Texas, USA).

10.3 Results

Four hundred and thirty two consecutive patients (median age 26, range 13–69 years) were treated for pancreatic injuries of whom 394 (91%) were men. (Table 1). Median RTS was 7.8 (range 1.8–7.8). Three hundred and thirteen patients had penetrating injuries (234 gunshot wounds, 79 stabs wounds) and 119 patients had blunt injuries (motor vehicle accidents n=62, assault n=41, pedestrian accidents n=9, bicycle accidents n=3, falls from a height n=2, train accident n=1, go-kart injury n=1). Three hundred and eighty seven (89.6%) patients were treated at the trauma centre within 24 hours of the injury. One hundred and sixty eight (38.9%) patients were in shock (systolic blood pressure <90mm Hg) on admission to hospital despite crystalloid volume replacement and resuscitation by paramedical staff (Table 1). Four hundred and twenty two patients underwent a laparotomy. Median time to surgery after hospital admission was 3 hours (range: 1 hour – 69 days).

Table 1 Clinical data of 432 patients with pancreatic injuries

	Total 432	Blunt 119 (27.5%)	GSW 234 (54.2%)	Stab 79 (18.3%)
Male	394	100	219	75
Female	38	19	15	4
Age				
Median (range)	26 (13-69)	30 (13-68)	26 (14-69)	26 (16-62)
RTS				
< 7.8 (range)	173 (1.8-7.5)	46 (1.8-7.5)	105 (3-7.5)	22 (2.1-7.1)
7.8	259	73	129	57
Shock on admission	168	43	103	22
Patients transfused	289	75	179	35
Blood transfusion				
Median units (range)	7 (1-124)	3 (1-82)	5 (1-124)	1 (1-32)
Time to operation				
Median (range)	3hrs (1-1656)	5hrs (1-1656)	3hrs (1-26)	3hrs (1-80)
DCS	69	11	56	2
Pancreatic injury site				
Head and neck of pancreas	137	37	84	16
Body of pancreas	167	51	77	39
Tail of pancreas	128	31	73	24
Associated abdominal injuries				
Nil (isolated injury)	59	49	3	7
1 or 2 organs injured	220	62	100	58
3 or more injured	153	8	131	14
Associated injured organs				
Liver	198	33	131	34
Stomach	172	4	133	35
Spleen	106	31	62	13
Diaphragm	101	5	71	25
Colon	100	9	79	12
Kidney	95	11	80	4
Duodenum	81	15	60	6
Associated vascular injuries	96	10	69	17
No of patients who had a repeat laparotomy	124	27	82	15

10.3.1 Anatomic site and severity of injury

Proximal pancreatic injuries in 137 patients involved the pancreatic head or uncinate process (n=107) or pancreatic neck (n=30). The body of the pancreas was injured in 167 patients and 128 injuries involved the pancreatic tail (Table 10.1). Two hundred and thirty three patients had AAST grade 1 or 2 pancreatic injuries, and 199 patients had AAST grade 3, 4 or 5 pancreatic injuries.

10.3.2 Associated organ injuries

An isolated pancreatic injury was present in 59 (14%) patients (Table 1). The 373 (86.3%) remaining patients had 868 associated intra-abdominal injuries involving predominantly liver (n=198, 45.8%), stomach (n=172, 39.8%), spleen (n=106, 24.5%), diaphragm (n=101, 23.8%), colon (n=100, 23.1%), kidney (n=95, 22%), and duodenum (n=81, 18.8%). Two hundred and twenty (50.9%) of the 432 patients had one or two associated injuries while 153 (35.4%) had three or more associated intra-abdominal injuries (Table 1). Significantly more associated abdominal injuries occurred in gunshot injuries than in blunt or stab injuries ($p<0.01$). Simultaneous extra-abdominal injuries in 178 patients involved the chest (n=116), spine (n=32), limbs (n=64), head (n=38) and neck (n=4).

10.3.3 Associated vascular injuries

Ninety six (22.2%) of the 432 patients had 1 or more associated vascular injuries involving IVC (n=42, 9.7%), superior mesenteric artery or vein (n=16, 3.7%), renal vessels (n=13, 3%), splenic vessels (n=6, 1.4%), aorta (n=7,

1.6%), portal vein (n=9, 2.1%), gastric and hepatic vessels n=4 (0.9%), middle colic artery (n=2) and phrenic artery (n=1).

10.3.4 Surgery

The 422 patients underwent a total of 732 laparotomies (n=298 had one laparotomy, n=63 each underwent two laparotomies, n=61 had 3 or more laparotomies). Two hundred and six patients (48.8%) underwent pancreas drainage after control of bleeding either as a primary (n=196) or secondary procedure (n=10). One hundred and eleven patients (26.3%) had a distal pancreatectomy and 19 (4.5%) had a pancreaticoduodenectomy.

10.3.5 Damage Control Surgery

Sixty-nine of the 432 patients (16%) with complex pancreatic and associated injuries had an initial damage control procedure (DCP) and received a median of 19 (range 4 – 89) units of blood. Sixty-one of the 69 patients were shocked on admission. Thirty-eight (55.1%) of the 69 patients also had major injuries to vascular structures, and 35 (50.7%) had injuries to 3 or more adjacent organs. During the initial damage control laparotomy 12 patients had a distal pancreatic resection as well as a splenectomy as the definitive management of the pancreatic injury while 57 patients had haemostasis and pancreatic drainage only. Nine patients had the definitive pancreatic procedure performed during a subsequent laparotomy (pancreaticoduodenectomy n=5; distal pancreatectomy and splenectomy n=2, spleen preserving distal pancreatectomy n=2). Thirty-nine (56.2%) of the 69 patients who had a DCP died. Twenty six of the 39 patients who died had associated major vascular injuries and 13 had associated

organ or head injuries and died of MOF, DIC, sepsis or as a consequence of the head injury. The need for a DCP resulted in a significantly increased mortality ($p < 0.01$). The 30 survivors in the damage control group underwent between 1 and 8 repeat laparotomies and required a median of 14 units of blood (range 4 – 47).

10.3.6 Combined pancreaticoduodenal injuries

Eighty one patients (18.8%) had both pancreatic and duodenal injuries. AAST grade 4 injuries were present in 15 patients had and 18 had grade 5 injuries. Eighteen patients had a pancreaticoduodenectomy (PD), of which 13 were completed during the first laparotomy, 6 of whom had major associated vascular injuries. Five PDs were delayed after DCP and completed once the patients were stable either at a second and third laparotomy within 72 hours of the initial injury. Three of the 18 patients who had a PD died (persistent coagulopathy and bleeding $n=1$, sepsis $n=2$). The remaining 45 patients with combined pancreaticoduodenal injuries had a primary duodenal repair and external drainage of the pancreatic injury.

The intensive care unit admission tally, median ICU and total hospital stay for all patients are provided in Table 2.

Table 2 Outcome in 432 patients with pancreatic injuries

	Total 432	Blunt 119 (27.5%)	GSW 234 (54.2%)	Stab 79 (18.3%)
No of patients with complications	275	77	161	37
Complications				
Systemic	199	50	121	28
Complications				
Intra-abdominal	115	20	81	14
Complications				
Pancreatic	91	34	44	13
Days in hospital				
Median (range)	12 (1-255)	18 (1-94)	13 (1-255)	9 (1-149)
ICU admission	192	63	111	18
Days in ICU				
Median (range)	6 (1-153)	6 (1-75)	5 (1-153)	9 (1-41)
Outcome				
Died	68	18	46	4

10.3.7 Morbidity

One hundred and fifty seven (36%) patients had no complications postoperatively (median hospital stay: 8 days, range 1-79). Two patients had prolonged hospitalisation (58 and 79 days) for treatment of spine and brain injuries. One hundred and ninety nine (72.4%) of the remaining 275 patients had systemic complications, 115 (41.8%) had intra-abdominal complications and 91 (33.1%) had complications related to the pancreas (Table 2). The systemic complications in 199 patients included pneumonia (n=50), respiratory failure (n=39), atelectasis (n=20), pleural effusion (n=16), acute respiratory distress syndrome (n=11), sepsis (n=40), renal failure (n=38), disseminated intravascular coagulopathy (n=51) and bleeding (n=43). In 115 patients the intra-abdominal complications were fluid collections (intra-abdominal and

subphrenic n=87), anastomotic leaks (n=18), enterocutaneous fistula (n=22), bowel obstruction (n=9), bile leak (n=9), wound sepsis (n=6), intra-abdominal compartment syndrome (n=4) and gastric outlet obstruction (n=2). One hundred and twenty four (28.7%) patients it was necessary to do a repeat laparotomy, most frequently to drain intra-abdominal sepsis refractory to percutaneous radiological treatment. (Table 1). Hospital stay for patients who had complications (median 24 days, range: 1–255) was significantly longer than those who did not have complications ($p < 0.05$).

Of the 91 patients who had pancreas-specific complications, 50 (55.6%) developed a pancreatic fistula, all of which were treated conservatively *ab initio* (Table 2). Of these 31 (62%) resolved after a median of 34 (IQR 14–46) days. Persistent fistulae in 19 patients required endoscopic intervention with retrograde cholangiopancreatography and pancreatic duct sphincterotomy and stenting. Seventeen resolved while 2 patients with recalcitrant fistulae underwent a pancreateojejunostomy. As per protocol 14 patients with symptomatic peripancreatic fluid collections seen on CT scan were treated radiologically with ultrasound-guided percutaneous 8 Fr pigtail catheter drainage. Of these 10 resolved. The remaining 4 patients had operative drainage of refractory infected multi-locular collections. Twelve patients later developed symptomatic pancreatic pseudocysts which required endoscopic transgastric drainage, 4 of which recurred and were treated surgically. The remaining patients had traumatic pancreatitis and resolved on conservative management.

Bivariate logistic regression analysis revealed that age, RTS, presence of shock, the need for a transfusion and the volume of blood transfused, damage control surgery, the AAST grade of pancreatic injury, the need for a relook laparotomy and an associated vascular injury were significant predictors of morbidity (Table 3). In the final multivariate logistic regression analysis model only 2 variables were significant predictors of morbidity: the AAST grade of pancreatic injury $p = 0.003$ [OR 2.7, CI 1.4-5.4], and the need for a repeat laparotomy $p = 0.001$ [OR 8.8, CI 2.4-32.6] (Table 4).

Table 3 Bivariate analysis of factors associated with overall morbidity

	Total no. of patients	Patients who developed Complications	Patients with no complications	<i>p-value</i>	OR	95% CI
	432	275	157	---	---	---
Age (years)						
Mean (SD)				0.0015	---	---
Median (range)	26 (13-69)	28 (13-64)	24 (13-69)			
Revised Trauma Score (RTS)						
<7.8	173	139 (50.5%)	34 (21.7%)	0.0000	3.7	2.3 - 6.0
7.8	259	136 (49.5%)	123 (78.3%)			
Presence of shock						
Yes	168	136 (49.5%)	32 (20.4%)	0.0000	3.8	2.4 - 6.2
No	264	139 (50.5%)	125 (79.6%)			
Patients transfused						
Yes	189	215 (78.2%)	74 (47.1%)	0.0000	4.0	2.6 - 6.3
No	143	60 (21.8%)	83 (52.9%)			
Blood transfusion (median units)						
	7 (1-124)	10 (2-124)	4 (1-28%)	0.0000	---	---
Damage control surgery						
Yes	69	67 (24.4%)	2 (1.3%)	0.0000	24.9	6.4 - 212.6
No	363	208 (75.6%)	155 (98.7%)			
AAST grade						
1, 2	233	111 (40.4%)	122 (77.7%)	0.0000	0.2	0.1 - 0.3
3, 4, 5	199	164 (59.6%)	35 (22.3%)			
No of patients with associated vascular injuries						
Yes	96	80 (29.1%)	16 (10.2%)	0.0000	3.6	1.9 - 6.9
No	336	195 (70.9%)	141 (89.8%)			
Patients who required a repeat laparotomy						
Yes	124	121 (44%)	3 (1.9%)	0.0000	40.3	12.9 - 201.3
No	308	154 (56%)	154 (98.1%)			

Table 4 Multivariate logistic regression model in patients who developed complications after pancreatic injuries

Risk factor	Odds ratio	95% CI	p-value
Gender	1.3	0.4 - 3.7	0.625
Age	0.9	0.9 - 1.0	0.186
RTS	1.6	0.2 - 13.9	0.679
Shock	1.1	0.1- 9.9	0.942
Blood transfusion	1.0	0.5 - 2.0	0.888
Total units transfused	0.9	0.9 - 1.0	0.943
Damage control surgery	1.6	0.2 - 10.1	0.630
AAST	2.7	1.4 - 5.4	0.003
Vascular injury	1.5	0.6- 3.8	0.328
Repeat laparotomy	8.8	2.4 - 32.6	0.001
Mechanism of injury			
GSW vs Blunt	1.1	0.3- 3.4	0.912
Stab vs Blunt	2.7	0.5 - 14.3	0.241
Hours to operation	0.9	0.9 - 1.0	0.316
Injury site			
Body vs head	0.8	0.4 - 1.6	0.498
Tail vs head	0.6	0.3 - 1.3	0.228

10.3.8 Mortality

Sixty-eight (15.7%) of the total of 432 patients died. Median RTS and median total blood transfusion requirements are provided in Table 10.2. Mortality in those who had sustained gunshot injuries was 19.6%, 15.1% for blunt abdominal trauma and 5% in patients who had abdominal stab wounds (Table 10.2). Only two of the 59 patients who had isolated pancreatic injuries died, both had complex brain injuries after blunt head injuries. It is noteworthy that 59 of the 68 patients who died were shocked on admission. The mortality rate for those patients who were shocked on admission to the Trauma Centre (systolic

blood pressure <90mm Hg) was 35.1% (59 of 168) versus 3.7% (9 of 264) ($P<0.05$) for those patients who were not shocked. Associated major vascular injuries were present in 37 of the 68 patients who died had and 39 had required a damage control operation before undergoing their definitive operation. Scrutiny revealed that 32 patients all of whom had concomitant vascular injuries as well as 3 or more adjacent organ injuries died of refractory coagulopathy compounded by bleeding after receiving a median of 18 (range 4-52) units of blood. The 21 patients who died between 5 and 150 days after the pancreatic injury succumbed from MOF ($n=12$), infection ($n=9$), head injury ($n=9$), myocardial infarction ($n=3$) after associated blunt cardiac trauma and necrotic small bowel ($n=2$). One patient died as a consequence of pancreatic necrosis, renal and respiratory failure and intra-abdominal infection. This death was the only one directly due to the pancreatic injury. This cohort underwent a median of 3 operations (range 1-8) and and developed a median of 4 complications (range 1-7).

When factors associated with mortality were considered, logistic regression analysis found that age, RTS, the presence of shock, patients who required a major blood transfusion, the median number of units transfused, the need for a damage control laparotomy, the presence of a severe pancreatic injury (AAST grade 3,4,5) associated vascular injuries and the number of associated injuries, patients with postoperative complications and days in ICU were significant (Table 5). However in the final stepwise multivariate logistic regression analysis model only 5 variables were significant factors associated with mortality: age: $p= 0.001$ [OR 0.9, CI 0.8-0.9], RTS: $p=0.006$ [OR 2.2, CI 1.2-

3.9], shock: $p = 0.043$ [OR 4.2, CI 1.0-16.7], the median number of units transfused: $p=0.03$ [OR 0.9, CI 0.9-1.0] and the presence of associated complications $p = 0.001$ [OR 12.2, CI 2.7-54.7] (Table 6).

Table 5 Bivariate analysis of factors associated with overall mortality

	Total no. of patients	Patients who died	Patients alive	<i>p</i> -value	OR	95% CI
	432	68	364	---	---	---
Age (years)						
Mean (SD)					---	---
Median (range)	26 (13-69)	30 (15-64)	26 (13-69)	0.0004		
Revised Trauma Score						
< 7.8	173	59 (86.8%)	114 (31.3%)	0.0000	14.3	6.7 - 33.9
7.8	259	9 (13.2%)	250 (68.7%)			
Presence of shock						
Yes	168	59 (86.7%)	109 (29.9%)	0.0000	138.0	22.9 - 5562.9
No	264	1 (13.2%)	255 (70.1%)			
Patients transfused						
Yes	289	67 (98.5%)	222 (61%)	0.0000	42.9	7.2 - 1729.2
No	29	1 (1.5%)	142 (39%)			
Blood transfusion (median units)	7 (1-124)	20 (2-102)	6 (1-124)	0.0000	---	---
Damage control surgery						
Yes	69	39 (57.4%)	30 (8.2%)	0.0000	14.9	7.8 - 28.8
No	363	29 (42.6%)	334 (91.8%)			
AAST grade						
1, 2	233	24 (35.3%)	209 (57.4%)	0.0008	0.4	0.2 - 0.7
3, 4, 5	199	44 (64.7%)	155 (42.6%)			
No of patients with associated vascular injuries						
Yes	96	37(54.4%)	59 (16.2%)	0.0000	6.2	3.4 - 11.1
No	336	31 (45.6%)	305 (83.8%)			
No of patients in ICU						
Yes	192	47 (69.1%)	145 (39.8%)	0.0000	3.4	1.9 - 6.2
No	240	21 (30.9%)	219 (60.2%)			
Days in ICU						
Median (range)	6 (1-153)	3 (1-150)	6 (1-253)	0.0027	---	---
No of patients with any complication						
Yes	275	65 (95.6%)	210 (57.7%)	0.0000	15.9	5.0- 80.1
No	3	3* (4.4%)	154 (42.3%)			

* 3 patients had no complications, but died as a result of head injuries

Table 6 Multivariate logistic regression model for death in patients after a pancreatic injury

Risk factor	Odds ratio	95% CI	p-value
Gender	1.5	0.3 - 8.7	0.643
Age	0.9	0.8 - 1.0	0.001
RTS	2.2	1.2- 3.9	0.006
Shock	4.2	1.0 - 16.7	0.043
Blood transfusion	8.2	0.9 - 75.0	0.063
Total units transfused	0.9	0.9- 1.0	0.032
Damage control surgery	2.7	0.9 - 8.2	0.066
AAST	1.2	0.5 - 3.1	0.648
Vascular injury	1.7	0.6 - 4.7	0.283
Repeat laparotomy	0.5	0.1- 1.5	0.215
Mechanism of injury			
GSW vs blunt	1.1	0.3 - 3.4	0.912
Stab vs blunt	2.7	0.5 - 14.3	0.241
Hours to operation	1.0	0.9 - 1.0	0.723
Injury site			
Body vs head	2.3	0.8 - 6.8	0.144
Tail vs head	1.8	0.6 - 5.8	0.312
Complications	12.2	2.7 - 54.7	0.001

10.4 Discussion

Despite a plethora of papers on pancreatic trauma, few have specifically assessed factors predictive of complications or death. The present study is, to our knowledge, the most comprehensive single centre series yet to use bivariate and multivariate logistic regression analyses to examine the factors

predicting complications and death in consecutive patients undergoing surgery for pancreatic trauma. The data in this study confirm that complications after major pancreatic injuries are common and occur in 25 to 50% of patients (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Wang, Li et al. 2007, Hwang and Choi 2008). Previous publications indicate that morbidity is increased in those patients who have severe pancreatic injuries (AAST grades 3-5), combined with other injuries, a delay of more than 24 hours in establishing the diagnosis and unsatisfactory or ineffective initial treatment (Chrysos, Athanasakis et al. 2002, Mayer, Tomczak et al. 2002, Subramanian, Dente et al. 2007, Hwang and Choi 2008, Antonacci, Di Saverio et al. 2011, Sharpe, Magnotti et al. 2012). In this study bivariate logistic regression analysis identified 9 candidate factors as significant predictors of morbidity although in the final multivariate analysis model only 2 variables, AAST grade of pancreatic injury and the necessity for a relaparotomy were significant predictors of morbidity.

The mortality in this study was 15.7% which is similar to other studies in which mortality rates were reported from 12% to 33% (Heitsch, Knutson et al. 1976, Kao, Bulger et al. 2003). As reported in other studies most of the early deaths which occurred in the first 24h after injury were due to collateral venous injuries (Heitsch, Knutson et al. 1976). When factors associated with mortality were considered in this study, logistic regression analysis found that 11 variables were significant but in the final stepwise multivariate analysis model only 5 variables, age, shock, median number of units transfused and the presence of associated complications were significant factors associated with mortality.

Surprisingly, in this analysis neither the site of pancreatic injury (head vs body vs tail) nor the number of associated abdominal injuries were significant.

Several previous studies have sought to detect predictors of morbidity and mortality in pancreatic trauma. In the first major study to delineate likely critical factors, Heitsch et al. from Louisville, Kentucky reported a 34% mortality rate in patients with pancreatic trauma and concluded that death was more common in the presence of duct injury ($p < 0.0001$) (Heitsch, Knutson et al. 1976). Pancreatic related mortality rate was 17%. Gram-negative sepsis was the most common cause of death ($p < 0.01$) and sepsis correlated with the presence of pancreatic duct ($p < 0.0001$) and bowel ($p < 0.001$) injury. In a subsequent study from Louisville which assessed determinants of outcome in pancreatic trauma, Smego et al. evaluated 72 consecutive patients and reported an overall mortality of 29% (Smego, Richardson et al. 1985). All grade I and most grade II injuries were treated by drainage alone; the grade III and IV injuries were treated by pancreatic resection. Fifty-seven patients survived longer than 24 hours. In 23 grade I injuries there were minimal pancreatic complications and no deaths. There was one death in 18 grade II injuries and 1 death in 16 patients with grade III and IV injuries treated by resection, although the complication rate rose with increasing severity of the pancreatic injury. The mortality rate from pancreatic causes was 3% (2/57). The authors concluded that recognition of a major ductal injury was crucial and that grade III and IV injuries required treatment by distal resection. Similarly, Bradley et al contended that mortality and morbidity increased when there was a delay in the detection of a pancreatic ductal injury (Bradley, Young et al. 1998).

In a retrospective review of 55 patients with pancreaticoduodenal injuries treated in Bologna, Italy, Antonacci found that age, AAST grade, organ involved, hemodynamic status, intra-operative cardiac arrest and operative time were strongly predictive of mortality on multivariate analysis (Antonacci, Di Saverio et al. 2011). The AAST grade was an independent prognostic factor predictive of overall morbidity on multivariate analysis, which was confirmed in our data.

Hwang and Choi from Korea reported overall mortality and morbidity rates of 13.3% and 49.3% in 75 patients with pancreatic injuries (Hwang and Choi 2008). Multivariate regression analysis showed that greater than a 12 unit blood transfusion and an initial base deficit of greater than -11 mM/L were significant predictors of mortality. The most important predictors of morbidity were surgical complexity and an initial base deficit of greater than -5.8 mM/L. The authors suggested that the severity of pancreatic injury per se influenced only morbidity (Hwang and Choi 2008).

In a retrospective review of 193 patients with a pancreatic injury admitted to their Level I trauma center in Seattle, Kao et al reported a 12% mortality and an overall morbidity rate of 50%, of which 22% were pancreas-related complications (Kao, Bulger et al. 2003). Multivariate analysis showed that the grade of pancreatic injury was an independent predictor of both pancreatic complications (odds ratio, 4.4; 95% CI 1.9 –10) and mortality (odds ratio, 2.6; 95% CI 1.2–5.8). In their study pancreatic and ICU complications were associated with longer ICU and hospital stays (Kao, Bulger et al. 2003).

This study is several significant limitations. These data were generated from and reflect the outcome in a select group of patients treated in a high volume well resourced tertiary academic Level I Trauma centre which has a particular interest in HPB trauma. In this unit senior multidisciplinary staff are involved in the constant care of patients. The assessment and management of complex pancreatic resections are done either by or under the supervision of experienced pancreatic surgeons. It is thus evident that the data in this study which are derived from a single specialist referral centre may differ substantially from the results emanating from smaller institutions which may have limited trauma management facilities or resource constraints and therefore may use different treatment strategies which consequently have differing outcomes.

In conclusion, this study showed that overall post-injury morbidity was 64% and the final multivariate logistic regression analysis model demonstrated that 2 variables, AAST grade of pancreatic injury and a repeat laparotomy were significant predictors of morbidity. Overall mortality in this study was 15.7% and most deaths were due to associated injuries and were unrelated to the pancreatic injury. In the final stepwise multivariate logistic regression analysis model 5 variables, age, shock, RTS, median number of units transfused and the presence of associated complications were significant factors associated with mortality. It should be stressed that the analysis and interpretation of these data pertain in particular to pancreatic injuries treated in an urban civilian population and reflect the outcome in a well resourced and amply staffed level 1 trauma centre.

CHAPTER 11

Emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum

11.1 Introduction

Severe injuries of the pancreatic head, duodenum and bile duct in hemodynamically unstable patients with associated injuries are complex to manage and tax the skill and ingenuity of even the most experienced trauma and pancreatic surgeons (Krige 1997, Krige, Beningfield et al. 2005). Previous reports indicate that outcome is determined by the complexity and site of the pancreatic injury, the number, extent, and magnitude of the associated injuries, the amount of blood loss and duration of shock, the rapidity and efficacy of resuscitation, and the speed and quality of surgical intervention (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Krige, Beningfield et al. 2005, Hwang and Choi 2008, Krige, Kotze et al. 2011, Krige and Thomson 2011). Overall morbidity rates for maximal pancreatoduodenal injuries are substantial and mortality is directly proportional to the number of injuries sustained and is highest in the elderly and those who are haemodynamically unstable (Scollay, Yip et al. 2006). Early mortality is due either to uncontrolled venous bleeding or major adjacent organ injuries (Krige, Beningfield et al. 2005, Krige, Kotze et al. 2011, Krige and Thomson 2011, Chinnery, Krige et al. 2012). Late mortality is generally a consequence of infection or multiple organ failure (Krige, Beningfield et al. 2005, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012).

Urgent intervention and resection of the pancreatic head and reconstruction in severely injured patients with complex pancreatic injuries aggravated by hypothermia, coagulopathy and acidosis has in the past resulted in prohibitive mortality rates (Wang, Li et al. 2007, Krige and Thomson 2011). Often life-threatening associated collateral injuries, especially those involving adjacent large splanchnic veins including inferior vena cava, portal and superior mesenteric veins take precedence in management (Wang, Li et al. 2007, Krige and Thomson 2011). In addition, there are technical difficulties resecting and reconstructing complex pancreatic injuries which require special surgical skills and expertise (Krige 1995, Krige, Beningfield et al. 2005, Krige and Thomson 2011). The answers to several issues regarding the role of pancreatoduodenectomy for major pancreatic injuries are unresolved. These questions include: what is the mortality for emergency Whipples resection using modern pancreatic and biliary operative techniques? Is a pylorus preserving pancreatoduodenectomy technically feasible and appropriate in acute trauma? Is there a beneficial role for pancreatogastrostomy in selected patients in reconstruction after an emergency Whipples? Although several substantial reviews (Chrysos, Athanasakis et al. 2002, Krige 2006, Subramanian, Dente et al. 2007) and original data from Cape Town (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012), have detailed aspects of the management of pancreatic injuries, no publications have specifically assessed the results of emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum when performed by or under the supervision of experienced HPB surgeons. The present study critically evaluated the outcome after pancreatoduodenectomy for non-reconstructable pancreatic injuries in a

cohort of consecutive patients treated at a level I trauma centre using established HPB techniques of resection and reconstruction adapted for the trauma situation.

11.2 Methods

11.2.1 Study population

The study design was a single center retrospective cohort analysis of prospective data on consecutive patients who had a pancreaticoduodenectomy for trauma between January 1990 and December 2011. The study used a registered fit for purpose departmental data base which documents the details of all patients with pancreatic injuries treated at the Level 1 Trauma Centre and the Hepatopancreatobiliary and Surgical Gastroenterology units at Groote Schuur Hospital, Cape Town. The study was approved by the University of Cape Town Human Research Ethics Committee and the protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, and revised in Tokyo 2004.

11.2.2 Data collection

During the 22-year study period, 426 patients were treated for pancreatic injuries of whom 19 (4.5%) underwent a pancreaticoduodenectomy for complex non-reconstructable injuries involving the proximal pancreas and duodenum (Figure 1). Data relating to each patient were entered prospectively on a standardised electronic password protected Microsoft Access data spread sheet and analyzed using Microsoft Access and Microsoft Excel. Data fields

comprised demographic information including age and gender, mechanism of injury, time from injury to Trauma Centre admission, vital signs on admission including systolic blood pressure in mmHg, heart rate and details of the clinical examination including details of associated extra-abdominal injuries. The trauma scores recorded included Glasgow Coma Scale (GCS), revised trauma score (RTS), abbreviated injury score (AIS), injury severity score (ISS), APACHE II and P-POSSUM scores. Pre-operative blood gas analysis and arterial blood pH, base deficit, temperature and coagulation profile including International Normalized Ratio (INR) were recorded. Operative findings and associated intra-abdominal injuries, anatomic location and grade of the pancreatic injury, surgical procedure performed, duration of the operation, post-operative course and duration of hospital stay were recorded. Intra-operative crystalloid and colloid volumes were recorded and the number of packed red cells, fresh frozen plasma and platelet packs given were documented and the accuracy reconciled with blood bank records.

All patients who had a pancreaticoduodenectomy had grade 5 pancreatic injuries according to the Organ Injury Scaling (OIS) of the American Association for the Surgery of Trauma (AAST) (Moore, Cogbill et al. 1990). Postoperative complications were classified according to the Clavien-Dindo grading system (Clavien, Barkun et al. 2009). For the purpose of data analysis, postoperative morbidity was subdivided into three categories, (i) pancreas-specific complications which included pancreatic fistula and pseudocyst, (ii) non-pancreatic abdominal complications including intra-abdominal abscesses, enterocutaneous fistulas and wound infections, and (iii) systemic complications

including acute respiratory distress syndrome, pneumonia, renal and multiple organ failure.

11.2.3 Definitions

Definitions used in this study were as defined and recorded in the study methodology in Chapter 3.

11.2.4 Operative management of pancreatic injury

Initial resuscitation was according to Advanced Trauma Life Support (ATLS®) guidelines. All patients in this study underwent an urgent laparotomy because of persisting shock with evidence of major intra-abdominal bleeding or an acute abdomen and signs of peritonitis. Operative management of the pancreatic injury was according to a specific operative strategy based on the hemodynamic stability of the patient, the magnitude and extent of associated injuries and the location and severity of the pancreatic injury. Details have been published previously (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012). In brief, the principles applied were urgent control of intra-abdominal bleeding, closure of visceral perforations to prevent contamination of the peritoneal cavity and rapid volume replacement to correct acidosis, coagulopathy and hypothermia. Patients who remained unstable or those *in extremis* with major associated organ and visceral vascular injuries had an initial damage control operation which comprised a truncated laparotomy followed by continued resuscitation and correction of haemodynamic, metabolic and physiological defects in the ICU and definitive surgery at a later, second or third operation.

A pylorus-preserving pancreatoduodenectomy (PPPD) was done in all patients except in those in whom the injury had irretrievably damaged the pylorus, in which case a classic Whipple resection was done. In patients in whom the jejunum was grossly oedematous, usually after prolonged portal vein clamping and large volume intra-operative crystalloid and blood transfusion, the pancreatic stump was anastomosed to the stomach. The bile duct was joined to the jejunum in the standard fashion for bile duct reconstruction. In situations where the bile duct measured less than 3mm and gross oedema jeopardised the bile duct to jejunum anastomosis, the gall bladder was preserved and used as the conduit for the biliary enteric anastomosis. In high risk stented biliary anastomoses the duodenojejunostomy was created as the first anastomosis using the Imanaga technique to allow post-operative ERCP and biliary stent retrieval (Imanaga 1960). All pancreatic anastomoses were stented internally with 8 cm long 5Fr silastic pediatric feeding tubes cut to size.

All biliary and pancreatic anastomoses were drained using closed silastic suction drains. Drainage volumes and amylase levels were measured daily postoperatively. Drains were left *in situ* while drain amylase levels were elevated or volume measured over 30 ml per day. All patients had intraoperative placement of double or triple lumen internal jugular central lines for venous access and TPN. Nasojejunal low residue enteral feeding was initiated as soon as the patient was haemodynamically stable, inotropes had been discontinued and intestinal continuity re-established. No dietary restrictions were imposed if a pancreatic fistula occurred and oral food intake was continued while the fistula drained. Suspicion of infected intra-abdominal

collections post-operatively was investigated by contrast-enhanced CT scan and treated by ultrasound guided 7Fr percutaneous catheter drainage.

11.3 Results

During the 22 year period from January 1990 to December 2011, 426 patients (389 (91.3%) men, median age 26 years (range 13 – 69 years) had confirmed pancreatic injuries. One hundred and eighteen (27.7%) were caused by blunt trauma (62 motor vehicle accidents, 41 assaults and 15 other), 229 (53.8%) were gunshot wounds and 79 (18.5%) were stab wounds. Of these, 19 (4.5%) had AAST grade V injuries involving the head of the pancreas and duodenum which were not reconstructable and required a pancreatoduodenectomy (Table 1). Thirteen of the 19 had penetrating injuries (12 low velocity gunshot wounds, 1 stab wound) and 6 had sustained blunt abdominal injuries due to motor vehicle accidents. Nine (47.4%) patients were in cardiovascular shock (systolic blood pressure <90mm Hg) on admission to hospital despite volume resuscitation by paramedical staff while in transit. On admission to the Trauma Centre, the patients' median recorded systolic blood pressure was 100 mmHg, (range 0-155) and median pulse rate was 94 per minute (range 80-128). The pre-operative trauma scores are shown in Table 1. Median delay from injury to Trauma Centre admission was 1 hour (range 0.5-17). Median delay from admission to initial operation was 2 hours (range 1-7 hours).

Table 1 Demographic and operative data

Demographic Data	
Total number of patients	19 (17 men, 2 women)
Median Age	28 years (range 14-53)
Pre-Operative Data	
Revised Trauma Score (RTS) median	7.84 (range 5.43-7.84)
Injury Severity Score (ISS) median	25 (range 25-75)
New Injury Severity Score (NISS) median	75 (range 49-75)
Abdominal trauma Index (ATI) median	56 (range 33-86)
APACHE II Score median	2 (range 0-18)
Intra-Operative Data	
Median duration of surgery	6h10min (range 4h20-10h45)
Median blood loss	1500ml (range 800-9000 ml)
Median intra-operative blood replacement	1200ml (range 0-8325 ml)
Median intra-operative crystalloid volume	6000ml (range 2000-14000 ml)
Median intra-operative colloid volume	1500ml (range 500-3000 ml)
Median fresh frozen plasma volume	1040 ml (range 520-2080 ml)
Post-Operative Data	
Median duration ICU stay	5 days (range 1-20 days)
Median duration hospital stay	29 days, (range 14-94 days)

11.3.1 Associated injuries

Two men who had sustained blunt abdominal trauma had isolated injuries confined to the head of the pancreas and duodenum. In addition to the grade 5 injuries of the pancreas and duodenum, 17 of the 19 patients had a total of 30 associated non-vascular intra-abdominal injuries (median 2, range 1-4) which involved bile ducts and gall bladder (n=10), liver (n=9), right kidney and ureter (5), stomach (n=3) and colon (n=3). Concurrent extra-abdominal trauma in three patients involved lung (n=1), spine (n=1) and left femur (n=1). Nine of the 19 patients had 1 or more associated vascular injuries involving IVC (n=8), portal vein (n=2), superior mesenteric vein (n=2), renal vein (n=1) and lumbar veins (n=1).

11.3.2 Surgery

All 19 patients had maximal injuries with destruction of the head of the pancreas involving the main pancreatic duct, the intrapancreatic portion of the distal common bile duct or had disruption or avulsion of the ampulla from the medial wall of the duodenum and duodenal devitalisation. Nine patients had, in addition, as indicated above, exsanguinating retroperitoneal or retropancreatic bleeding due associated major splanchnic venous injuries involving the inferior vena cava and/or portal vein, superior mesenteric vein and in one patient the superior mesenteric artery.

11.3.2.1 Initial damage control operation

Five patients in whom complex pancreatic injuries were aggravated by severe associated injuries and major blood loss, acidosis, coagulopathy, hypothermia and persisting hypotension despite vigorous resuscitation, had an initial damage control operation (median duration 102 minutes, range 92–165 minutes), followed by a subsequent pancreatoduodenectomy and reconstruction when stable. These 5 patients had a median Apache II score of 11, (range 0-18) and received a median of 10 (range 8-12) units of blood intraoperatively. Four of the 5 were shocked on admission to hospital and four had associated vascular injuries. The pancreaticoduodenectomy was completed at a median of 15 hours (range 11-96 hours) after the initial damage control laparotomy. Three had relook laparotomies.

11.3.2.2 Pancreatic resection

Twelve patients had a PPPD and seven a standard Whipple resection. In two patients the reconstruction arrangement used the Imanaga technique to allow a postoperative ERCP to retrieve or replace the biliary stent because of an

associated major liver injury with a segmental intrahepatic ductal injury. In three patients the bile duct measured 3mm or less in diameter and because the jejunum was grossly oedematous, the bile duct was ligated and the gallbladder was used as the conduit for biliary drainage into the jejunum. In eight patients the back wall of the stomach was used to drain the pancreatic stump with a single layer pancreatogastrostomy and in 11 patients an end-to-side pancreatojejunostomy was used. The relevant intra-operative data are shown in Table 1. Sixteen patients survived, 13 of whom had substantial morbidity.

11.3.3 Morbidity

The Clavien–Dindo complication grades were as follows: 1 patient had a grade I complication, 7 (13.8%) patients had grade II complications, 2 (17.5%) had grade IIIa, 6 (10%) had grade IVa, and 3 (16.3%) had grade V complications and died. The surviving 16 patients had a total of 31 complications which included 10 systemic complications (pneumonia n=5, multi-organ failure n=2, renal failure n=1, central line sepsis n=1, jaundice n=1), 18 intra-abdominal complications (intra-abdominal and subphrenic abscess n=6, anastomotic leak n=2, enterocutaneous fistula n=2, bowel obstruction n=1, bile leak n=1, delayed gastric outlet emptying n=3, wound sepsis n=3). Three patients developed a pancreatic fistula after the pancreatoduodenectomy. All were treated conservatively and resolved spontaneously after a median of 22 (IQR 12–38) days. Six patients had infected fluid collections identified on CT scan which were treated with percutaneous ultrasound-guided 8 Fr catheter drainage. Four resolved and two required surgical drainage for persistent multi-locular collections despite percutaneous drainage.

11.3.3.1 Late complications

One patient was admitted to hospital on three occasions over a period of 18 months with acute pancreatitis after an alcohol binge. Each event resolved on conservative treatment. One patient had symptomatic malabsorption which resolved on pancreatic replacement therapy. Three patients required a further operation after discharge from hospital. One patient returned 6 months after the pancreatoduodenectomy for closure of a defunctioning colostomy and two patients in whom the gallbladder had been retained and used for biliary drainage returned 3 and 6 years after the pancreatoduodenectomy with cholangitis due to hepatic duct stones. Both had a cholecystectomy and a formal hepaticojejunostomy.

11.3.4 Mortality

Three of the 19 patients died, 2 of whom had damage control operations. All 3 were shocked on admission; 2 were *in extremis* on arrival at the Trauma Centre with no recordable blood pressure and both underwent an initial damage control operation before later definitive surgery. All 3 patients who died had associated major splanchnic venous injuries involving IVC, PV and SMV and had APACHE II scores on admission of 15, 18 and 18. Root-cause analysis showed that 2 patients died of multi-organ failure and disseminated intravascular coagulopathy within 48 hours of the resection after receiving a median of 27 units of blood during the damage control operation. The third patient died after 24 days of multi-organ failure, ARDS, and resistant *acinetobacter* and *pseudomonas* related intra-abdominal sepsis.

11.4 Discussion

This prospective single centre observational cohort analysis is unique in several respects. This is the largest series documenting emergency pancreatoduodenectomy in injured patients with severe trauma of the proximal pancreas and duodenum. There are no existing data on the results of proximal pancreatic resection and reconstruction in severely injured patients performed by or under the supervision of experienced HPB surgeons using established pancreatobiliary operative techniques adapted for trauma. In this cohort of patients reconstruction is frequently technically difficult as the ducts are nondilated and the surrounding organs damaged or oedematous which necessitates modification of conventional biliary and pancreatic anastomoses (Krige 1995, Krige 1997, Krige, Beningfield et al. 2005, Krige and Thomson 2011). Unlike previous publications, a novel feature in this study was the ability to do a pylorus-preserving pancreatoduodenectomy in a substantial proportion of injured patients. Importantly, in those patients who, in addition to maximal injuries to the pancreas, also had severe injuries to adjacent vascular, biliary, enteric, colonic or solid organs and had persistent shock, an initial damage control operation was followed by delayed pancreatoduodenectomy and reconstruction when the patient was stable.

Most authors agree that a pancreatoduodenectomy for trauma is seldom necessary and should be reserved for the select small group of patients with severe injuries of the head of pancreas and duodenum in whom lesser procedures with preservation of pancreas and duodenum is not possible (Chrysos, Athanasakis et al. 2002, Subramanian, Dente et al. 2007). However,

the mortality rate for a Whipple resection in severely injured and unstable patients is prohibitive, and in this and other series, those who survive also have a high postoperative complication rate (Krige 1997, Krige 2006). When faced with a devitalized head of the pancreas and duodenum, an avulsed ampulla or a near-completetraumatic resection, a surgeon may have no recourse but to proceed and complete the resection provided the patient is haemodynamically stable and the necessary surgical expertise is available (Krige, Beningfield et al. 2005, Krige and Thomson 2011). McKone has proposed specific indications for pancreatoduodenectomy for trauma: 1) extensive devitalization of the head of the pancreas and duodenum in whom there is no prospect of a repair; 2) ductal disruption in the pancreatic head with AAST grade 5 injuries of the duodenum and distal common bile duct; 3) injury to the ampulla of Vater, with disruption of the main pancreatic duct from the duodenum (McKone, Bursch et al. 1988). It should be emphasized that only patients who had devitalised non-reconstructable injury were considered for a pancreatoduodenectomy in the study. Other authors (van der Wilden, Yeh et al. 2014) have recently suggested that lesser procedures may be applicable for grade V injuries but this is not an option in patients with a disrupted and devitalised duodenum and pancreas.

The reputation of an emergency pancreatoduodenectomy is tarnished by high mortality rates reported in the literature. In an analysis of 61 publications which reported 220 pancreatoduodenectomies for trauma, Krige *et al* found an overall mortality of 34% (Krige 1997). Substantial experience is scant. Only seven series have previously treated ten or more patients with pancreatoduodenectomy for trauma (Yellin and Rosoff 1975, Jones 1978,

Balasegaram 1979, Oreskovich and Carrico 1984, Feliciano, Martin et al. 1987, Asensio, Petrone et al. 2003, Thompson, Shalhub et al. 2013) (Table 2).

Table 2 Pancreatoduodenectomy for trauma

Author	Year	Site	No of patients	Mortality
Yellin	1975	LAC + USC Medical Center, Los Angeles, USA	10	6
Balasegaram	1979	General Hospital, Kuala Lumpur, Malaysia	12	5
Jones	1985	Parkland Memorial Hospital, Dallas, USA	12	7
Oreskovich	1984	Harbourview Medical Center, Seattle, USA	10	0
Feliciano	1987	Ben Taub General Hospital, Houston, USA	13	6
Asensio	2003	LAC + USC Medical Center, Los Angeles, USA	18	6
Thompson	2013	Harbourview Medical Center, Seattle, USA	15	2
This study	2014	Groote Schuur Hospital, Cape Town, South Africa	19	3

A pancreatoduodenectomy for trauma is perhaps the most demanding of all pancreatic resections because the procedure is performed under the most difficult circumstances with severe operative constraints. Management of the associated and collateral damage is crucial in ensuring survival in this group of desperately injured patients and, in particular, injuries to adjacent large visceral splanchnic veins are frequently immediately life-threatening and require priority intervention (Wang, Li et al. 2007). Urgent vascular access to a lacerated retropancreatic portal or superior mesenteric vein in an exsanguinating patient

is often problematic and accelerated exposure and rapid control is necessary (Krige 1997). Assessment of the extent of the pancreatic injury and the need for resection requires mature judgement and skilled evaluation and in these situations intra-operative appraisal by an HPB surgeon provides invaluable assistance to the trauma surgeon. The decision to do a pancreatoduodenectomy may be obvious, especially if blunt injury has resulted in a near complete *de facto* resection (Krige 1997). However in gunshot injuries of the pancreatic head, assessment may be difficult and crucial strategic decisions benefit from the opinion of an experienced pancreatic surgeon. In some circumstances a lesser procedure is both appropriate and technically feasible without resorting to a pancreatoduodenectomy.

The conduct and execution of an emergency pancreatoduodenectomy for trauma differs from the elective operation (Krige 1997, Krige, Beningfield et al. 2005). There is general agreement that patients who have a major pancreatic injury with associated major visceral injuries and are haemodynamically unstable despite vigorous resuscitation and are coagulopathic, acidotic and hypothermic and have received a massive intra-operative blood transfusion should have an abbreviated laparotomy with a damage control procedure and subsequent re-exploration, resection and reconstruction when stable (Glancy 1989, Chrysos, Athanasakis et al. 2002, Wang, Li et al. 2007, Nicol, Navsaria et al. 2010, Thompson, Shalhub et al. 2013). While some authors recommend that pancreatoduodenectomy for trauma should be always performed as a two-stage procedure, this suggestion is not supported by the data in this study. In this series five patients who were unstable despite optimal resuscitation had an

initial damage control operation to achieve haemostasis with staple closure of hollow viscera and external drainage of pancreas and common bile duct. Resection and anastomoses were completed at either the second or third reoperation 48 or 72 hours later when the patient was stable.

This study has several specific limitations. Despite the fact that the data generated are from a high volume tertiary academic center, the patient numbers are small and may reflect an inherent referral and treatment bias. The analysis is based on a select high-risk surgical cohort treated in a centre with constant access to specialist multidisciplinary HPB care which may not be representative of or applicable to lesser resourced hospitals where such facilities are not freely available. A strength of this study is the prospective documentation of a robust dataset conducted in a single center using uniform criteria in a defined and homogenous population of consecutive patients supervised by a single surgeon (JEK) for the duration of the study period.

In conclusion, pancreatoduodenectomy for trauma is seldom necessary and is reserved for maximal injuries involving the head of the pancreas and duodenum in which repair is not feasible and where the decision to do a pancreatoduodenectomy is unavoidable. This study has shown that a pylorus-preserving pancreatoduodenectomy is technically feasible in the trauma situation. Pancreatogastrostomy is an option when conventional pancreatojejunostomy is difficult due to an oedematous jejunum. Initial damage control with delayed resection and reconstruction is applicable in a select group of patients. While an emergency pancreatoduodenectomy has significant morbidity and appreciable mortality due to complicating factors, associated

injuries and shock, resection may be the only option in complex injuries with ampullary destruction or devitalised duodenum. The pancreas is an unforgiving organ, especially if severely damaged and it is prudent to call an experienced HPB surgeon to assist with operative decisions as the procedure is technically demanding and crucial procedural decisions must be made during resection and reconstruction. For the patients benefit, this is not the time for a trauma surgeon to be doing his or her first unsupervised Whipple resection. The current data show that these are patients with complex problems associated with significant postoperative morbidity and should be managed collaboratively by both trauma and HPB surgical teams.

CHAPTER 12

Surgical Management and Outcomes of Combined

Pancreatoduodenal Injuries: 75 Consecutive Cases Analyzed

12.1 Introduction

Severe injuries involving both pancreas and duodenum continue to be a considerable cause of morbidity and mortality, even when treated in well-resourced high volume trauma referral centers (Ragulin-Coyne, Witkowski et al. 2014, O'Reilly, Bouamra et al. 2015). Most deaths occur early and are due to associated injuries and the consequences of uncontrolled blood loss and shock (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). Late deaths are usually due to resistant intra-abdominal sepsis and multisystem organ failure (Tyburski, Dente et al. 2001, Krige, Beningfield et al. 2005). The five most crucial factors influencing management and outcome are (i) the grade of pancreatic head damage, (ii) the degree of ischemia and viability of the duodenum, (iii) the extent of ampullary damage, (iv) the presence of visceral vascular injuries and (v) the magnitude of associated organ injuries. These issues determine both the scale of intervention and ultimate survival. Both the early use of damage control surgery and the need for pancreatic and duodenal resection are important considerations when treating complex combined pancreatoduodenal injuries but have not been applied consistently in high risk situations (van der Wilden, Yeh et al. 2014).

The optimal surgical management of complex combined pancreatoduodenal injuries is currently characterized by continued controversy and contradiction.

The reasons for the lack of clear guidelines and the paucity of reliable and robust data are manifold. Synchronous combined duodenal damage seldom occurs in tandem with injuries to the head of the pancreas (O'Reilly, Bouamra et al. 2015). In the prospective TARN and STAG databases combined pancreatoduodenal injuries occurred in only 0.2% and 0.3% of predominantly blunt abdominal injuries, while a large cohort study from Cape Town reported double the number of combined pancreatoduodenal injuries after abdominal gunshot wounds compared to blunt trauma (Scollay, Yip et al. 2006, van der Wilden, Yeh et al. 2014). The relative infrequency of this type of injury suggests that most surgeons will have had minimal operative exposure and limited personal experience when dealing with complex combined pancreatoduodenal injuries (CPDI). These deficiencies are compounded by the lack of data and clarity in surgical publications which consist mostly of small retrospective or outdated series and collective reviews which do not provide an authoritative or comprehensive analysis of the problem. In addition, the lack of a practical and universally relevant classification that can be applied to accurately predict the outcome of combined pancreatoduodenal injuries has further hampered progress. Both the widely used Lucas (Lucas 1977) and AAST (Moore, Cogbill et al. 1990) classifications have flaws which hinder a detailed comparison of treatment choices in major combined pancreatoduodenal injuries. For example, in the pancreatic injury AAST classification, no provision is made for associated duodenal injuries which may be a critical factor determining the need for a pancreatoduodenectomy (Krige, Beningfield et al. 2005).

This study addressed three of the major unresolved issues in severe combined pancreatoduodenal injuries, namely (i) survival after initial damage control surgery, (ii) outcome following pancreatoduodenectomy, and (iii) evaluation of predictive factors for morbidity and mortality in a large cohort of consecutive patients using a CPDI grading score. The hypothesis in this study was that bivariate analyses would accurately identify factors influencing morbidity and mortality. In addition the study sought to define specific criteria for the selection of the type of surgery for complex combined injuries using robust and reliable methodology and objective and reproducible end-points.

12.2 Methods

12.2.1 Study population

The study design was a retrospective observational cohort analysis using a faculty approved and registered prospective database which documents the information of all patients with pancreatic injuries treated in the Level 1 Trauma Centre and the Hepatopancreatobiliary and Surgical Gastroenterology units in Groote Schuur Hospital, Cape Town. After approval by the University of Cape Town Human Research Ethics Committee, an analysis was done of consecutive patients who were treated for combined pancreatic and duodenal injuries between January 1990 and April 2015 at Groote Schuur Hospital in Cape Town.

12.2.2 Data collection

All clinical records including surgical details, intensive care, radiology and endoscopy reports of patients with pancreatic injuries were reviewed and

updated monthly since inception of the database. Comprehensive details of the database have been documented previously (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014, Krige, Kotze et al. 2014). A synopsis is provided here. Data were abstracted by a specially trained nurse reviewer and recorded using a standardised data form after affirmation by a senior study surgeon. Details of the methodology used to record the variables for each patient have been published (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014, Krige, Kotze et al. 2014) and included demographic data, revised trauma score (RTS), presence of shock on admission, anatomic location and grade of the pancreatic injury, associated intra- and extra-abdominal injuries, injury to operation interval, surgical procedure used, duration of hospital stay, presence and type of pancreas-related and other complications and mortality. In this study the admission to operation time recorded included all referrals from other hospitals with the clock starting from the first admission at a referral hospital and therefore included helicopter and ambulance transfer times. Longer admission to operation times occurred in haemodynamically stable patients with polytrauma who required head CT scans, neurosurgery consults, and other essential procedures. Hospital length of stay and ICU length of stay were recorded as calendar days. The primary study endpoint was death. The secondary endpoint was morbidity assessed by the Clavien-Dindo classification (Dindo, Demartines et al. 2004).

12.2.3 Definitions

Definitions used in this study were as is defined and recorded in the study methodology in Chapter 3.

12.2.4 Initial management

Initial resuscitation was implemented using Advanced Trauma Life Support (ATLS) guidelines. Patient management was as is outlined in the study methodology in Chapter 3. This study used a novel composite grading system for CPDI (Table 1).

Table 1 Composite grading system for combined pancreaticoduodenal injuries

Grade	Duodenum	Pancreas
1	Partial thickness injury with no perforation	Superficial pancreatic injury with minimal tissue damage and no associated MPD injury
2	Full thickness, disruption <50% of circumference D1-D4	Major laceration without MPD injury or tissue loss
3	D1,D3,D4: disruption 50%-100% of circumference D2: disruption 50%-75% of circumference	Distal transection or major parenchymal injury with MPD injury
4	Disruption >75% of circumference of D2 involving ampulla or distal common bile duct	MPD disruption in head, proximal transection or parenchymal injury involving the ampulla
5	Devitalising injury with ischemic non-viable duodenum	Devitalising injury with cavitation or destruction of pancreatic head

12.2.5 Operative management of pancreatic and duodenal injuries

Operative management of pancreatic and duodenal injuriesinjury was based on the hemodynamic stability of the patient, the magnitude and extent of associated injuries and the location and severity grades of the both the

pancreatic and duodenal injuries, details of which are outlined in the study methodology in Chapter 3.

12.2.6 Damage control laparotomy

Details of the damage control process are not repeated here and are outlined in the study methodology in Chapter 3.

12.2.7 Management of postoperative intra-abdominal, pancreatic and duodenal complications

Postoperative intra-abdominal collections were drained with 5 Fr percutaneous catheters using ultrasound or CT guided placement. Endoscopic 7 Fr pancreatic duct stents were used for persistent pancreatic fistulas (Thomson, Krige et al. 2014) and an endoscopically placed covered self-expanding metal duodenal stent was used for prolonged large volume drainage of lateral duodenal fistulas (Chinnery, Bernon et al. 2011).

12.2.8 Data analysis

Descriptive statistics reporting medians with ranges, and frequency distributions, were used to characterize the cohort. Between-group comparisons were made using the Student t-test or Wilcoxon sum rank test for normal and non-normally distributed data respectively. The Pearson's χ^2 or Fisher's exact tests were used for analysis of categorical variables, and odds ratios (ORs) with 95 per cent confidence intervals (CI) were calculated. Univariate and then forward stepwise multivariate logistic regression analyses were performed to identify factors associated with the occurrence of death. A p value of <0.05 was

considered statistically significant. The data were analysed using Stata software version 11 (StataCorp LP, College Station, Texas, USA).

12.3 Results

During the period under review, 453 consecutive patients were treated for pancreatic injuries, 85 of whom had both duodenal and pancreatic injuries. For the purposes of this study only patients with contiguous pancreatic and duodenal injuries were considered and therefore 10 patients who had a distal pancreatic injury and a duodenal injury were excluded from the analysis. The remaining 75 patients (69 men, median age 27 years, range 14-56) who had combined pancreatoduodenal injuries, sustained 62 penetrating (57 GSW, 5 stab wounds) and 13 blunt injuries (MVA pedestrian 6, MVA driver 3, MVA passenger 1, assault 3 patients) (Table 1). Thirty eight (50.7%) patients were hypotensive on admission to the Trauma Centre (systolic blood pressure <90mm Hg). Median RTS was 7 (range: 3.5-7.1) (Table 2). Median time from admission to surgery was 3 hours (range: 1-17 hours).

Table 2 Clinical data for 75 patients with combined pancreaticoduodenal injuries using the composite grading system

	Grade 1 n=2	Grade 2 n=7	Grade 3 n=28	Grade 4 n=12	Grade 5 n=26	TOTAL n=75
Mechanism of Injury						
Gunshot Wounds	--	5	23	11	18	57 (76%)
Blunt	2	1	3	--	7	13 (17.3%)
Stab	--	1	2	1	1	5 (6.7%)
Shock	1	1	11	10	15	38 (50.7%)
Revised Trauma Score Median (range)	7.8 (4.5-7.8)	7.8 (7.1-7.8)	7.1 (3.5-7.8)	7.1 (6.3-7.8)	7.1 (4.5-7.8)	7.1 (3.5-7.8)
Number of patients transfused	2	6	22	12	23	65 (86.7%)
Damage Control Surgery	1	1	7	6	14	29 (38.7%)
Vascular Injuries	--	1	12	7	15	35 (46.7%)
No of patients with complications	2	2	22	12	25	63 (84%)
Complications						
Systemic	2	2	15	9	22	50 (66.7%)
Intra-abdominal	1	--	14	7	10	32 (42.7%)
Duodenal	--	--	7	5	3	15 (20%)
Pancreatic	--	--	9	3	2	14 (18.7%)
Days in hospital Median (range)	11 and 22	13 (5-68)	22 (3-178)	19 (1-105)	20 (1-94)	20 (1-178)
ICU admission	2	3	17	9	21	52 (69.3%)
Days in ICU Median (range)	6 and 16	3 (3-17)	8 (2-46)	9 (1-19)	4 (1-20)	6 (1-46)
Outcome						
Died	--	--	3	7	11	21 (28%)

All 75 patients underwent a laparotomy. Sixty three patients had injuries involving the pancreatic head, six involved the pancreatic neck and six the proximal pancreatic body. The AAST grade for pancreatic injuries were: grade 1 = 11, grade 2 = 21, grade 3 = 5, grade 4 = 11 and grade 5 = 27. The site of the duodenal injuries were D1 = 13, D2 = 50, D3 = 5 and D4 = 7. The AAST grading for the duodenal injuries were: grade 1 = 3, grade 2 = 8, grade 3 = 45, grade 4 = 13, grade 5 = 6. The 75 patients had composite injury grades as follows: grade 1 = 2, grade 2 = 7, grade 3 = 28, grade 4 = 12 and grade 5 = 26 (Table 2). In 30 (40%) patients the pancreas was the more severely injured organ, in 26 (34.7%) patients the duodenum was more severely injured and 19 (25.3%) patients had an equally severe injury score involving both pancreas and duodenum.

Sixty nine (92%) of the 75 patients had other associated intra-abdominal injuries. The liver was the most frequently injured organ n=42 (56%), followed by stomach n= 26 (34.7%) and colon n=23 (30.7%) (Table 3).Thirty five (46.7%) of the 75 patients had associated vascular injuries of which the IVC was the most frequent major vascular injury (Table 4).

Table 3 Associated intra-abdominal injuries in 75 patients with pancreatoduodenal injuries

	Total n=75	Died n=21	Alive n=54
Liver	42	13	29
Stomach	26	7	19
Colon	23	11	12
Kidney	18	4	14
Jejunum	14	2	12
Gallbladder	10	2	8
Diaphragm	5	9	4
Spleen	2	0	2

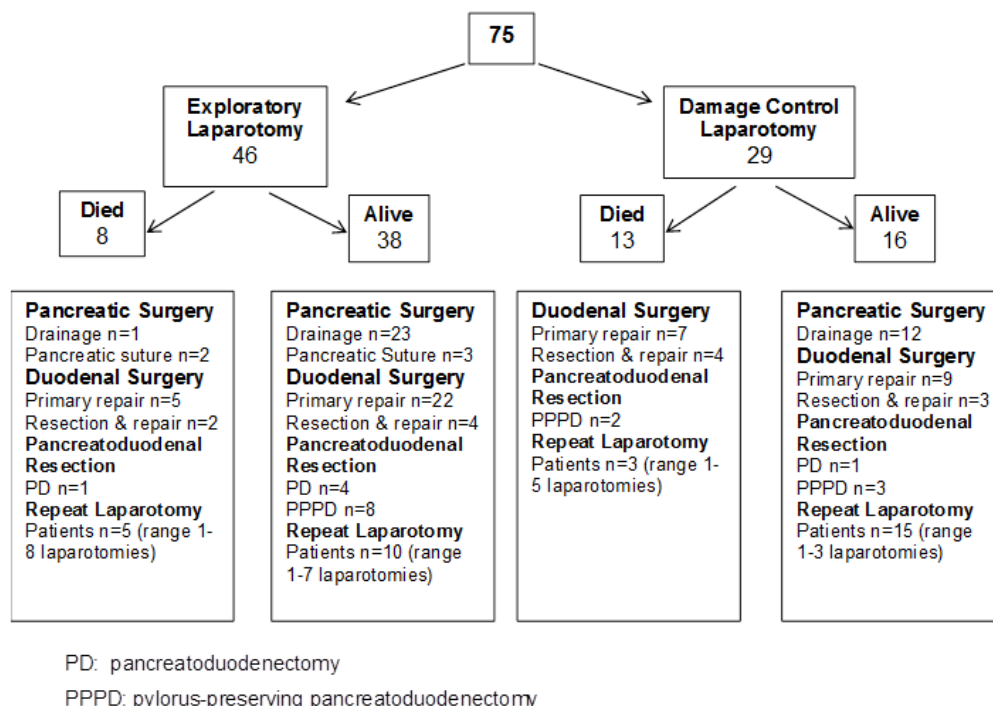
Table 4 Associated vascular injuries in 35 of 75 patients with pancreatoduodenal injuries

	Total n=35	Died n=15	Alive n=20
Inferior Vena Cava	23	8	15
Portal Vein	5	4	1
Superior Mesenteric Vein	5	5	0
Superior Mesenteric Artery	4	4	0
Hepatic artery	2	1	1
Renal artery	2	0	2
Renal vein	2	1	1
Colic artery	2	0	2
Celiac trunk	1	0	1

12.3.1 Operative management

The 75 patients underwent a total of 161 (range 1-9) operations. Forty six patients had definitive treatment of the CPDI during the initial operation while 29 patients with multiple complex injuries had DCS followed by planned re-operation and definitive management when stable (Fig 1). Nineteen of the 75 patients underwent a pancreatoduodenectomy, either during the initial operation (n=13) or later after the DCS (n=6). In the remaining 56 patients, the duodenal injuries were managed with debridement and single layer primary suture in 43 patients while 13 had resection of the injured part of the duodenum and primary end-to-end anastomosis with a feeding jejunostomy and intraluminal tube drainage. In the same 56 patients the pancreatic injury was managed by suture to control bleeding and large bore external drainage using Silastic suction drains (Fig 1). Forty two of the 75 patients also had significant liver injuries which were treated with packing and temporary intra-operative vascular inflow control.

Figure 1 Surgical management in 75 patients with combined pancreatoduodenal injuries



12.3.1.1 Definitive surgery during the index operation

Thirteen patients (12 men, 1 woman, median age 27, range 14-53 years, mean Apache II score 2, range 0-4) underwent a pancreaticoduodenectomy and reconstruction as part of their initial definitive management. Eight patients had a pylorus-preserving pancreatoduodenectomy and five a standard Whipple resection. In three patients the reconstruction arrangement used a modified Flautner-Imanaga technique (Imanaga 1960, Flautner, Tihanyi et al. 1985) to allow postoperative ERCP access to retrieve the transanastomotic biliary stent used to drain an associated major intrahepatic ductal injury. In three patients the bile duct was ligated and the gallbladder was preserved and used as the conduit for biliary drainage into the jejunum as the bile duct measured <3mm and the jejunum was grossly oedematous which jeopardized a conventional

anastomosis. In six patients the pancreatic stump was joined to the back wall of the stomach as a single layer pancreatogastrostomy and in seven patients an end to side stented pancreatojejunostomy was fashioned. The median duration of intensive care was 5 days (range 1-20 days). Twelve patients survived. Median duration of hospital stay for survivors was 29 days, (range 14-94 days). Eleven of the 12 survivors had substantial morbidity.

12.3.1.2 Damage Control

Thirteen (45%) of the 29 patients who underwent DCS died, 10 without having a second operation (Fig 1). Twenty one of the 29 were severely shocked on admission and 20 had associated major vascular injuries. Twenty eight of the 29 required a median 18 (range 4-49) unit blood transfusion. The composite injury grading score was grade 1=1, grade 2=1, grade 3=7, grade 4=6, grade 5=14. Six patients (5 men, 1 woman, median age 20, range 16-39 years, mean Apache II score 12, range 4-18) who, in addition to non-reconstructable AAST grade 5 pancreatoduodenal injuries, also had associated major visceral venous injuries involving the portal vein, IVC, renal and lumbar veins underwent the initial DCS followed by physiological stabilisation in ICU (median duration 38 hours, range 11- 92 hours) subsequently underwent a pancreaticoduodenectomy and reconstruction (Fig 1). All 6 had associated abdominal injuries with a mean of 3.3 (range 3-6) organs involved. Five patients had a pylorus-preserving pancreatoduodenectomy. One patient who had an extensive pancreatoduodenal injury involving the pylorus which precluded pylorus preservation had a standard Whipple resection. The median duration of intensive care treatment was 7 days, (range 1-21 days) and median hospital

stay was 28 days, (range 3-93 days). The proportion of patients undergoing damage control increased from 17 of 40 (42.5%) during 1995 to 2004 to 12 of 20 (60%) between 2005 and 2015 while the pancreatoduodenectomy rate decreased from 25% to 10%.

12.3.2 Morbidity

Postoperative complications occurred in 63 (84%) patients (Table 2). Significantly more complications related to bleeding, DIC and hypovolaemic shock occurred in those patients who eventually died (Table 5) and significantly more fistulas occurred in patients who survived (Table 6). Postoperative complications according to the Clavien–Dindo Classification (Dindo, Demartines et al. 2004) were as follows: 5 (7.9%) had a grade I complication, 11 (17.5%) patients had grade II complications, 6 (9.5%) had grade IIIa, 11 (17.5%) had grade IIIb, 7 (11.1%) had grade IVa, 2 (3.2%) had grade IVb and 21 (33.3%) had grade V complications.

Pancreatic and duodenal complications

Fourteen of the 54 patients who survived developed a pancreatic complication. Eleven patients had pancreatic fistulas and 3 patients developed acute pancreatitis. One patient received somatostatin analogue therapy. Seven of the pancreatic fistulas resolved on conservative treatment and four required an ERP and pancreatic duct sphincterotomy and endoscopic stenting before resolution. Seventeen of the 75 patients developed duodenal complications. Ten duodenal fistulas and one duodenal stenosis occurred in the group of patients who survived (Table 5). Fifty two patients (69.3%) required intensive care unit

(ICU) admission. Median ICU and total hospital stay (range) were 6 (1–46) and 20 (1–178) days respectively.

Table 5 Morbidity

	Died	Alive
	n=21	n=54
Complications related to bleeding Bleeding/ Disseminated Intravascular Coagulation / hypovolemic shock/ acidosis	21	23 <i>P value 0.046</i>
Systemic complications		
Respiratory failure/pneumonia	4	22
Renal failure	4	5
Systemic sepsis	5	5
Wound infection and wound dehiscence	0	10
Deep Vein Thrombosis	0	2
Urinary Tract Infection	0	1
Jaundice	0	1
Intra-abdominal non-pancreatic-duodenal complications		
Abdominal sepsis	4	11
Abdominal collections (all)	0	6
Biliary fistula	1	5
Abdominal compartment syndrome	0	1
Bowel ischemia	1	0
Bowel obstruction	0	4
Pancreaticoduodenal complications		
Acute pancreatitis	0	3
Pancreatic fistula	0	11
Duodenal fistula	6	10
Duodenal stenosis	0	1

Table 6 Bivariate analysis of factors associated with overall morbidity

	Total number of patients	Patients who developed Complications	Patients with no complications	<i>p-value</i>	OR	95% CI
	75	63 (84%)	12 (16%)	---	---	---
Trauma						
Gunshot Wounds	57	48 (76.2%)	9 (75%)	0.669	0.9	- 4.6
Blunt	13	11 (17.5%)	2 (16.7%)	0.649	1.4	0.0 - 14.7
Stab	5	4 (6.3%)	1 (8.3%)			
Revised Trauma Score (RTS)						
<7.8	39	36 (57.1%)	3 (25%)	0.041	4.0	1.0 - 15.0
7.8	36	27 (42.9%)	9 (75%)			
Presence of Shock						
Yes	38	36 (57.1%)	2 (16.7%)	0.010	6.7	1.2 - 66.0
No	37	27 (42.9%)	10 (83.3%)			
Patients transfused						
Yes	65	56 (88.9%)	9 (75%)	0.195	2.7	0.6 - 11.5
No	10	7 (11.1%)	3 (25%)			
Damage Control Surgery						
Yes	29	29 (46%)	0	0.002	-	-
No	46	34 (54%)	12 (100%)			
Composite Grading						
1, 2	9	4 (6.3%)	5 (41.7%)	0.004	0.09	0.02 - 0.4
3, 4, 5	66	59 (93.7%)	7 (58.3%)			
Associated Abdominal Injuries						
Nil*, 1 or 2 organs	56	47 (74.6%)	9 (75%)	0.644	0.9	0.2 - 3.8
3 or more organs	19	16 (25.4%)	3 (25%)			
Number of patients with associated						
Vascular Injuries						
Yes	35	32 (50.8%)	3 (25%)	0.091	3.1	0.8 - 11.5
No	40	31 (49.2%)	9 (75%)			

* 6 patients had pancreatoduodenal injuries only

12.3.3 Mortality

Overall 21 (28%) patients (GSW n=18, blunt n=1, stab wounds n=2) died as a result of the injuries at a median of 3 days after the injury (range: 1-42 days). Seventeen patients who died were shocked on admission and had a RTS range of 4.5–7.1 (Table 7). Five of the 21 patients who died had three or more associated abdominal injuries (Table 7), 13 had liver injuries, 11 had colon

injuries, 9 had diaphragm and 7 had stomach injuries (Table 7). Fifteen patients had an associated major venous injury in addition to a grade 5 pancreatoduodenal injury. Five patients died in the operating theatre of uncontrolled bleeding due to bullet injuries involving a combination of complex visceral vascular injuries of both IVC and portal vein and pancreas and liver. Three patients died subsequently after reconstruction of complex injuries involving the celiac axis, SMA and SMV. Nine of the 29 died as a consequence of multiple injuries involving closed head injury (n=1), cervical and thoracic spine (n=2) and chest (n=6) in addition to the pancreatic and intra-abdominal injuries. Eight patients developed multi-organ failure secondary to intra-abdominal sepsis and died after a prolonged hospital stay. All 8 required further laparotomies (1 repeat laparotomy n=4, 4 repeat laparotomies n=2, 5 repeat laparotomies n=1, 8 repeat laparotomies n=1) for multilocular intra-abdominal sepsis which did resolve after percutaneous ultrasound-guided catheter drainage. Two patients died of cardiac events, 2 died of DIC and one of septic shock. The composite injury scores were grade 3: n=3, grade 4: n=7 and grade 5: n=11.

Table 7 Bivariate analysis of factors associated with overall mortality

	Total number of patients	Patients who died	Patients alive	p-value	OR	95% CI
	75	21 (28%)	54 (72%)	---	---	---
Trauma						
Gunshot Wounds	57	18 (85.7%)	39 (72.2%)	0.074	5.5	0.7 - 250
Blunt	13	1 (4.8%)	12 (22.2%)	0.172	0.125	0 - 1.4
Stab	5	2 (9.5%)	3 (5.6%)			
Revised Trauma Score (RTS)						
<7.8	39	17 (81%)	22 (40.7%)	0.002	6.2	1.9 - 19.8
7.8	36	4 (19%)	32 (59.3%)			
Presence of Shock						
Yes	38	17 (81%)	21 (38.9%)	0.002	6.7	2.0 - 21.5
No	37	4 (19%)	33 (61.1%)			
Patients transfused						
Yes	65	20 (95.2%)	45 (83.3%)	0.163	4.0	0.5 - 184
No	10	1 (4.8%)	9 (16.7%)			
Damage Control Surgery						
Yes	29	13 (61.9%)	16 (29.6%)	0.010	3.8	1.4 - 10.9
No	46	8 (38.1%)	38 (70.45)			
Composite Grading						
1, 2	9	0	9 (16.7%)	0.042	0.0	0.0 - 0.9
3, 4, 5	66	21 (100%)	45 (83.3%)			
Associated Abdominal Injuries						
Nil*, 1 or 2 organs	56	16 (76.2%)	40 (74.1%)	0.551	1.1	0.3 - 3.5
3 or more organs	19	5 (23.8%)	14 (25.9%)			
Number of patients with associated Vascular Injuries						
Yes	35	15 (71.4%)	20 (37%)	0.007	4.2	1.4 - 12.3
No	40	6 (28.6%)	34 (63%)			

* 6 patients had pancreaticoduodenal injuries only

Sixteen of the 19 patients who underwent a pancreatoduodenectomy and reconstruction survived. Twelve of the 13 patients who had a pancreatoduodenectomy during the initial laparotomy survived. One patient who had IVC, portal vein and SMV repairs died of MOF 3 days after the pancreatoduodenectomy and reconstruction. On review he should have had initial DCS and delayed definitive surgery. Four of the six patients who had an initial DCS and delayed definitive surgery. Four of the six patients who had an initial DCS and a delayed PD survived. The 2 patients who died had received massive blood transfusions for severe associated vascular injuries. The first

died of refractory coagulopathy and multi-organ failure after 48 hours while the second died of drug-resistant intra-abdominal sepsis, fungemia, ARDS and multi-organ failure after 24 days. In four patients complications were managed non-operatively.

Mortality was significantly associated with $RTS < 7.8$ ($p=0.002$), shock on presentation ($p=0.002$), increased composite grade of injury ($p=0.04$), the need for damage control surgery ($p=0.01$) and the presence of vascular injuries overall ($p < 0.007$) and major visceral venous injuries ($p < 0.011$) as well as the combination of vascular plus the total number of associated organs injured ($p < 0.046$). Thirty five (46.7%) of the 75 patients had associated vascular injuries of whom 15 (43%) died. The IVC was the most frequent major vascular injury with a survival rate of 15/23 (Table 4). One of the fourteen patients who had portal vein, SMV and SMA injuries survived.

12.4 Discussion

This analysis of a large prospectively documented cohort of patients with severe combined pancreatoduodenal injuries treated in a high volume Level 1 Trauma Center reports the increasing role of damage control laparotomy in complex injuries and the substantial use of primary pancreatoduodenectomy in stable patients and delayed secondary pancreatoduodenectomy in unstable patients with grade V injuries. This study shows that only one-sixth of patients who had sustained pancreatic injuries overall had synchronous duodenal injuries and while most CPDI had associated intra-abdominal injuries, importantly, almost half also had major vascular injuries with significant portend. Unlike previous reports on pancreatoduodenal injuries, one quarter of patients in this study

underwent a pancreatoduodenectomy and 40% had an initial damage control laparotomy. A feature in this study is the use of a composite grading system for CPDI. Further salient findings in this paper are the impact of associated life-threatening visceral vascular injuries on survival and the outcome of simplified duodenal repair and the avoidance of previously recommended protective bypass surgery to redirect gastric content into the jejunum.

The lack of consensus on the current optimal treatment of CPDI has hampered progress and several factors in particular have prevented a detailed and accurate comparative analysis of the treatment options. Historically, morbidity and mortality data reporting CPDI has varied widely due to selection bias, exclusion of patients with associated vascular injuries and deaths occurring intra-operatively or within the first 24 hours (Kao, Bulger et al. 2003, Recinos, DuBose et al. 2009, Sharpe, Magnotti et al. 2012). The management of complex injuries has also differed substantially and remains mired in historical dogma (Flynn, Cryer et al. 1990). A wide spectrum of surgical options have been recommended for CPDI, ranging from conservative to radical and have included simple closure and drainage, debridement and primary repair, resection and end-to-end anastomosis, a selection of duodenal diversions and pancreatoduodenectomy (Graham, Mattox et al. 1979, Moore and Moore 1984, Feliciano, Martin et al. 1987, Mansour, Moore et al. 1989, Lopez, Benjamin et al. 2005). There remains disagreement in the current literature regarding the relative merits of the various options. Earlier studies recommended that additional surgical procedures to bypass and protect the duodenal repair using pyloric exclusion or diverticulization of the duodenum were always necessary in

complex injuries. Most authorities now believe this approach has been overused and current data would suggest that complex prolonged supplementary procedures in severely injured patients are inappropriate and are often unnecessary (Ivatury, Nallathambi et al. 1985, Flynn, Cryer et al. 1990).

Although the pancreas and duodenum are intimately connected and function anatomically and physiologically as a unit, most publications analyze pancreatic and duodenal injuries separately without considering combined injuries as a single entity. Published mortality rates for pancreatoduodenal injuries vary widely ranging from 3% to 38% due to variable referral patterns in the respective datasets, inclusion of differing ratios of blunt-to-penetrating PD trauma and data dilution by inclusion of low grade injuries treated non-operatively (Table 8). In a report from Ben Taub General Hospital, Houston, Texas, 308 pancreatic injuries and 175 duodenal injuries were treated over a nine year period of whom 68 had combined pancreatic and duodenal injuries (Graham, Mattox et al. 1979). Eighteen patients had a primary repair and external drainage while 50 required more extensive procedures which included duodenal diversion and pyloric exclusion (n=32), pancreatoduodenectomy (n=6), and a variety of other procedures (n=12). Operative mortality rate was 26.4%, including five patients who died intraoperatively. Only one death was directly attributable to the pancreatoduodenal injury. Similarly, in a study from Denver, Colorado, 34 patients with CPDI were treated operatively (Moore and Moore 1984). Twelve patients had sump drainage and repair while 22 required more extensive procedures including pyloric exclusion with or without pancreatic resection in

14, and pancreatoduodenectomy in one patient. Overall mortality rate was 9% with 2 early deaths secondary to associated injuries and 1 late death due to the pancreatoduodenal injury. Complications directly related to the combined injury occurred in 47% of the patients including a 20% incidence of pancreatic fistulas (Moore and Moore 1984).

In a subsequent updated report by Feliciano from Ben Taub General Hospital 129 patients with combined pancreatoduodenal injuries were treated, of whom 104 (81%) had penetrating wounds (Feliciano, Martin et al. 1987). Primary repair or resection of one or both organs with pyloric exclusion and gastrojejunostomy (68 patients) and drainage was used in 79 patients (61%). Simple primary repair was used in 31 patients (24%), and 19 patients (15%) had either a pancreatoduodenectomy (13 patients) or no repair before exsanguination (6 patients). Major pancreatoduodenal complications including pancreatic fistulas (26%), intra-abdominal abscess (17%), and duodenal fistulas (7%) occurred in 108 (84%) patients who survived more than 48 hours. Thirty-eight (30%) of the 129 patients died (Feliciano, Martin et al. 1987). In a later 12-year review of 62 patients with CPDI from Denver, Colorado, grade I and II injuries (39%) were treated with simple repair and drainage, grades III and IV (51%) were managed primarily by pyloric exclusion, while grade V injuries (10%) underwent pancreatoduodenectomy (Mansour, Moore et al. 1989). Pancreatic and duodenal complications developed in 35% and 2% respectively. The overall mortality was 19% of whom 83% died within the first 24 hours from exsanguination or severe head injuries (Mansour, Moore et al. 1989). In a report by Lopez from Ryder Trauma Center in Miami, 33 of 240 patients who

sustained a pancreatic or duodenal injury had CPDI (Lopez, Benjamin et al. 2005).The majority of patients (82%) had penetrating injuries of whom 72% had sustained gunshot wounds and 45% had an associated major vascular injury. Thirteen of the 33 (39%) patients presented in extremis and underwent an abbreviated laparotomy. Overall complication rate was 36% including fistula (Donadon, Costa et al. 2016), abscess, pancreatitis and organ dysfunction with an 18% mortality rate.

Table 8 Published morbidity and mortality of pancreatoduodenal injuries

Study	Number of patients	Gunshot Wounds	Blunt	Stab	Whipple	Duodenal complications	Pancreatic complications	Overall morbidity	Mortality
Graham, 1979*	68	50	13	5	5	3 (4.4%)	24 (35.3%)	44 (64.7%)	18 (26.5%)
Moore, 1984	34	18	15	1	1	1 (2.9%)	14 (41.2%)	12 (35.3%)	3 (8.8%)
Feliciano, 1987*	129	89	25	15	10	7 (5.4%)	28 (21.7%)	No data	38 (29.5%)
Mansour, 1989	62	30	25	7	4	1 (1.6%)	22 (35.5%)	No data	12 (19.4%)
Lopez, 2005	33	24	6	3	0	2 (6.1%)	3 (9.1%)	No data	6 (18.2%)
This study, 2015	75	57	13	5	19	17 (22.6%)	14 (18.7%)	63 (84%)	21 (28%)

**both papers from Ben Taub General Hospital, Houston, Texas and contain overlapping data*

This study emphasizes the lethality of complex CPDI especially when combined with major visceral vascular injuries involving the portal vein, the superior mesenteric vein and the inferior vena cava. Almost half the patients had associated visceral vascular injuries and 45% of the DCS group died without having a second definitive operation. Previous studies from Cape Town reported an overall mortality rate of 15.7% (Krige, Kotze et al. 2015) for pancreatic injuries and mortality rates of 5.1% (Krige, Kotze et al. 2014), 16.4% (Krige, Kotze et al. 2011) and 21% (Chinnery, Krige et al. 2012) for stab wounds, blunt injuries and gunshot wounds of the pancreas. In an analysis of the TARN database which is the largest trauma database in Europe, the mortality for blunt PD trauma was 17.6% and was 12.2% for penetrating PD trauma. Variables predicting mortality after pancreatic trauma were increasing age, ISS, haemodynamic compromise and not having undergone an operation (O'Reilly, Bouamra et al. 2015). However, unlike this study, the results and outcome of the TARN database are skewed as the majority of patients had only AAST grade I pancreatic and duodenal injuries and a third of patients had no operation during their hospital admission (O'Reilly, Bouamra et al. 2015). Overall mortality in this study was 28% which reflects a selected group of patients with multiple injuries in which one third of deaths were due to exsanguination as a consequence of unsalvageable vascular injuries. The results of this study represent the full spectrum of CPDI and included the very worse end of the injury continuum and incorporated patients who arrived in the operating room in extremis, some of whom died soon after initiation of the laparotomy. This study demonstrated that $RTS < 7.8$, shock on presentation, increased composite grade of injury, the need for damage control surgery and the presence of vascular

injuries overall and major visceral venous injuries as well as the combination of vascular plus the total number of associated organs injured are inter-related risk factors which influence mortality (Lucas 1977, Tyburski, Dente et al. 2001, Krige, Beningfield et al. 2005). Other authors have similarly noted major bleeding from associated vascular injuries to be a significant factor in early deaths (Wang, Li et al. 2007, Antonacci, Di Saverio et al. 2011).

A major difference in this study, compared to other series, is the number of patients who had a pancreatoduodenectomy. There are very few detailed reports on pancreatoduodenectomy in patients with CPDI (Table 8). Most authorities agree that a pancreatoduodenectomy for trauma is seldom necessary and should only be undertaken in stable patients with grade 5 injuries of the head of pancreas and duodenum in whom a repair is not feasible (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). While there are clear guidelines on the timing of pancreatoduodenectomy, details regarding the optimal reconstruction method after a trauma Whipple are scant. Data show that a severe pancreatic injury compounded by visceral and vascular injuries exponentially increases the complexity and mortality of the operative intervention (Wang, Li et al. 2007). There is consensus that patients with major pancreatic injuries and hemodynamic instability due to uncontrollable bleeding, coagulopathy, hypothermia, or acidosis should have an abbreviated laparotomy with DCS and subsequent re-exploration, resection and reconstruction when stable (Thompson, Shalhub et al. 2013). While this practice is now self evident, the procedure has not been universally applied. In an analysis of the National Trauma Data Bank pancreaticoduodenal injury register from 2008-2010, 13

(33%) of 39 patients who underwent a trauma Whipple died at a median of 7 days (range 1-180 days). In the majority of cases the Whipple was performed during the index operation and most procedures were done within 6 hours of admission (van der Wilden, Yeh et al. 2014). Similarly, in an analysis of 11,011 patients in the US Nationwide Inpatient Sample (NIS) who required an operation for pancreatic and duodenal injuries over a 12 year period, 48.9% underwent a distal pancreatectomy, 3% had a total pancreatectomy and 3% had a radical pancreatoduodenectomy or a radical pancreatectomy, a notion which is contrary to and deviates markedly from current principles espoused for pancreatic trauma surgery (Ragulin-Coyne, Witkowski et al. 2014).

As neither the optimal implementation of pancreatoduodenectomy for CPDI nor the timing of reoperation after initial DCS have been standardized, both require careful strategic consideration. The criteria used in the selection of patients who would benefit from an abbreviated laparotomy in this study were based on data from our Trauma Center which found that base excess, pH and core temperature were significant pre-operative predictors of death and recommended that specific trigger points at which DCS should be implemented were pH <7.20, base excess exceeding -10.5 and core temperature <35°C²⁰. In this study we have shown the usefulness of a staged procedure with initial damage control surgery followed by a delayed secondary pancreatoduodenectomy and reconstruction in critically injured patients with associated major vascular trauma. In a study from Seattle 12 of 15 patients with severe pancreatoduodenal injuries underwent DCS with or without the initial stage of a Whipple resection as their first operation (Thompson, Shalhub

et al. 2013). The pancreatoduodenectomy was completed in two stages in eight patients (67%) and in three stages in four patients (33%). Two of the 12 died (17%) of bleeding and MOF (Thompson, Shalhub et al. 2013).

Although this study represents the largest current series of patients with CPDI, there are several caveats and limitations that should be considered when interpreting these results. A substantive limitation is that these data were generated from and reflect the outcome of a highly select cohort of patients treated in a large volume well-resourced tertiary referral academic Level I Trauma Center with a special interest in HPB trauma and access to “round-the-clock” experienced pancreatic surgical assistance. Although these data may be similar to other major academic institutions or trauma centres, it is not applicable to community-based hospitals. In contrast to other studies which have not included consecutive patients or have incomplete follow-up, this study design avoided these pitfalls by excluding non-measurable biases and included all patients who had a laparotomy and included those who died in the operating room either during or after completion of DCS. Furthermore, in this longitudinal cohort study the detailed prospective documentation of complications and any cause of death within 30 days of surgery provided consistent and objective endpoints. The unvalidated composite grading system used in this study demonstrates a difference in complications and mortality between grades 1-2 vs 3-5 which may be an important component for assessing and comparing future reports on complex combined injuries as this feature has been lacking in past papers.

In conclusion, this study demonstrates a paradigm shift in the overall management of complex combined pancreatoduodenal injuries and emphasizes that no single operation is appropriate for all pancreatoduodenal injuries²⁹. Operative intervention in each patient should ideally be individualized and surgeons need to have a flexible strategy and should be familiar with the full range of surgical techniques required for repair (Graham, Mattox et al. 1979). The data and outcome in this study are in keeping with current concepts in DCS (Roberts, Bobrovitz et al. 2015, Roberts, Bobrovitz et al. 2016) and in line with recent authoritative guidelines for duodenal injuries (Malhotra, Biffl et al. 2015). The optimal management of grade 1-3 duodenal injuries is primary repair or resection of the damaged segment of duodenum and anastomosis without the need for elaborate bypass procedures or pyloric exclusion to exclude the duodenum and protect the duodenal repair. Once haemostasis has been achieved, most pancreatic head injuries with an intact ampulla and no devitalization can effectively be managed with external sump drainage. If an ensuing pancreatic fistula persists, treatment with endoscopic stenting is safe. Pancreatoduodenectomy should be reserved for a select group of patients who have complex combined pancreatoduodenal injuries in whom repair is not feasible and who are haemodynamically stable (Antonacci, Di Saverio et al. 2011). In the small cohort of patients who require initial damage control, both the pancreatoduodenectomy and the reconstruction should be delayed until the subsequent definitive operation. Despite using DCS in CPDIs, morbidity (84%) and mortality (28%) remain substantial. Careful selection of patients undergoing PD resulted in 84% survival. Associated vascular injuries, major visceral venous injuries and combined vascular and associated organs injured influenced

outcome and mortality. This study strongly supports the closely integrated and collegial collaboration between trauma and pancreatic surgeons in managing complex pancreatic injuries. In this study all the pancreatic head resections were done by pancreatic surgeons working in conjunction with trauma surgeons which should be the model applied in modern trauma surgery. We advocate that there should be a low threshold to involve an experienced pancreatic surgical team with complex pancreatic injuries day and night or if that level of access is not directly available, the prudent surgeon should apply DCS principles and transfer a stable patient expeditiously to the closest major centre which has the necessary facilities and expertise.

CHAPTER 13

Management of pancreatic injuries during damage control surgery. An observational outcomes analysis of 79 patients treated at an academic Level 1 Trauma Centre

13.1 Introduction

Since the initial publication by Stone et al (Stone, Strom et al. 1983) and the subsequent seminal description by Rotondo et al (Rotondo, Schwab et al. 1993), damage-control methodology has transformed the way trauma surgery is implemented. The concept is now widely accepted as an essential strategy in the management of complex trauma aggravated by coagulopathy, hypothermia and acidosis (Shapiro, Jenkins et al. 2000). Despite these advances mortality rates in patients who have life-threatening pancreatic trauma combined with injuries to contiguous organs including liver, bile ducts, duodenum and vena cava, superior mesenteric and portal veins remain substantial (Chrysos, Athanasakis et al. 2002, Recinos, DuBose et al. 2009). A severe pancreatic injury compounded by visceral and vascular injuries exponentially increases the complexity of operative intervention (Krige, Beningfield et al. 2005). Outcome is influenced by the amount of blood lost, the magnitude and duration of shock, the speed and efficacy of resuscitation and the quality and nature of the ultimate surgical intervention (Farrell, Krige et al. 1996, Wang, Li et al. 2007). In combined pancreatic and visceral injuries early mortality is usually the result of major blood loss from associated vascular injuries or severe adjacent organ injuries (Krige, Beningfield et al. 2005). Late mortality is largely a consequence

of persistent or resistant intra-abdominal sepsis and multiple organ failure (Wang, Li et al. 2007).

In a recent expert appropriateness rating study on indications for use of damage control surgery, there was expert opinion consensus that DCS was useful in combined pancreaticoduodenal injuries with intraoperative hemodynamic instability or in devascularisation or massive destruction of the pancreatic head/pancreaticoduodenal complex (Roberts, Bobrovitz et al. 2015, Roberts, Bobrovitz et al. 2016). There is however no published strategy nor are there clear guidelines on the management of a pancreatic injury during damage control surgery. Equally, few published series have specifically addressed outcome of damage control surgery in patients with an associated pancreatic injury. This study evaluated the role of damage control surgery to determine which factors influenced mortality in a large cohort of patients who sustained pancreatic injuries and underwent DCS at a major trauma centre using a previously defined protocol.

13.2 Patients and Methods

13.2.1 Study design

The study design was a retrospective cohort analysis of prospective data of all patients with a pancreatic injury who underwent damage control surgery. The study used a large institutional database which documents all patients with pancreatic injuries treated at the Level 1 Trauma Centre and the Hepatopancreatobiliary and Surgical Gastroenterology units in Groote Schuur Hospital, Cape Town. Other aspects of pancreatic injury management using this

data base have been published (Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014, Krige, Nicol et al. 2014). After approval by the University of Cape Town Human Research Ethics Committee, an analysis was done using data on consecutive patients who had pancreatic injuries and damage control surgery at Groote Schuur Hospital between January 1995 and April 2014.

13.2.2 Data collection

Patient data were collected and validated by a trained surgical clinical reviewer. Standardized data definitions and reliability audits were conducted on a routine basis to ensure data quality. For the purposes of this study all clinical records including operative, intensive care, radiology, endoscopic and multidisciplinary clinic reports of patients with pancreatic injuries were accessed from the database and reviewed (Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014, Krige, Nicol et al. 2014). The data recorded for each patient used a specifically designed binary and narrative form comprising 60 items with 54 data fields. Variables recorded in the database included patient demographic data, mechanism of injury, revised trauma score (RTS), associated intra- and extra-abdominal injuries, anatomic site and grade of pancreatic injury, operative findings and surgical management, presence and type of pancreas-related and other complications, duration of hospital stay and mortality. Hospital length of stay and ICU length of stay were expressed in calendar days. No patient was excluded from the analysis and included every operation even if the patient had exsanguinated on the operation table during DCS.

13.2.3 Definitions

DCS was defined as an abbreviated emergency trauma laparotomy that required temporary abdominal closure and secondary definitive surgery. Patient undergoing DCS were critically injured and *in extremis* and underwent a staged triple phase procedure which incorporated an initial truncated laparotomy to control bleeding and bowel contamination with temporary vacuum-assisted abdominal wall closure (phase 1) followed by physiological resuscitation and optimization in the ICU (phase 2) and further definitive management during a subsequent operation (phase 3). Shock was defined as a systolic blood pressure less than 90mm Hg. In this study definitions and criteria for pancreatic injury grade (Moore, Cogbill et al. 1990), pancreatic fistula (Bassi, Derveniz et al. 2005), organ dysfunction (Moore, Sauaia et al. 1996), infectious complications (Bone, Balk et al. 1992) and septic shock (Dellinger, Levy et al. 2008) used internationally validated guidelines. Mortality was defined as any cause of death in hospital after a pancreatic injury.

13.2.4 Damage control laparotomy

Initial resuscitation was according to Advanced Trauma Life Support (ATLS) guidelines. Rapid pre-operative evaluation included relevant physical examination, endotracheal intubation when necessary, insertion of resuscitation lines, selected trauma abdominal and cardiac sonography and chest radiographs. Urgent surgery was performed in patients who had an acute abdomen with signs of peritonitis, or evidence of major intra-abdominal bleeding. Damage control laparotomy was applied in critically injured patients with severe metabolic acidosis indicated by a pH <7.20, lactate levels >5

mmol/L, hypothermia with a core temperature <35 °C, coagulopathy as evidenced by the onset of non-mechanical bleeding or patients requiring a massive transfusion of more than 10 units of packed red blood cells (Kairinos, Hayes et al. 2010, Timmermans, Nicol et al. 2010). In brief, the fundamental principles included an abbreviated laparotomy and the use of sutures, staples and packs to rapidly control intra-abdominal bleeding and close visceral perforations. The laparotomy was concluded with temporary abdominal wall closure (Navsaria, Bunting et al. 2003) and transfer to an intensive care unit for invasive monitoring, cardiopulmonary support and urgent volume replacement to correct acidosis, coagulopathy and hypothermia and restore normal physiology.

13.2.5 Operative management of pancreatic injury

The philosophy underpinning management was not to embark on complex and prolonged definitive surgery in a hypotensive, hypothermic, coagulopathic and acidotic patient but to abbreviate intervention to essential intra-operative life-saving procedures by applying modern damage control principles (stop bleeding, control contamination, restore physiology to normality) and delay the pancreatic resection and reconstruction until more favourable conditions were present. Emergency laparotomy used a midline incision to provide access to the abdomen. Treatment of life-threatening priority injuries took precedence over the operative management of pancreatic injuries. Intra-abdominal bleeding was controlled by suture and packing, and bowel contamination was contained by sutures or staples. Only then was the site and extent of the pancreatic injury systematically assessed.

For pancreatic injuries to the left of the portal-mesenteric axis, the anterior surface of the pancreas was examined by entering the lesser sac through the gastrocolic ligament and the posterior aspect was assessed by dividing the peritoneum along the inferior border which allowed elevation of the pancreas. Patients who had a major laceration of the body or tail of the pancreas with a likely pancreatic duct injury and bleeding from an associated splenic vein, splenic artery or splenic injury had a rapid stapled completion distal pancreatectomy and splenectomy as part of the procedure to control bleeding. Non-life threatening injuries of the pancreatic body were drained and no attempt was made to escalate the intervention or prolong the primary DCS. Grade 3 injuries of the body and tail of the pancreas without bleeding were managed by temporary external Silastic catheter drainage with the intention of later resection.

Operative management of pancreatic head or combined pancreatic head and duodenal injuries was based on the hemodynamic stability of the patient, the magnitude and extent of associated injuries and the location and severity grades of the both the pancreatic and duodenal injuries, strategic details of which have been published (Krige, Beningfield et al. 2005, Chinnery, Krige et al. 2012, Krige, Nicol et al. 2014). The duodenum was exposed using an extended Kocher manoeuvre. The ligament of Treitz was divided to allow assessment of the fourth part of the duodenum. When indicated, the ascending colon and small bowel were mobilized to allow full assessment of the third part of the duodenum and uncinate process of the pancreas, especially if vascular injuries were suspected. Minor lacerations of the pancreas without visible duct damage

and without devitalization of pancreatic tissue (grade 1 and 2 injuries) were managed by closed external suction drainage. Combined injuries involving the pancreas and duodenum were treated on the specific merits of the individual case. Duodenal injuries were treated with debridement of the edges and a single layer primary repair (grade 1 and 2), or with resection of ischemic tissue and a primary end-to-end anastomosis (grade 3) with intraluminal tube drainage. A feeding jejunostomy was fashioned when there was involvement of greater than 50% of the duodenal circumference and a primary repair or resection and anastomosis was undertaken. Pancreatoduodenectomy was restricted to patients who had non-reconstructable injuries with destruction of the head of the pancreas, duodenum and ampulla (grade 4 and 5) and was always done as a secondary staged procedure after the DCL. Immediate concern was control of bleeding and containment of bile and bowel content. The bile duct was ligated below the cystic duct entry and the gallbladder drained externally with a 16Fr Foley catheter. Injured duodenum was repaired or if irretrievably damaged was stapled closed at the level of the pylorus and jejunum. After conclusion of the laparotomy with temporary abdominal wall closure, the ventilated patient was transferred to an intensive care unit for invasive monitoring, cardiopulmonary support and continued damage control resuscitation with blood component therapy to correct acidosis, coagulopathy and hypothermia and restore normal physiology. The patient was returned to the operating room for the definitive procedure only after correction of coagulation, base deficit and hypothermia and when inotrope support was no longer necessary.

Definitive management of the pancreatic injury in a stable patient during the second laparotomy commenced with a careful re-evaluation of the extent of the pancreatic and duodenal injuries. Grade 3 injuries of the body and tail of the pancreas with a likely main pancreatic duct injury were treated by a stapled distal pancreatic resection. Duodenal injuries were treated with debridement of the edges and a single layer primary repair (grade 1 and 2), or with resection of ischemic tissue and a primary end-to-end anastomosis (grade 3) with intraluminal tube drainage. A feeding jejunostomy was fashioned when there was involvement of greater than 50% of the duodenal circumference and a primary repair or resection and anastomosis was undertaken. In patients who had grade 4 or 5 injuries of the head of the pancreas, duodenum and ampulla in whom a pancreatoduodenectomy was inevitable, the resection was expedited using a harmonic scalpel. The uncinate process of the pancreas was not resected to reduce operating time and to avoid the superior mesenteric vessels. A pylorus preserving pancreatoduodenectomy (PPPD) was done in all patients in whom the pylorus was not irretrievably damaged. In those requiring a gastric resection a classic Whipple resection was done. The end-to-side pancreatojejunostomy was stented internally with an 8 cm 5Fr silastic paediatric feeding tube cut to size. 4 cm of stent were inserted into the pancreatic duct and the remaining 4 cm placed in the jejunum. In patients in whom the jejunum was grossly oedematous after prolonged resuscitation and unsuitable for an anastomosis, the pancreatic stump was drained into the stomach. The biliary anastomosis was a modification of the standard method used for bile duct reconstruction after iatrogenic injuries (Hofmeyr, Krige et al. 2015). The duct was spatulated to increase anastomotic size using an anterior vertical incision

positioned to avoid the 3 and 9 o'clock bile duct arteries. All biliary anastomoses were stented with an 8 cm long 5Fr silastic paediatric feeding tube. In situations where the bile duct measured less than 3mm in width and gross oedema jeopardised the bile duct to jejunum anastomosis, the gall bladder was preserved and used as the conduit for the biliary-enteric anastomosis. In high-risk stented biliary anastomoses a modified Imanaga reconstruction technique was used in which the duodenojejunostomy was created end-to-side as the most proximal jejunal anastomosis to allow post-operative ERCP and biliary stent retrieval (Imanaga 1960).

13.2.6 Management of postoperative intra-abdominal, pancreatic and duodenal complications

Intra-abdominal collections were drained with 5Fr percutaneous catheters using ultrasound or CT guided placement. Endoscopic 7 Fr pancreatic duct stents were used for persistent pancreatic fistulas (Thomson, Krige et al. 2014) and an endoscopically placed covered self expanding metal duodenal stent was used for prolonged large volume drainage of lateral duodenal fistulas (Chinnery, Bernon et al. 2011).

13.2.7 Data analysis

Descriptive statistics reporting medians with ranges, and frequency distributions, were used to characterize the cohort. Between-group comparisons were made using the Student t-test or Wilcoxon sum rank test for normal and non-normally distributed data respectively. The Pearson's χ^2 or Fisher's exact tests were used for analysis of categorical variables, and odds ratios (ORs) with

95 per cent confidence intervals (CI) were calculated. Univariate and then forward stepwise multivariate logistic regression analyses were performed to identify factors associated with the occurrence of death. A p value of < 0.05 was considered statistically significant. The data were analysed using Stata software version 11 (StataCorp LP, College Station, Texas, USA).

13.3 Results

13.3.1 Patient characteristics

Three hundred and twelve patients were treated for pancreatic injuries during the study period of whom 79 (71 men, 8 women, median age: 26 years, range 16–73 years) underwent an initial damage control laparotomy. In each of the 79 patients a pancreatic injury was confirmed at laparotomy. Sixty two (78%) patients had sustained gunshot injuries, 14 (18%) had blunt abdominal injuries due to high speed motor vehicle accidents either as pedestrians (n=7) unrestrained drivers (n=4) or passengers (n=1), or assault (n=1) or polytrauma after being struck by a train (n=1) and in 3 (4%) patients the pancreatic injury was due to an abdominal knife wound (Table 1).

13.3.2 Anatomic site and severity of injury

Thirty-five (44%) patients had proximal pancreatic injuries, involving the head (n=30) or neck (n=5) of the pancreas. Forty-four patients had an injury of the body or tail of the pancreas. Twenty (25.3%) patients had AAST grade 1 or 2 pancreatic injuries and 59 (74.7%) patients had AAST grade 3, 4 or 5 pancreatic injuries (Table 1).

Table 1 Bivariate Analysis of factors associated with mortality

	Total no. of patients	Patients who died	Patients alive	<i>p-value</i>	OR	95% CI
	79	43 (54.4%)	36 (45.6%)			
Trauma						
GSW	62	33 (76.7%)	29 (80.5%)	0.53	----	
Blunt	14	9 (20.9%)	5 (13.9%)			
Stab	3	1 (2.3%)	2 (5.6%)			
RTS						
<7.8	63	36 (83.7%)	27 (75%)	0.34	1.7	0.6 - 5.0
7.8	16	7 (16.3%)	9 (25%)			
Presence of shock						
Yes	63	36 (83.7%)	27 (75%)	0.34	1.7	0.6 - 5.0
No	16	7 (16.3%)	9 (25%)			
No of patients transfused						
Yes	76	41 (95.3%)	35 (97.2%)	1.00	0.6	0.0 - 4.7
No	3	2 (4.7%)	1 (2.8%)			
BTF (median units)	18 (4-89)	20 (4-89)	18 (4-47)	0.07	----	
Lapsed time to DCS (median hours)	3 (1-17)	3 (1-17)	3 (1-8)	0.37	----	
AAST						
1, 2	20	9 (20.9%)	11 (30.6%)	0.33	0.6	0.2 - 1.6
3, 4, 5	59	34 (79.1%)	25 (69.4%)			
Associated injured organs						
Liver	52	27 (62.8%)	25 (69.4%)	0.12	----	
Stomach	30	16 (37.2%)	14 (38.9%)			
Duodenum	30	14 (32.6%)	16 (44.4%)			
Colon	26	16 (37.2%)	10 (27.8%)			
Spleen	26	13 (30.2%)	13 (36.1%)			
Kidney	23	9 (20.9%)	14 (38.9%)			
Diaphragm	17	10 (23.2%)	7 (19.4%)			
No of patients with associated vascular injuries						
Yes	41	28 (65.1%)	13 (36.1%)	0.01	3.3	1.3 - 8.3
No	38	15 (34.9%)	23 (63.9%)			
Associated injured vascular structures						
IVC	18	10 (23.2%)	8 (22.2%)	0.01	----	
Aorta	4	3 (7%)	1 (2.8%)			
Portal Vein	8	7 (16.2%)	1 (2.8%)			
Splenic Vein / Artery	3	3 (7%)	0			
Renal Vein / Artery	9	5 (11.6%)	4 (11.1%)			
SMA / SMV	7	7 (16.3%)	0			
Other	9	6 (14%)	3 (8.3%)			

13.3.3 Associated injuries

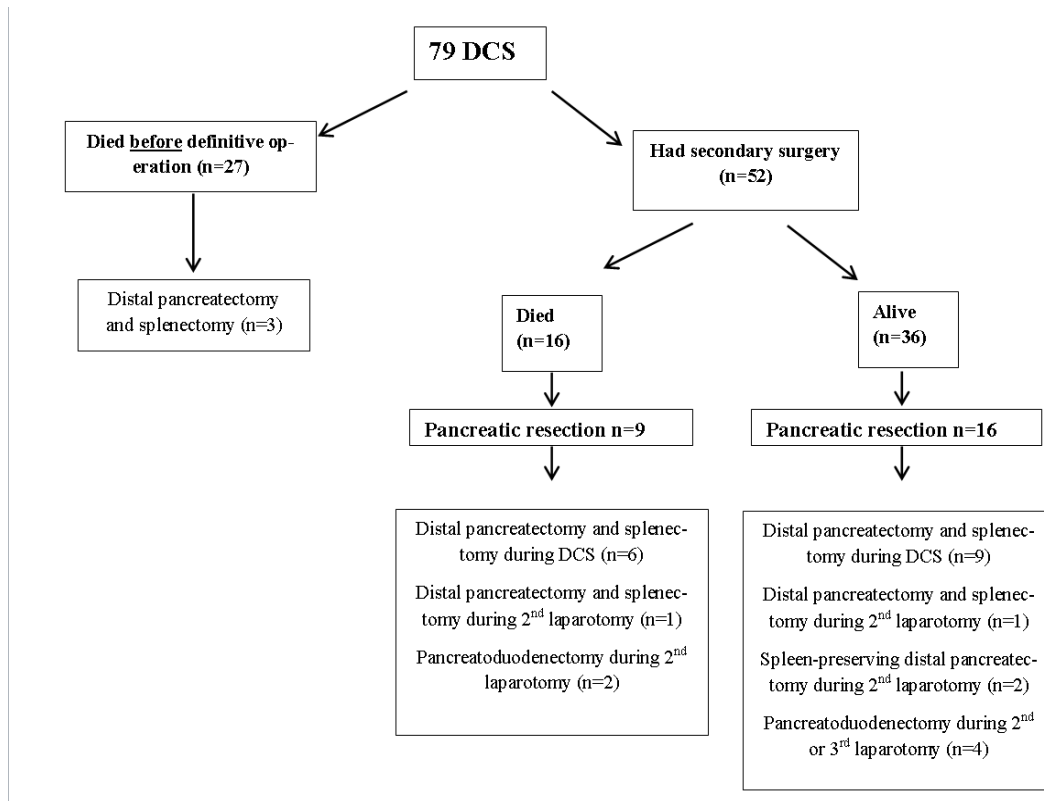
The 79 patients had a total of 327 associated injuries (Table 1). Intra-abdominal injuries accounted for most (200/327, 61.2%) of the associated injuries. The mean number of organs injured was 3 per patient (range 0-6), and vascular injuries (60/327, 18.3%) occurred in 41 (52%) patients (Table 1). The associated extra-abdominal injuries (67/327, 20.5%) involved mainly chest (n=27), head (n=11), limbs (n=14), neck (n=2) and spine (n=13).

13.3.4 Operative management

The 79 patients underwent a total of 187 (range 1-7) operations. Twenty-seven (34.2%) patients died without having a second operation (Figure 1). The remaining 52 patients had two or more laparotomies (range 2-7). Overall 28 (35%) patients underwent a pancreatic resection either during the index damage control operation or subsequently as a secondary procedure when stable. During initial DCS, 18 patients who had grade 3 pancreatic injuries with either near-complete transection or a severely damaged body or tail of pancreas with evidence of a main duct injury had a completion distal pancreatectomy and splenectomy. Subsequently a further 10 patients had definitive completion pancreatic surgery during a subsequent laparotomy when stable. Of these 10 patients, two had a distal pancreatectomy and splenectomy, two had a spleen-preserving distal pancreatectomy and six patients had a pancreatoduodenectomy and reconstruction. Fifty two of the 79 patients also had significant liver injuries which were treated with temporary intra-operative vascular inflow control and perihepatic packing (Krige 2000, Nicol, Hommes et al. 2007). In addition to the 17 splenectomies done in

conjunction with the pancreatic resection, nine other patients had splenic injuries requiring splenectomy and drainage of lesser pancreatic injuries.

Figure 1 Operative management and pancreatic specific surgery



13.3.4.1 Pancreatoduodenectomy

Six patients (5 men, 1 woman, median age 20, range 16-39 years, mean Apache II score 12, range 4-18) who, in addition to non-reconstructable AAST grade 5 pancreatoduodenal injuries, also had associated major visceral venous injuries of the portal vein, IVC, renal and lumbar vein injuries underwent the initial damage control surgery followed by ICU stabilisation (median duration 38 hours, range 11- 92 hours) subsequently underwent a pancreatoduodenectomy and reconstruction. All six had associated abdominal injuries with a mean of

3.3 (range 3-6) organs involved. Five underwent a pylorus preserving pancreatoduodenectomy and one patient who had a pancreatoduodenal injury which involved the pylorus and precluded pylorus preservation had a standard Whipple resection. The median duration of intensive care was 6 days, (range 1-20 days) and median hospital stay was 29 days, (range 3-94 days).

13.3.4.2 Combined pancreatoduodenal injuries

Thirty patients had combined pancreatoduodenal injuries, 16 of whom had AAST grade 5 injuries with maximal disruption of the pancreatic head and duodenum and 6 underwent delayed pancreatoduodenectomy and reconstruction (see above). The remaining 14 patients had grade II and III duodenal injuries and grade I and II pancreatic injuries. The duodenal injuries were treated with debridement, single layer primary repair, intraluminal tube drainage and a nasojejunal enteric feeding tubes and the pancreatic injuries were treated with closed suction drainage.

13.3.5 Morbidity

13.3.5.1 Overall

Postoperative complications occurred in 77 of the 79 (97%) patients. Significantly more complications related to bleeding, DIC and hypovolaemic shock occurred in patients who eventually died and significantly more abdominal sepsis and fistulas developed in patients who survived (Table 2).

Table 2 Post-operative complications

	DIED	ALIVE	<i>p Value</i>
	n=43	n=36	
Acute complications related to bleeding			
Bleeding/DIC/hypovolemic shock/acidosis	37	12	0.02
Systemic complications			
Respiratory failure	12	19	0.20
Renal failure	11	7	0.79
Septic shock	6	13	0.12
Intra-abdominal complications			
Abdominal sepsis	8	17	0.06
Enterocutaneous and biliary fistulas	1	7	0.03
Anastomotic disruption	2	3	0.66
Other complications	2	6	0.15

13.3.5.2 Pancreatic complications

Ten of the 36 patients who survived developed a pancreatic complication. Nine patients had pancreatic fistulas and one had a peripancreatic fluid collection which was drained percutaneously. Seven of the nine patients with pancreatic fistulas resolved on conservative treatment which included nasojejunal enteral feeding and intravenous octreotide. Two patients with prolonged persistent pancreatic fistula drainage required endoscopic intervention and pancreatic duct stenting before resolution.

13.3.6 Mortality

Overall 43 (GSW n=33, blunt n=9, stab=1) (54.4%) of the 79 patients died as a result of injuries sustained at a median of 1.5 days after the injury (range: 1 - 23 days, mean 5.8 days). Thirty six of the 43 were shocked on admission and had a RTS <7.8 (Table 1). Twenty of the 43 patients who died had three or more

associated abdominal injuries and 27 had major liver injuries (Table 1). Twenty-seven (34.2%) patients died without having a second operation, 24 of whom were shocked on admission, 20 of whom had an associated major vascular injury (Figure 1). Nine (multiple GSW n=7, pedestrian MVA n=2) of the 27 died of uncontrolled bleeding in the operating theatre due to a combination of complex visceral vascular injuries involving SMA, SMV and portal vein, pancreas and liver. Eighteen of the 27 died subsequently in the ICU before definitive surgery as a consequence of multiple injuries involving head (n=6), cervical and thoracic spine (n=4), chest (n=16) and limb (n=8) in addition to the pancreatic and intra-abdominal injuries. Sixteen patients underwent a total of 56 laparotomies and died at a median of 7 days (range: 5-52) due to MOF (n=6), sepsis (n=7), head injury (n=2) and ischemic small bowel (n=1) after a second, third or fourth laparotomy (Fig 1).

Two of the six patients who underwent a pancreatoduodenectomy and reconstruction after DCS died (Fig 1). Both had received massive blood transfusions for complex associated vascular injuries; the first patient received 18 units of packed cells and blood products including fresh frozen plasma, platelets and cryoprecipitate but died of refractory coagulopathy and multi-organ failure after 48 hours. The second patient died of drug resistant infection after 24 days complicated by recurrent intra-abdominal sepsis, fungemia, multi-organ failure and ARDS despite percutaneous drainage and 3 laparotomies. The remaining four patients had complications which were managed non-operatively.

Mortality was significantly (3-fold) related to the presence of associated vascular injuries overall ($p<0.01$), the presence of major visceral venous injuries ($p<0.01$) as well as the combination of vascular plus the total number of associated organs injured ($p<0.04$). Neither RTS nor shock on presentation were predictive of death (Table 1). Thirty six of 43 patients who had a systolic BP of $<90\text{mmHg}$ on admission to hospital subsequently died compared to 27 of the 36 patients who were shocked and did not die. In a univariate logistic regression model, not only vascular injury ($p=0.03$), but also the number of vascular structures ($p=0.01$) and total units of blood transfused were significantly associated with mortality. On multivariate regression analysis, however, correcting for collinearity, the only risk factor that approached significance was the total units of blood transfused ($p=0.05$).

13.4 Discussion

This single centre observational cohort study is distinctive in several respects. To my knowledge this is the largest series documenting damage control laparotomy in a subset of severely injured, exsanguinating patients with a pancreatic injury and multiple other competing injuries. Four-fifths of the patients had sustained abdominal gunshot injuries and three-quarters had AAST grade 3, 4 or 5 pancreatic injuries. This study shows the lethality of complex injuries of the head and neck of the pancreas when combined with major visceral vascular injuries involving the portal vein, the superior mesenteric vein and the inferior vena cava. More than half the patients had associated visceral vascular injuries and one-third of the total group died without having a second definitive operation. In a previous report from Cape Town the overall

mortality rate was 15.7% for pancreatic injuries and mortality rates were 5.1% (Krige, Kotze et al. 2014), 16.4% (Krige, Kotze et al. 2011) and 21% (Chinnery, Krige et al. 2012) for stab wounds, blunt injuries and gunshot wounds of the pancreas. Overall mortality in this study was 54% which reflects a highly selected group of patients with multiple injuries in which one third of deaths were due to exsanguination as a consequence of unsalvageable vascular injuries. The degree of pre-operative shock, the presence of major vascular injuries, the number of associated injuries, and the location and complexity of the pancreatic injury are inter-related risk factors which influence mortality (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005, Wang, Li et al. 2007). Other authors have noted major bleeding from associated vascular injuries to be a significant factor in early deaths (Kao, Bulger et al. 2003, Wang, Li et al. 2007).

Neither the optimal timing of DCS nor the timing of reoperation after initial DCS have been standardized in previous publications and both require careful strategic consideration. Other authors have sought to identify criteria which would refine the selection of patients who would benefit from an abbreviated laparotomy (Morris, Eddy et al. 1993, Cosgriff, Moore et al. 1997, Johnson, Gracias et al. 2001, Lee and Peitzman 2006. A wide range of objective measurements including pH <7.30, transfusion of 10 or more units of packed red cells with an estimated blood loss of >4 L, temperature <35°C temperature, base deficit >14 pH, the presence of coagulopathy, early use of damage-control laparotomy [Morris, 1993 #407].(Morris, Eddy et al. 1993) A previous study from our Trauma Centre found that base excess, pH and core

temperature were significant pre-operative predictors of death and recommended that specific trigger points at which DCS should be implemented were pH <7.20, base excess exceeding -10.5 and core temperature <35°C. In this study once the predetermined endpoints of effective resuscitation were achieved with restoration of physiological haemostasis including core temperature, normal coagulation and biochemistry, the patient was returned to the operating room for definitive treatment. Patients who are returned to the operating room within 72 hours have been shown to have improved morbidity and mortality, compared with patients who return later and premature return to the operating room may result in increased rebleeding and the need for additional operations (Nicol, Hommes et al. 2007).

While the principles of DCS are well-defined and the procedure forms an integral part of the management of the multiply injured patient, there is limited clinical or published experience when DCS is applied in the presence of major pancreatic injuries. Despite irrefutable data, some studies provide no evidence of using DCS in patients undergoing major surgery for pancreatic injuries (Ragulin-Coyne, Witkowski et al. 2014). In an analysis of 11,011 patients recorded in the US Nationwide Inpatient Sample (NIS) over a 12 year period with pancreatic and duodenal injuries who required an operation, in the surgical resection group 48.9% underwent a distal pancreatectomy, 3% had a total pancreatectomy and 3% had a radical pancreatoduodenectomy or a radical pancreatectomy, a notion which deviates markedly from current principles espoused for pancreatic trauma surgery (Ragulin-Coyne, Witkowski et al. 2014).

In the present study two-thirds of patients had a completion distal pancreatectomy as part of the initial DCS to control bleeding. Only essential pancreatic surgery was undertaken as part of the procedure to obtain haemostasis by suturing major peripancreatic vessels during the DCS phase. In six patients a delayed pancreatoduodenectomy and reconstruction were done subsequently once stable. This is not a uniform experience and in most studies the major resections were done during the DCS. In the only other substantial report on DCS in patients with pancreatic injuries, a retrospective two centre study from Philadelphia compared DC pack and drain with resection in 42 patients with pancreatic injuries (Seamon, Kim et al. 2009). Overall 14 of the 42 patients had a pancreatic resection. Of the 12 patients who underwent an initial pancreatic resection (11 distal pancreatectomies, 1 pancreatoduodenectomy), all distal pancreatectomies were performed during the initial DC laparotomy while the pancreatoduodenectomy reconstruction was delayed until the subsequent laparotomy (Seamon, Kim et al. 2009). Mortality was substantial and 18 (43%) of the 42 patients died (packing only, 70%; packing with drainage, 25%, distal pancreatectomy, 55%). In this study 12 (86%) of the 14 pancreatic resections were done during initial DCS. The authors reported that the presence of shock or major vascular injury dictated the extent of pancreatic operative intervention (Seamon, Kim et al. 2009). In their study increased mortality rates in patients who were packed without drainage during DCS indicated that this method was ineffective and should be abandoned (Lee and Peitzman 2006).

A pancreatoduodenectomy for trauma is seldom necessary and should only be undertaken in stable patients with grade 5 injuries of the head of pancreas and duodenum in repair is not feasible (Krige, Nicol et al. 2014). There are no clear guidelines on when to do the pancreatoduodenectomy and the optimal reconstruction method after resection of the pancreatic head. Data show that a severe pancreatic injury compounded by visceral and vascular injuries exponentially increases the complexity and mortality of the operative intervention (Krige, Nicol et al. 2014, Krige, Kotze et al. 2015). There is consensus that patients with major pancreatic injuries and haemodynamic instability due to uncontrollable bleeding, hypothermia, acidosis or coagulopathy should have an abbreviated laparotomy with DCS and subsequent re-exploration, resection and reconstruction when stable (Thompson, Shalhub et al. 2013, Krige, Nicol et al. 2014). While this practice should be self evident this is not universally applied. In an analysis of the National Trauma Data Bank pancreatoduodenal injury register from 2008-2010, 13 (33%) of 39 patients who underwent a trauma Whipple died at a median of 7 days (range 1-180 days). In the majority of cases the Whipple was performed during the index operation and most procedures were done within 6 hours of admission (van der Wilden, Yeh et al. 2014).

This study shows the usefulness of a staged procedure with initial damage control surgery followed by a delayed secondary pancreatoduodenectomy and reconstruction in critically injured patients with associated major vascular trauma. Despite being near to death on arrival, four of the six patients survived. Five of the six patients had a pylorus-preserving pancreatoduodenectomy and

the reconstruction was modified to overcome the technical difficulties encountered with an oedematous jejunum and a small pancreatic and bile duct. In a study from Seattle 12 of 15 patients with severe pancreatoduodenal injuries underwent DCS with or without the initial stage of a Whipple resection as their first operation. The pancreatoduodenectomy was completed in two stages in eight patients (67%) and in three stages in four patients (33%). Two of the 12 died (17%) of bleeding and MOF (Thompson, Shalhub et al. 2013).

Major injuries to the pancreas remain a significant source of morbidity even when treated in well-resourced high volume specialist trauma referral centers. Overall reported morbidity rates following pancreatic injury range from 30% to 70% and are primarily related to associated vascular, liver and bowel injuries (Seamon, Pieri et al. 2007, Wang, Li et al. 2007, Thompson, Shalhub et al. 2013, Krige, Nicol et al. 2014, van der Wilden, Yeh et al. 2014). In the current study postoperative complications occurred in 77 of 79 patients and reflects the consequences of a group of severe multiply injured patients. A pancreatic fistula was the most common complication and occurred in 30% of pancreatic resections despite using a stapled transection technique and further closure of the transection margin with figure of 8 sutures and an omental buttress. Most pancreatic fistulas resolved on conservative management and the minority required endoscopic intervention for resolution.

This study has several limitations which require consideration when interpreting the information. Although the data were collected prospectively, this is a non-randomized, single centre study. In addition, these data were generated from and reflect the outcome of a highly select cohort of patients treated in a large

volume well-resourced tertiary referral academic Level I Trauma Centre with a special interest in HPB trauma. In order to achieve a homogenous and clinically valid study population, consecutive patients were evaluated without exclusions and the use of complications and death as the main outcomes provided consistent and objective end-points in the study. Unlike some other studies, no patients were excluded from the analysis and this study included all patients who had a laparotomy and died in the operating room either during or after completion of the DCS. These data are therefore likely to differ substantially from that emanating from smaller institutions with limited trauma management facilities. A further important and relevant consideration is that during the study period there have been substantial advances in intensive care management with invasive monitoring and cardiopulmonary support and improved damage control resuscitation with careful attention to blood component and volume replacement to correct acidosis, coagulopathy and hypothermia and restore normal physiology before definitive surgery (Duchesne, Kimonis et al. 2010).

In conclusion, damage control surgery has substantively changed the conduct of trauma surgery and the management of the severely injured patient (Nicol, Navsaria et al. 2010). However, the effective treatment of complex pancreatic injuries in the presence of both vascular and collateral injuries despite DCS continues to be a major challenge for surgeons dealing with abdominal trauma. This study reports a distressingly high mortality in a subset of severely injured patients who had complex pancreatic injuries combined with major visceral vascular injuries. One-third of the total group did not survive long enough for a definitive operation. However, despite the magnitude of their injuries and the

degree of physiological insult, DCS salvaged 45% of critically injured patients. The indications for DCS in this study (Table 2) mirror those in a recent expert appropriateness rating studies (Roberts, Bobrovitz et al. 2015, Roberts, Bobrovitz et al. 2016). It should be emphasized that these conclusions specifically apply to civilian pancreatic trauma and reflect the experience of a level 1 academic urban trauma referral centre.

CHAPTER 14

Damage control laparotomy and delayed pancreatoduodenectomy for complex combined pancreatoduodenal and venous injuries

14.1 Introduction

Grade 5 injuries of the proximal pancreas with destruction of the pancreatic head are among the most devastating abdominal injuries trauma surgeons are likely to encounter (Krige, Beningfield et al. 2005, Krige, Nicol et al. 2014). The complexity of these critical injuries is further compounded by the consequences of associated collateral vascular damage, especially when involving the vena cava and portal venous system (Krige, Beningfield et al. 2005, Krige, Nicol et al. 2014). Survival is influenced by the severity of associated injuries, the magnitude and duration of shock and the speed and efficacy of surgical intervention (Smego, Richardson et al. 1985, Kao, Bulger et al. 2003, Seamon, Kim et al. 2009). Mortality in severe pancreatic injuries may reach 46% and is highest in those who are hemodynamically unstable (Scollay, Yip et al. 2006). Early mortality is due either to uncontrolled venous bleeding or major adjacent organ injuries (Chrysos, Athanasakis et al. 2002, Subramanian, Dente et al. 2007). Late mortality is usually a consequence of infection or multiple organ failure (Krige, Kotze et al. 2011, Krige and Thomson 2011, Chinnery, Krige et al. 2012).

In the small cohort of patients who have maximal injuries of the pancreatoduodenal complex and in whom there is no other rational surgical

option for survival, a salvage pancreatoduodenectomy may be necessary (Koniaris, Mandal et al. 2000, Koniaris 2004, Krige, Nicol et al. 2014, van der Wilden, Yeh et al. 2014). However, surgical intervention of such magnitude in those who are severely injured can only be contemplated in haemodynamically stable patients. The concept of damage control surgery (DCS) is now an essential element in the management of severely injured patients who are haemodynamically unstable and has dramatically improved outcome (Wang, Li et al. 2007, Nicol, Navsaria et al. 2010, Timmermans, Nicol et al. 2010, Savage and Fabian 2014). In the largest series to date of an emergency pancreatoduodenectomy in patients with complex non-reconstructable pancreatoduodenal injuries we reported an overall survival in 84% (Krige, Nicol et al. 2014). However, there is a lack of accurate and robust data assessing the role of DCS in patients who have combined severe pancreatic and vascular injuries. To date there has been no detailed or comprehensive evaluation of the efficacy of an initial damage control laparotomy followed by a proximal pancreatic resection in this high risk group of patients, nor has there been a critical analysis of the timing of the pancreatoduodenectomy. In order to address this deficiency, this single centre study evaluated patient outcome after initial DCS and subsequent pancreatoduodenectomy and reconstruction with particular appraisal of the advantages of delaying resection in unstable patients with associated major vascular injuries.

14.2 Patients and methods

The study design was a single centre retrospective cohort analysis of prospective data on consecutive patients who underwent damage control

surgery for trauma followed by a pancreatoduodenectomy between May 1, 1995 to April 30, 2014. The study used a registered departmental data base which documents the details of all patients with pancreatic injuries treated at the Level 1 Trauma Centre and the Hepatopancreatobiliary and Surgical Gastroenterology units at Groote Schuur Hospital, Cape Town. Other aspects of pancreatic injury management using this data base have been published previously (Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Nicol et al. 2014). Approval for this study was granted by the institutional review board at the University of Cape Town Health Sciences Faculty.

14.2.1 Data collection

Patient information in the registered departmental data base which is entered prospectively on a standardised electronic *Access* data spread sheet was analysed. During the 20-year study period, 312 patients were treated for pancreatic injuries of whom 14 underwent a pancreatoduodenectomy for complex injuries involving the proximal pancreas and duodenum. Six of the 14 patients who had associated vascular injuries underwent an urgent laparotomy to control intra-abdominal bleeding. All 6 patients had initial DCS because of massive blood loss, hypothermia, acidosis and evidence of coagulopathy. These 6 patients later had a pancreatoduodenectomy when stable and constitute the study group. The remaining 8 patients were haemodynamically stable and underwent a pancreatoduodenectomy and immediate reconstruction during the first laparotomy (Krige, Nicol et al. 2014).

Data fields analysed comprised demographic information, mechanism of injury, time from injury to Trauma Center admission, vital signs on admission including

systolic blood pressure in mmHg, heart rate and details of the clinical examination including details of associated extra-abdominal injuries. The trauma scores recorded included revised trauma score (RTS), injury severity score (ISS) and APACHE II scores. Operative findings and associated intra-abdominal injuries, grade of the pancreatic injury, surgical procedure performed, duration of the operation, post-operative course including the presence and type of pancreas-related and other complications and mortality were recorded. The duration of both ICU and hospital stay were documented. Intra-operative crystalloid and colloid volumes were recorded and the number of packed red cells, fresh frozen plasma and platelet packs given were documented and the accuracy reconciled with blood bank records.

14.2.2 Definitions

Definitions used were as defined and recorded in the study methodology in Chapter 3.

14.2.3 Initial management

Initial resuscitation was implemented using Advanced Trauma Life Support (ATLS) guidelines. Patient management was as outlined in the study methodology in Chapter 3.

14.2.4 Operative management of pancreatic injuries

Initial resuscitation was according to Advanced Trauma Life Support (ATLS) guidelines. Operative management of pancreatic injuries was based on the haemodynamic stability of the patient, the magnitude and extent of associated injuries and the location and severity grades of the both the pancreatic and

duodenal injuries, details of which are outlined in the study methodology in Chapter 3. In this study all 6 patients underwent urgent surgery because of evidence of major intra-abdominal bleeding. All were haemodynamically unstable with major abdominal vascular injuries and multiple visceral injuries which required a massive transfusion aggravated by severe metabolic acidosis, hypothermia and coagulopathy. During the index operation a damage control procedure was performed before delayed definitive intervention, details of which are in the study methodology in Chapter 3.

14.3 Results

Six patients (5 men, 1 woman, median age 20, range 16-39 years) with non-reconstructable AAST grade 5 pancreatoduodenal injuries underwent damage control surgery followed by ICU transfer and physiological stabilisation and subsequent pancreatoduodenectomy and reconstruction when stable (Table 1). Median delay from the time of injury to initial operation was 2 hours, range 1-4 hours. Mean RTS score was 6.508 (range 6.171-7.108), mean ISS was 38 (range 25-75) and mean Apache II score was 12 (range 4-18). All six patients had associated abdominal injuries with a mean of 3.3 (range 3-6) organs involved. All had non-reconstructable injuries of the head of the pancreas involving the main pancreatic duct, intra-pancreatic distal common bile duct with devitalisation and destruction of the blood supply or combinations of both. In addition all six patients had associated major visceral venous injuries with profuse retropancreatic bleeding due to portal vein, IVC, renal and lumbar vein injuries (Table 1).

Five patients had injuries to the IVC (Table 1). In three patients the IVC was partially lacerated and was repaired with sutures. In one of these patients lacerations in both the anterior and posterior caval walls were sutured. In two patients extensive damage precluded repair and the IVC was ligated. In three of these 5 patients a right renal vein laceration extended to the IVC and was repaired in addition to the IVC repair. Two of these patients required a right nephrectomy. In one patient both renal veins were injured and ligated. Patient #5 had in addition problematic bleeding from retroperitoneal lumbar veins. Bleeding from the injured pancreas was controlled. A portal vein laceration was suture repaired in patient #3. Collateral bowel damage was repaired by sutures or staples to avoid contamination. The bile duct was ligated and a tube cholecystostomy inserted to drain the bile externally. The operative site was widely drained with silastic *PenSil* drains. The duration of surgery and fluid requirements during the DCS are given in Table 2.

Table 1 Clinical details of patients who underwent a pancreatoduodenectomy for trauma

Patient no	Age years	Type injury	Associated injuries	Vascular injuries	Type of resection	Postoperative complications (Clavien-Dindo grade)	Duration of hospital stay (days)	Follow-up
1	16 M	MVA	D,K,BD	IVC, right renal vein	PPPD	Pancreatic leak (2)	21	Alive 52 m
2	39 M	GSW	D,L,BD	IVC	PPPD	Coagulopathy MOF (5)	2	Died 2 d
3	36 M	MVA	D,L,BD	PV	Whipple	Wound sepsis (2)	15	Alive 12 m
4	20 F	Stab	D,C,BD	IVC, right renal vein	PPPD	I/A sepsis, MOF, ARDS (5)	24	Died 24 d
5	16 M	GSW	D,C,BD	IVC, lumbar veins	PPPD	Pneumonia, DIC, sepsis (4)	64	Alive 14 m
6	20 M	GSW	D,S,K,BD	IVC, right and left renal veins	PPPD	Renal failure (3)	14	Alive 2 m

Legend

MVA: motor vehicle accident
 C: colon
 D: duodenum
 BD: bile duct
 L: liver
 PPPD: pylorus preserving pancreatoduodenectomy
 MOF: multi-organ failure
 DIC: disseminated intravascular coagulopathy
 ARDS: adult respiratory distress syndrome

GSW: gunshot wound
 S: stomach
 K: kidney
 IVC: inferior vena cava
 PV: portal vein

Median time in ICU for continued resuscitation and physiological stabilisation, before returning to the operation room, was 38 hours (range 11- 92 hours). Five patients had a delayed pylorus preserving pancreatoduodenectomy and one patient who had a pancreatoduodenal injury which involved the pylorus and precluded pylorus preservation underwent a standard Whipple resection. Four patients had a side-to-side hepaticojejunostomy with a stented anastomosis. In two the bile duct measured 2 mm in diameter and in these 2 the gall bladder was preserved, the bile duct ligated below the cystic duct insertion and the

biliary reconstruction completed using a cholecystojejunostomy. In four patients the pancreatic stump was oedematous and the anastomosis was completed by draining the pancreatic remnant into the back wall of the stomach as a pancreaticogastrostomy. Two patients had a conventional end-to-side stented pancreaticojejunostomy. The duration of surgery and fluid requirements during the secondary pancreatoduodenectomy and reconstruction are given in Table 2.

Table 2 Comparison of fluid and blood requirements during the initial DCS and the secondary delayed pancreatoduodenectomy

	Index DCL	Delayed resection
Duration of surgery	113 minutes (range 90-140 minutes)	335 minutes (range 260-395 minutes)
Estimated blood loss	5 456ml (range 2 318-7 665 ml)	1 250ml (850-3 600 ml)
Mean total intra-operative fluid administered	11 150ml (range 8 450-13 320)	6 850ml (range 3 350-9 020)
Crystalloid	5 000ml (range 3 000- 8 500)	3 000ml (range 2 000-6 000)
Blood units packed cells	10 units (range 6-16 units)	6 units (range 0-10 units)
Colloid	1 500ml (range 1 000-2 500)	1 000ml (range 500-1 500)
Fresh frozen plasma	7 units (range 6-8 units)	4 units (range 2-8 units)
Platelets	4 packs (range 2-6)	1 (range 0-4)
Cryoprecipitate	2 (range 0-6)	1 (range 0-2)

Four of the six patients survived. Two patients died in hospital. Both had received massive blood transfusions for complex associated vascular injuries; the first patient received 18 units of packed cells and blood products including fresh frozen plasma, platelets and cryoprecipitate but died of refractory coagulopathy and multi-organ failure after 48 hours. The second patient died of drug resistant infection after 24 days complicated by recurrent intra-abdominal sepsis, fungemia, multi-organ failure and ARDS despite percutaneous drainage and 3 laparotomies. The remaining four patients had complications which were managed non-operatively (Table 2). The median duration of intensive care was

6 days, (range 1-20 days) and the median hospital stay was 29 days, (range 3-94 days).

14.4 Discussion

The surgical management of severe grade 5 injuries of the pancreas and duodenum is complex and demanding, especially if all the elements comprising the pancreatic head are irreparably damaged (Krige, Beningfield et al. 2005, Krige, Nicol et al. 2014). In the small cohort of patients with irretrievable pancreatic head injuries, the only rational surgical option for salvage is a pancreatoduodenal resection and reconstruction (Krige 1997). However, the mortality of an emergency pancreatoduodenectomy in critically injured patients is disproportionately high and exceeds 30% in collected series (Krige 1997, Asensio, Petrone et al. 2003). The main factor responsible for this high mortality is the number and severity of the associated vascular injuries coupled with inappropriately prolonged surgery in haemodynamically unstable patients (Krige, Beningfield et al. 2005, Krige, Nicol et al. 2014).

A previous study from Cape Town reported that a primary pancreatoduodenectomy and reconstruction could be performed safely during the index laparotomy provided the patient was haemodynamically stable without continued blood loss after initial control (Krige, Nicol et al. 2014). Most experts agree that in a critically injured patient who has received a massive blood transfusion and is haemodynamically unstable, hypothermic, coagulopathic and acidotic, prolonged and complex surgery is ill-advised and unlikely to have a satisfactory outcome (Seamon, Pieri et al. 2007, Thompson, Shalhub et al. 2013). Under these adverse conditions, it is crucial to apply damage control

principles and stage the procedure by truncating the initial operation and returning later to complete the resection in a favourable environment and a stable patient (Biffi, Moore et al. 2013, Thompson, Shalhub et al. 2013). This study shows the usefulness of a staged procedure with initial damage control surgery followed by a delayed secondary pancreatoduodenectomy and reconstruction in critically injured patients with associated major vascular trauma. Despite being near to death on arrival, four of the six patients survived.

While there are several small published series (Asensio, Petrone et al. 2003, Thompson, Shalhub et al. 2013) confirming the worth of initial damage control surgery in complex pancreatoduodenal injuries, there is no agreement on how to manage severe pancreatic injuries during the damage control phase. In particular, there are no published data detailing the benefits of instituting an initial damage control operation and delaying the pancreatoduodenectomy and reconstruction in terms of fluid management and blood requirements. Nor are there accurate data on the timing of the relook and reconstruction after ICU resuscitation. Analysis of the existing published data shows that several strategies of dealing with the pancreatic injury during the damage control laparotomy have been proposed and implemented (Table 3). All these methods involve an initial DCS to achieve control of bleeding and prevention of bowel contamination. The management of the pancreatic injury has differed substantially with either a primary resection and delayed reconstruction or a delayed secondary resection with reconstruction (Table 3). The first category involves the initial DCS and an immediate pancreatoduodenectomy with stapled closure of the pancreas, bowel and bile duct. Reconstruction is completed in a

stable patient 36 hours later. This technique was used by Eastlick and colleagues. In their report the pancreas was not anastomosed during the reconstruction and the patient received permanent exocrine replacement (Eastlick, Fogler et al. 1990). Koniaris (Koniaris, Mandal et al. 2000) reported reconstruction 72 hours later and Yong (Yong, Concejero et al. 2008) reconstruction 96 hours later. In a series from India, Gupta, Wig and Garg undertook reconstruction in 4 patients between 6 and 28 weeks after the initial pancreatoduodenectomy (Gupta, Wig et al. 2008). In a report by Mistry and Durham, DCS was performed with a secondary pancreatoduodenectomy 30 hours later and the final reconstruction delayed until 10 weeks later. Pancreatic drainage was never re-established (Mistry and Durham 1996).

Table 3 Pancreatoduodenal resection strategies for complex pancreatic injuries

Category	Pancreatoduodenectomy and reconstruction strategy
A	No damage control laparotomy. Primary pancreatoduodenectomy and reconstruction during the index operation
B	Damage control operation. Primary pancreatoduodenectomy during the index operation. Delayed reconstruction.
C	Damage control operation only. Staged delayed secondary pancreatoduodenectomy with reconstruction.
D	Damage control operation only. Delayed pancreatoduodenal resection. Multistaged delayed reconstruction.

In the USC Medical Centre series reporting 18 patients who had a pancreatoduodenectomy for trauma, 5 (28%) underwent initial damage control and staged reconstructive procedures (Asensio, Petrone et al. 2003). However no data or details are provided on the technique or timing of the reconstruction (Asensio, Petrone et al. 2003). In a two-centre retrospective study from Philadelphia and Columbus, Ohio, detailing 42 patients who had sustained

pancreatic injuries and had DCS, 3 patients underwent a pancreatoduodenectomy, one during the DCS with delayed reconstruction, and 2 had a delayed pancreatoduodenectomy and reconstruction (Seamon, Kim et al. 2009) (Table 3). In a Seattle study 12 patients had DCS as their initial operation and the pancreatoduodenectomy performed in two stages in 8 patients and in three stages in four patients. No information is provided regarding the timing of reconstruction (Biffl, Moore et al. 2013).

The benefits of DCS in the literature are self evident and substantial (Wang, Li et al. 2007, Chovanes, Cannon et al. 2012, Ball 2014). The objective is survival of the patient and the prevention and correction of those factors which threaten survival. It is prudent and safer to delay primary definitive care and use a staged approach especially if the patient has significant physiological derangement (Savage and Fabian 2014). A previous study from the Cape Town Trauma Centre found that age, base excess, pH and core temperature were significant pre-operative predictors of death (Timmermans, Nicol et al. 2010). The study recommended that the specific trigger points at which DCS should be implemented were when pH falls below 7.20, the base excess exceeds -10.5 and the core temperature is less than 35⁰C (Timmermans, Nicol et al. 2010). This is especially important when associated vascular repair has necessitated cross-clamping of major vessels with consequent reduced tissue perfusion.

The optimal timing of reoperation after initial DCS has not been standardized in previous publications and requires careful strategic consideration. The Cape Town policy has been that once the predetermined endpoints of effective

resuscitation were achieved with restoration of physiological haemostasis including core temperature, normal coagulation and biochemistry, the patient was returned to the operating room for definitive treatment. Premature return to the operating room may result in increased rebleeding and the need for additional operations (Nicol, Hommes et al. 2007). Patients who are returned to the operating room within 72 hours have been shown to have improved morbidity and mortality, compared with patients who return later.

The effective treatment of complex pancreatic injuries associated with vascular damage continues to be a major challenge for surgeons dealing with abdominal trauma. The surgical decision to implement a damage control strategy is not regarded as a surgical retreat but recognition that successful trauma surgery demands attention not only to the extent and magnitude of collective injuries sustained but also demands a careful assessment of the physiological status of the patient. It is important to identify the need for DCS at an early stage. Careful patient selection is crucial for survival and prolonged surgical procedures consciously avoided. It is essential to appreciate that a damage control approach can be used in smaller hospitals where experience with complex pancreatic and vascular injuries may be limited or where the necessary resources are not available. After control of bleeding and contamination the patient should be transferred to a major trauma center where both trauma and HPB surgeons experienced in the management of proximal pancreatic resections and reconstruction are available.

CHAPTER 15

Management of complex pancreatic injuries: benchmarking postoperative complications using the Accordion classification

15.1 Introduction

Major pancreatic resections are technically complex procedures, especially so when performed as an emergency in severely injured patients who also have multiple other injuries (Thompson, Shalhub et al. 2013, van der Wilden, Yeh et al. 2014). There are wide variations in the reported overall postoperative morbidity rates after pancreatic injuries due to non-standardised analyses and a lack of comprehensive datasets which specifically document outcome after resection of complex pancreatic injuries (Scollay, Yip et al. 2006, Antonacci, Di Saverio et al. 2011, Sharpe, Magnotti et al. 2012). The absence of an appropriate and defined methodology to measure and register peri-operative outcome, precludes the generation of validated outcome data, fundamental to accurate benchmarking of surgical performance and internal quality control (Yoon, Chalasani et al. 2013). Both the number and severity of postoperative complications are recognised key short-term surrogate markers of the quality of operative intervention and surgical outcome (Martin, Brennan et al. 2002).

The development and application of internationally accepted and validated International Study Group of Pancreatic Surgery (ISGPS) definitions of complications in elective pancreatic surgery has provided accurate, robust and consistent data which has allowed reliable comparisons of, for example, the incidence of post-operative pancreatic fistulas (Bassi, Dervenis et al. 2005),

bleeding (Wente, Veit et al. 2007) and delayed gastric emptying (Wente, Bassi et al. 2007) (DGE). Similarly, the 6-scale Accordion Severity Grading System (ASGS) which discriminates post-operative complication severity following elective surgery on the basis of escalating interventional criteria, is now widely accepted as a credible, scoring system which is easy to apply and is reproducible with minimal inter-observer variability (Strasberg, Linehan et al. 2009).

Earlier studies assessing outcome after pancreatic resections for major pancreatic injuries have applied unqualified primary endpoints with differing descriptions and definitions which consequently have resulted in flawed conclusions. The Cape Town group has previously evaluated other aspects of pancreatic trauma and, as one of the world's busiest high volume academic trauma centres, has sufficient prospective granular data available to investigate organ-specific research questions (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2015). The aim of this research project was to provide a detailed analysis to benchmark the severity of complications after pancreatic resection for severe trauma in a civilian patient population using the ASGS.

15.2 Methods

15.2.1 Study design

A retrospective analysis of prospectively collected data derived from a comprehensive and dedicated institutional pancreatic trauma database which includes clinical, operative and postoperative information on all patients treated

for pancreatic trauma was performed of all adult patients who had a resection for a pancreatic injury between January 1990 and April 2015. Current guidelines of good clinical practice were followed and data collection and analysis were approved by the departmental, institutional and university research and ethics review boards. A statistical review of the study was performed by a biomedical statistician.

15.2.2 Data collection

Details of the methodology used are provided in the study methodology in Chapter 3

15.2.3 Classification of surgical complications

Postoperative complications were scored using the expanded ASGS (Strasberg, Linehan et al. 2009) (Table 1). In this study grade 1 and 2 complications were regarded as minor, grade 3 as moderate, 4 as serious and grade 5 complications as life-threatening. Grade 6 complications resulted in the death of the patient and included death from any cause within 30 days of surgery. The overall complication rate was reported as the number of patients with at least one complication. In patients with several complications, the highest graded complication was used for analysis of the complication severity.

Table 1 Expanded Accordion Classification

		Expanded Accordion Classification (Levels of Severity)
1	Mild	Requires only minor invasive procedures that can be done at the bedside. Physiotherapy and the following drugs are allowed: antiemetics, antipyretics, analgesics and electrolytes
2	Moderate	Requires pharmacologic treatment with drugs other than such allowed for minor complications, for instance antibiotics. Blood transfusions and total parenteral nutrition are also included.
3	Severe	Invasive procedure / No GA, requires management by an endoscopic, interventional procedure or re-operation without general anesthesia
4	Severe	Invasive procedure under GA or single organ system failure, Requires management by an operation under general anesthesia or results in single organ system failure
5	Severe	Organ system failure and invasive procedure under GA or multisystem organ failure, such complications would normally be managed in an increased acuity setting but in some cases patients with complications of lower severity might also be admitted to an ICU
6	Deaths	Postoperative death

15.2.4 Definitions

Details of definition applied are provided in the study methodology in Chapter 3.

15.2.5 Initial and operative management of pancreatic injuries

Details of initial and operative management of pancreatic injuries and damage control laparotomy are given in the study methodology in Chapter 3.

15.2.6 Management of postoperative intra-abdominal, pancreatic and duodenal complications

Postoperative intra-abdominal collections were drained percutaneously using ultrasound- or CT-guided catheter placement. Endoscopic therapy techniques

were used to treat persistent pancreatic and duodenal fistulas and pancreatic fluid collections (Chinnery, Bernon et al. 2011, Thomson, Krige et al. 2014).

15.2.7 Data analysis

The data were analysed using Stata version 11 (StataCorp. 2009. Stata: Release 11. Statistical Software. College Station, TX: StataCorp LP). For bivariate analysis the Pearson chi-square or Kruskal-Wallis tests were used for categorical variables, and the non-parametric Wilcoxon rank-sum test for numerical variables. Univariate and multivariate logistic regression models were used to evaluate the odds ratios (OR) and 95% confidence intervals of clinical variables (while excluding collinearity). All statistical tests were two-tailed and a p-value < 0.05 was considered statistically significant.

15.3 Results

15.3.1 Patient demographics

Between January 1990 and April 2015 a total of 461 patients were treated for pancreatic injuries of whom 130 had a pancreatic resection for either grade 3, 4 or 5 injuries. Most patients were men and 74% had sustained penetrating injuries, predominantly gunshot wounds (GSW) (Table 2). One third of patients were shocked on admission and 30 patients (23.1%) had an emergency operation.

15.3.2 Anatomic site and severity of injury

One-fifth of patients had pancreatic head or neck injuries and four-fifths had injuries involving either the pancreatic body or tail. More than 80% sustained AAST grade 3 injuries and 18% had grade 4 or grade 5 injuries (Table 2).

15.3.3 Associated injuries

Fifty-two patients (40%) had 77 extra-abdominal injuries of whom 65 (50%) had three or more associated adjacent organ injuries, predominantly involving the liver and spleen. Fourteen patients had an isolated pancreatic injury. Twenty-four patients (18%) had associated vascular injuries, of whom 15 had an IVC injury. The presence of an associated vascular injury correlated significantly ($p=0.007$) with shock at presentation.

Table 2 Demographic and clinical data for patients with and without complications

	Total (n=130)	Those with complications (n=95)	Those without complications (n=35)	p-Value
Age Median (range)	26 (13-73)	28 (13-73)	24 (15-59)	0.0064*
Mechanism of Injury GSW Stab Blunt	88 (67.7%) 7 (5.4%) 35 (26.9%)	63 (66.3%) 6 (6.3%) 26 (27.3%)	25 (71.43%) 1 (2.86%) 9 (25.71%)	0.6490 [#]
Hospital stay Median (range)	8 (1-255)	23 (1-255)	9 (5-58)	0.0000*
ICU stay	77 (59.23%)	68 (71.58%)	9 (25.71%)	0.0000**
Number ICU days Median (range)	3 (0-153)	4 (0-153)	3 (0-7)	0.0000*
RTS < 7.8 7.8	49 (37.69%) 81 (62.3%)	44 (46.32%) 51 (53.68%)	5 (14.29%) 30 (85.71%)	0.001**
No of patients shocked on admission	46 (35.4%)	42 (44.21%)	4 (11.43%)	0.001**
No of patients who received a blood transfusion	103 (79.2%)	79 (83.16%)	24 (68.57%)	0.069**
Units of blood transfused Median units (range)	8 4.5 (0-124*)	8 (0-124)	2 (0-28)	0.0000*
Damage Control Surgery	30 (23.1%)	27 (28.42%)	3 (8.57%)	0.0176**
Pancreatic injury site Head and neck of pancreas Body of pancreas Tail of pancreas	24 (18.5%) 57 (43.8%) 49 (37.7%)	20 (21.05%) 44 (46.32) 31 932.63)	4 (11.43%) 13 (37.14%) 18 (51.43%)	0.0443 [#]
AAST Grade 3 Grade 4 Grade 5	107 (82.3%) 4 (3.1%) 19 (14.6%)	74 (77.89%) 3 (3.16%) 18 (18.95%)	33 (94.28%) 1 (2.86%) 1 (2.86%)	0.0297 [#]
Associated abdominal injuries Nil (isolated injury) 1 or 2 organs injured 3 or more injured	14 (10.8%) 51 (39.2%) 65 (50%)	10 (10.53%) 37 (38.95%) 48 (50.53%)	4 (11.43%) 14 (40%) 17 (48.57%)	0.8833 [#]
Associated injured organs Liver Kidney Spleen Stomach Diaphragm Colon Duodenum	53 (40.7%) 53 (40.7%) 52 (40%) 49 (37.7%) 38 (29.2%) 32 (24.6%) 22 (16.9%)	40 (42.11%) 34 (35.79%) 39 (41.05%) 32 (33.68%) 28 (29.47%) 27 (28.42%) 20 (21.05%)	13 (37.14%) 19 (54.29%) 13 (37.14%) 17 (48.57%) 10 (28.57%) 5 (14.29%) 2 (5.71%)	0.6109 0.0579 0.6876 0.1217 0.9204 0.0983 0.0393*
Pancreatic resection type Pancreatoduodenectomy Distal pancreatectomy and	20 (15.4%) 95 (73%)	19 (20%) 70 (73.68%)	1 (2.86%) 25 (71.4%)	0.0004 [#]

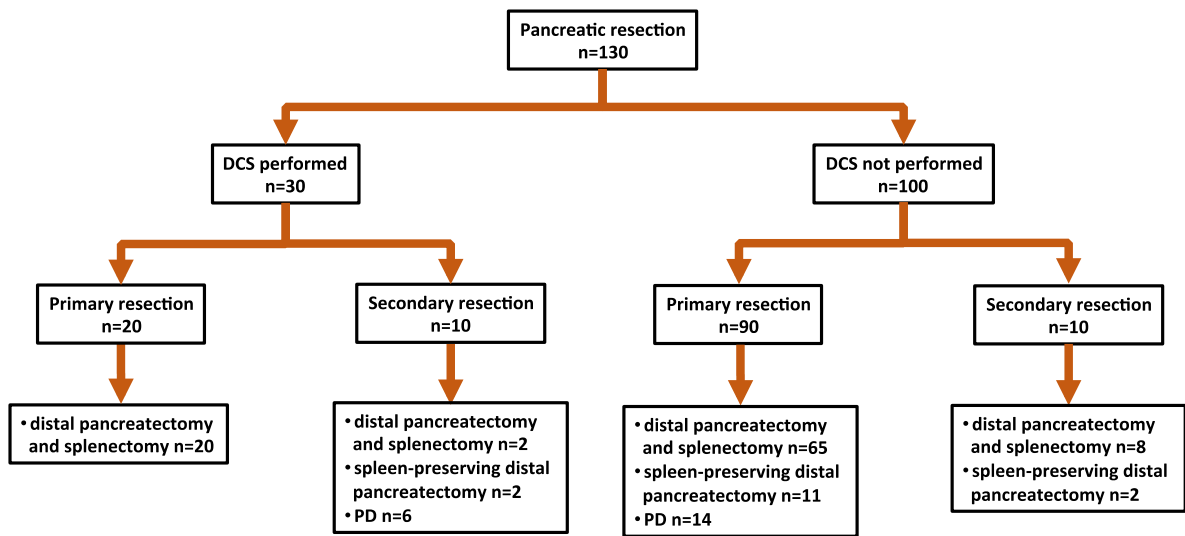
splenectomy Distal pancreatectomy with spleen preservation	15 (11.5%)	6 (6.32%)	9 (25.7%)	
Associated vascular injuries	24 (18.5%)	24 (25.26%)	0 (0%)	0.001**
No of patients who had a repeat laparotomy	58 (44.6%)	55 (57.89%)	3 (8.57%)	0.0000**
No of repeat laparotomies done Median (range)	0 (1-10)	1 (0-10)	0 (0-1)	0.0000*
Death	19 (14.62%)	19 (20%)	0 (0%)	0.004**

**WRS - Wilcoxon rank sum, **CS - Chi square, #KW - Kruskal-wallis, RTS revised trauma score, GSW gunshot wound*

15.3.4 Surgery

The 130 patients underwent a total of 287 laparotomies. Their surgical therapy is detailed in Figure 1. Thirty of the 130 patients (23%) had an initial DCL. Twenty patients had a PD, 14 of which were completed during the index laparotomy and 6 at a second laparotomy. Thirteen patients underwent a pylorus-preserving PD, and 7 had a conventional PD. Fifty-eight patients (44.6%) had a repeat laparotomy (range 1-10), 25 following an initial DCL, 16 for intra-abdominal infection unresolved by percutaneous catheter drainage, 10 for control of intra-abdominal bleeding and 7 for small bowel obstruction. Ninety five patients (73.1%) had a distal pancreatectomy and splenectomy, and 15 (11.5%) had a spleen-preserving distal pancreatectomy.

Figure 1 Pancreatic resection for trauma in 130 patients



15.3.5 Complications

Of the 130 patients who had a pancreatic resection, 35 made an uneventful recovery without any postoperative complications. A total of 238 complications occurred in the remaining 95 patients. The severity of postoperative complications as classified using the ASGS is summarized in Table 3. Twenty-nine events were related to bleeding (intra-abdominal bleeding n=11, DIC n=18) 52 patients had respiratory related complications (21.8% of all events) and 20 had renal complications (8.4% of all events). Systemic sepsis occurred in 19 patients, intra-abdominal infections in 42 and wound infection in nine. Overall complications occurred in 95% of patients who had a PD compared to 69% who had a distal pancreatectomy (p=0.0004).

Thirty-three patients had a total of 36 pancreatic complications following pancreatic resection (Table 4). Twenty-four patients developed a pancreatic fistula, 15 of which resolved on conservative management alone. Nine patients with persistent fistulae had ERCP with sphincterotomy and pancreatic duct

stenting (n=7) or pancreatic duct sphincterotomy only (n=2). Two patients developed symptomatic pseudocysts which were treated with endoscopic ultrasound-guided transgastric stent drainage. Eight patients had peri-pancreatic fluid collections of which seven were successfully drained percutaneously. One patient with a complex pancreato-colo-cutaneous fistula underwent a left hemicolectomy. Three of 20 patients (15%) developed a pancreatic fistula after PD compared to 21 of 110 (19%) after a distal pancreatectomy (Table 4).

Table 3 Accordion Severity Grade in 130 patients

Accordion Severity Grade	Mild	Moderate	Severe: invasive / no GA	Severe: invasive / GA	Severe: organ failure	Death	Total
	1	2	3	4	5	6	n=130
SURGICAL COMPLICATIONS							
Pancreatic							
1. Fistula	1	11	6	6 ^a	--	--	24 (18.5%)
2. Peri-pancreatic collection	--	3	4	1	--	--	8 (6.6%)
3. Pseudocyst	--	--	1	1	--	--	2 (1.5%)
4. Pancreatic necrosis	--	--	--	2	--	--	2 (1.5%)
Intra-abdominal							
1. Postoperative ileus	2	--	--	--	--	--	2 (1.5%)
2. Intra-abdominal infection	--	9	17	16	--	--	42 (32.3%)
3. Biliary fistula	--	1	--	1	--	--	2 (1.5%)
4. Small bowel obstruction	--	1	--	7	--	--	8 (6.6%)
5. Enterocutaneous fistula	--	9	--	--	--	--	9 (6.9%)
6. Anastomotic leak	--	--	--	3	--	--	3 (2.3%)
7. Abdominal compartment syndrome	--	--	--	3	--	--	3 (2.3%)
Wound							
1. Wound infection	--	7	--	2 ^b	--	--	9 (6.9%)
2. Wound dehiscence	--	1	--	1	--	--	2 (1.5%)
Bleeding							
1. Intra-abdominal	--	4	--	6	--	1	11 (8.5%)
2. DIC	--	7	--	--	6	5	18 (13.8%)
NON-SURGICAL COMPLICATIONS							
Respiratory							
1. Pleural effusion	9	2	--	--	--	--	11 (8.5%)
2. Atelectasis	2	--	--	--	--	--	2 (1.5%)
3. Pneumonia	--	14	--	--	--	--	14 (10.7%)

4. Respiratory failure	--	--	--	10	6	9	25 (19.2%)
Renal							
1. Renal failure	--	--	--	8	10	1	19 (14.6%)
2. Intra-abdominal urine leak	--	--	--	1	--	--	1 (0.8%)
Systemic sepsis	--	12	--	--	4	3	19 (14.6%)
Other	1 ^c	1 ^d	--	--	--	--	2 (1.5%)
TOTAL	15 (6.3%)	82 (34.5%)	28 (11.8%)	68 (28.6%)	26 (10.9%)	19 (8.0%)	238

^a*Pancreatic-colo-cutaneous fistula (one patient)*

^b*Abdominal wall sepsis*

^c*Jaundice*

^d*Bedsore*

GA general anaesthetic

Table 4 Outcome according to type of pancreatic resection performed

	Pancreatoduodenectomy (n=20)	Distal Pancreatectomy and Splenectomy (n=95)	Distal Pancreatectomy with Spleen Preservation (n=15)	p-Value [#]
No. of patients with any complication	19 (95%)	70 (73.7%)	6 (40%)	0.0014
Complications Non-surgical	15 (75%)	58 (61.1%)	2 (13.3%)	0.0006
Complications Surgical (Other)	12 (60%)	37 (38.9%)	4 (26.7%)	0.1111
Complications Pancreatic	3 (15%)	25 (26.3%)	5 (33.3%)	0.4339
Days in hospital Median (range)	22 (3-94)	17 (1-255)	15 (5-58)	0.1797
ICU admissions	19 (95%)	55 (57.9%)	3 (20%)	0.0001
Days in ICU Median (range)	4 (1-20)	7 (1-153)	7, 9, 16 respectively	0.0099
Outcome Died	4 (20%)	14 (14.7%)	1 (6.7%)	0.5445

[#] *Kruskal Wallis*

Duration of hospital stay was analysed for the different ASGS grades. In patients with more than one complication the highest grade was used. Those with no post-operative complications (grade 0, n=35) had a median 9 (range: 5-58) day post-resection hospital stay. Grade 1 patients (n=3) spent 14, 23 and 34 days in hospital, grade 2 (n=14, median 22, range 6-94 days), grade 3 (n=17, median 24, r 9-58 days), grade 4 (n=40, median 33, r 7-255 days), grade 5 (n=2, 9 and 19 days) and grade 6 (n=19, median 14, r 1-52).

15.3.6 Mortality

Nineteen patients (14.6%) died post-operatively (GSW 15, blunt 3, stab 1) of whom 13 were shocked on admission, 10 had major vascular injuries, 11 had 3 or more associated abdominal organ injuries required a median of 25 units of blood (range 4-89). Five deaths occurred within the first 24 hours as a result of complications related to bleeding, DIC and shock due to a combination of complex peri-pancreatic visceral vascular injuries. Fourteen patients died after 24 hours (median 17 days, range 2-52 days) of multi-organ failure (MOF), respiratory failure (n=9), DIC (n=5), septic shock (n=3), renal failure (n=1) and abdominal bleeding (n=1). Four patients (20%) died after PD, including two of the six patients who underwent a delayed PD and reconstruction after DCL (Table 4).

Patients who were older, those who had a RTS ≥ 7.8 , were shocked on admission, had grade 5 injuries with associated vascular or duodenal injuries, required a DCL, received a larger blood transfusion, had a PD or repeat laparotomies were more likely to have complications after pancreatic resection (Table 2). Applying univariate logistic regression analysis mechanism of injury, RTS ≥ 7.8 , shock on admission, DCL, greater AAST grade and type of pancreatic resection (PD) were significant variables for complications (Table 5). Multivariate logistic regression analysis, however showed only age and type of pancreatic resection (PD) to be significant (Table 5).

Table 5 Logistic regression analysis of risk factors for developing complications

Risk Factor	Univariate Logistic Regression			Multivariate Logistic Regression		
	Odds Ratio	95% CI	p-Value	Odds Ratio	95% CI	p-Value
Age median, range	0.9	0.58 - 1.43	0.699	0.9	0.82 - 0.99	0.031
Mechanism of injury	0.9	0.89 - 0.98	0.017	0.4	0.12 - 1.39	0.155
RTS (<7.8)	5.1	1.85 - 14.5	0.002	10.8	0.15 - 788	0.277
No. of patients shocked on admission	6.1	2.0 - 18.8	0.001	0.5	0.00 - 30.2	0.728
No. of patients who received a blood transfusion	2.3	0.93 - 5.53	0.073	0.5	0.00 - 3.64	0.486
Damage control surgery	1.6	1.18 - 2.2	0.030	1.36	0.68 - 2.69	0.373
Pancreatic injury site	1.8	0.99 - 3.15	0.050	2.4	0.57 - 100	0.231
AAST	0.5	0.23 - 0.92	0.028	3.8	0.67 - 21.9	0.131
Pancreatic resection type	4.8	1.91 - 12.0	0.001	65.7	3.13 - 1381	0.007
Associated abdominal injuries	1.1	0.32 - 3.7	0.883	12.9	0.39 - 423	0.152

15.4 Discussion

The present study is the largest series to date of consecutive patients undergoing a pancreatectomy for trauma and represents a select cohort of severe pancreatic injuries with the common denominator a main pancreatic duct injury. This is the first study to examine ASGS metrics to assess the usefulness of the scoring system to benchmark the spectrum and severity of complications after pancreatic resection for trauma. Unlike the planning and precision of elective pancreatic resections performed under controlled conditions with prior

knowledge of co-morbidities, extent of pathology and anatomical considerations, the complexities and unpredictable operative demands surgeons are faced with during a pancreatic resection for trauma frequently require flexible or innovative strategies (Navsaria, Bunting et al. 2003). There seldom is the opportunity to evaluate and study the details of the injury pre-operatively and resection is often undertaken under unfavourable circumstances when other competing life-threatening injuries are present and take precedence (Krige, Nicol et al. 2014).

The accurate intra-operative assessment of major pancreatic injuries may be complex and the surgeon may be faced with a range of uncertainties, some of which only become apparent during the procedure (Krige and Thomson 2011, Krige, Nicol et al. 2014, Krige, Kotze et al. 2016). When major blood loss and shock occur, strategies including rapid haemostasis and damage control intervention become imperative, necessitating deferred resection and/or reconstruction at a more opportune time when abnormal physiological parameters have been restored (Krige, Kotze et al. 2016, Roberts, Bobrovitz et al. 2016). After resection, technical difficulties may arise in the reconstruction of the pancreatic and biliary anastomoses due to a mismatch in size with non-dilated biliary and pancreatic ducts, often aggravated by gross oedema of the jejunum and small bowel mesentery and soft pancreatic parenchyma. Although 20 patients in this study had a PD for grade 5 injuries, a procedure of this magnitude is seldom necessary and should only be undertaken in stable patients when lesser operations are not feasible. Although pancreas-specific complications were surprisingly low after PD, the overall complication rate in

this category of resection was high. This emphasizes the need for combined and integrated involvement of both trauma and HPB surgeons familiar with the full spectrum and exigencies of pancreatic trauma(Krige, Kotze et al. 2016).

The salient features of this study are the high proportion of patients who required a pancreatic resection for major injuries and the substantial morbidity and mortality associated with it. Major injuries to the pancreas remain a significant source of morbidity even when treated in well-resourced high-volume specialist trauma referral centres (Kao, Bulger et al. 2003). Outcome is influenced by the mechanism, anatomical location, grade and complexity of the pancreatic injury, the amount of blood lost, duration of hypovolaemic shock, the quality of resuscitation, number of associated injuries and the appropriateness and quality of surgical intervention (Kao, Bulger et al. 2003, Wang, Li et al. 2007, Antonacci, Di Saverio et al. 2011, Krige, Kotze et al. 2015). Overall reported morbidity rates following pancreatic injury range from 30% to 70% with the higher reported percentages generally being the result of severe trauma with higher AAST grades, associated injuries, diagnostic delay and inadequate or inappropriate initial treatment (Kao, Bulger et al. 2003, Wang, Li et al. 2007, Krige, Kotze et al. 2015). In the current study the number and severity of post-operative complications reflect the consequences of surgery in severe multiply injured patients. Associated injuries were common, in keeping with collateral damage seen with abdominal gunshot injuries. One half of patients had three or more associated injuries and the complexities of management were further compounded by associated vascular injuries present in one of every five patients. The dominant complications were infective, both intra-abdominal and

systemic, respiratory, renal and related to bleeding. A substantial number of patients required a repeat laparotomy either for definitive management following an initial DCL (i.e. delayed resection) or for intra-abdominal infection unresolved after percutaneous catheter drainage, control of intra-abdominal bleeding, or for small bowel obstruction.

A variety of factors specifically contribute to the development of pancreas-related complications following trauma, including the mechanism and grade of the injury, especially GSWs and associated vascular, hollow viscus and solid organ injuries and neglect of a main pancreatic duct injury may lead to local complications including pseudocysts, fistulas, sepsis and secondary haemorrhage (Recinos, DuBose et al. 2009). Pancreatic fistulas occur in up to 38% of patients and intra-abdominal abscesses in 34% (Recinos, DuBose et al. 2009). In a study from Los Angeles County Hospital pancreas-related complications developed in 27.9%, including pseudocysts in 14.9% and fistulas 1.9% (Recinos, DuBose et al. 2009).

The data in this study concur with the findings of others in that early deaths after major pancreatic trauma are related to the number and severity of associated injuries (Seamon, Kim et al. 2009). Overall mortality in this study was 14.6% with the presence of shock, due to associated vascular injuries being significantly related to early mortality. Late deaths were due to sepsis and MOF. Deaths specifically related to the pancreas were uncommon. A substantial number of patients required a repeat laparotomy either for definitive management following an initial DCL or for postoperative complications that could not be managed by percutaneous or endoscopic intervention. The DCL

patients had a mortality of 31%. In a two-centre study from Philadelphia and Columbus, Ohio which sought to determine the optimal initial operative management in damage control operations, 42 patients with pancreatic injuries underwent either packing, drainage or resection. Mortality in their study population was substantial (packing only, 70%; packing with drainage, 25%, distal pancreatectomy, 55%) (Seamon, Kim et al. 2009).

Although this study represents the largest detailed analysis of pancreatectomies for trauma to date, there are several specific limitations that should be considered when interpreting the results. The most substantive limitation is that this is a single centre study in a high-volume tertiary referral centre and although these data are likely to be similar to other major academic institutions, the data are not applicable to community-based hospitals with lesser resources. The study design sought to avoid possible non-measurable biases that may arise from patient selection, referral policies and local variations in treatment strategies by using complications and death as the main outcomes to provide consistent and objective end-points. A further concern is that the ASGS scores only the highest grade complication, without considering the burden of multiple but lesser complications in the same patient (Lee, Lewis et al. 2014). Specific strengths of the current study and of the analysis are the size of the cohort and the use of validated ISGPS definitions to score postoperative complications which have provided consistent and robust data and allowed reliable comparisons (Bassi, Dervenis et al. 2005, Wente, Bassi et al. 2007, Wente, Veit et al. 2007, Strasberg, Linehan et al. 2009).

In conclusion, postoperative morbidity after pancreatic resection for trauma in this study was considerable and an increasing complication severity grade, as measured by the ASGS, required escalation of intervention and prolonged hospitalisation. The injured pancreas is an unforgiving organ, especially if severely damaged. Accurate intraoperative decision-making is crucial for a favourable outcome. A wide spectrum of options need to be considered, including initial damage control with delayed resection and/or reconstruction which is applicable as the default option in a select group of unstable patients. In applying the ASGS, we have established a benchmark for pancreatic resections for trauma by using current standardized definitions for grading severity of pancreatic complication. This will facilitate future comparative assessments and serve as a reference for improving outcome. Benchmarking is not restricted to comparative analyses of outcome, but should serve as a mechanism for transforming surgical practice and enhancing quality of care. To further develop this, future studies should include the calculation of the total burden of multiple complications in individual patients by utilising the comprehensive complication index, a factor which is relevant in trauma patients with several injured organs (Slankamenac, Nederlof et al. 2014).

CHAPTER 16

Morbidity and mortality after distal pancreatectomy for trauma: a critical appraisal of 107 consecutive patients undergoing resection at a Level 1 Trauma Centre

16.1 Introduction

Pancreatic injuries to the left of the superior mesenteric portal vein axis involving the neck, body and tail of the pancreas are uncommon and occur in less than 1% of patients with abdominal trauma (Mayer, Tomczak et al. 2002). Outcome is determined primarily by the cause and grade of the pancreatic injury, the number and severity of associated injuries and secondarily by complications related to main pancreatic duct injury (Chrysos, Athanasakis et al. 2002, Scollay, Yip et al. 2006). Severe pancreatic injuries result in substantial morbidity and mortality rates (Subramanian, Dente et al. 2007, Sharpe, Magnotti et al. 2012) and serious sequelae follow if the injury is underestimated or inappropriately treated (Vasquez, Coimbra et al. 2001, Kao, Bulger et al. 2003, Ahmed and Vernick 2009, Chinnery, Krige et al. 2012). Disregard for a main pancreatic duct injury inevitably results in serious complications which include pseudocysts, fistulas, intra-abdominal sepsis and secondary haemorrhage (Kao, Bulger et al. 2003, Scollay, Yip et al. 2006, Ahmed and Vernick 2009). Uncontrolled bleeding from major splanchnic peripancreatic veins or severe adjacent solid organ injuries are generally the cause of early deaths in pancreatic trauma while delayed mortality is due to the consequences of intra-abdominal sepsis and multi-organ failure (Vasquez, Coimbra et al. 2001,

Recinos, DuBose et al. 2009, Heuer, Hussmann et al. 2011, Chinnery, Krige et al. 2012).

Although several substantial reports (Kao, Bulger et al. 2003, Heuer, Hussmann et al. 2011, Sharpe, Magnotti et al. 2012) including those from Cape Town (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012), have detailed aspects of the management of pancreatic injuries, few series have specifically assessed complications and outcome after distal pancreatectomy for trauma (Wind, Turet et al. 1999, Malgras, Douard et al. 2011). While mortality is an objective and finite endpoint, different grades of severity of postoperative morbidity are poorly defined and less easily quantifiable (DeOliveira, Winter et al. 2006). Most previous studies have used subjective criteria to assess postoperative complications, which have hampered accurate comparative studies. Morbidity rates differ substantially within these series and reflect intrinsic biases of smaller hospitals compared to high volume tertiary referral centres as data generated from these reports are influenced by both referral and ascertainment bias. The present study critically evaluated morbidity and mortality after distal pancreatectomy for major pancreatic injuries in a large cohort of consecutive patients treated at one of the busiest trauma centres in the world and assessed the severity of pancreas-specific postoperative complications using objective, reliable, and reproducible internationally accepted graded classification systems (Table 1) (Moore, Cogbill et al. 1990, Clavien, Barkun et al. 2009).

Table 1 Clavien-Dindo classification of surgical complications adapted for pancreatic surgery

Grade	Definition
1	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics and electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside.
2	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
3	Requiring surgical, endoscopic or radiological intervention
3 a	Intervention not under general anesthesia
3 b	Intervention under general anesthesia
4	Life-threatening complication (including CNS complications)‡ requiring IC/ICU-management
4 a	Single organ dysfunction (including dialysis)
4 b	Multi organ dysfunction
5	Death of a patient
Suffix 'd':	If the patients suffers from a complication at the time of discharge, the suffix “d” (for ‘disability’) is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

16.2 Methods

16.2.1 Study population and data collection

Details of the study population, data collection and variables recorded for each patient are outlined in the methodology section in Chapter 3.

16.2.2 Definitions

Details of definitions applied are provided in the study methodology in Chapter 3.

16.2.3 Initial and operative management of pancreatic injuries

Details of initial and operative management of pancreatic injuries and damage control laparotomy are given in the study methodology in Chapter 3.

16.2.4 Perioperative management

Perioperative management for all patients was according to the Trauma Centre's standard protocol for pancreatic resection. All patients' drain amylase levels and output volumes were measured postoperatively. Drains were left *in situ* while drain amylase levels were elevated or volume measured over 30 ml per day. No dietary restrictions were imposed and oral food intake was continued while the fistula drained. ERCP with pancreatic duct sphincterotomy was used in patients who had pancreatic fistulas which persisted for more than 3 weeks (Thomson, Krige et al. 2014).

16.2.5 Statistical analyses

Means, standard deviations, ranges, and frequencies were used to describe the data. Interquartile ranges, medians and the extreme values were shown with box and whiskers plots. Pearson's chi-square test was used for analysis of categorical variables, and odds ratios (ORs) with 95 per cent confidence intervals (CI) were calculated. Continuous data were expressed as means and standard deviations. Categorical variables were analyzed with the chi-squared test or Fisher exact test, and continuous variables were analyzed with the *t* test. Two-tailed $P < 0.05$ was considered statistically significant. When appropriate statistical analysis was performed using non-parametric Mann–Whitney, or Student's *t*-test when appropriate. $P < 0.05$ was considered statistically

significant. The data were analysed using Stata version 11 (*StataCorp LP, College Station, Texas, USA*).

16.3 Results

During the study period, 426 consecutive patients were treated for pancreatic injuries, of whom 107 had a distal pancreatectomy (Table 2). Median age of the 107 patients was 26 (range 15–64) years, 94 (88%) were men and the median RTS was 7.8 (range 3.3–7.8). Sixty nine patients had penetrating injuries (63 gunshot wounds, 6 stabs wounds). Thirty eight patients had blunt injuries (assault n=20, motor vehicle accidents n=9, falls from a height n=3, pedestrian accidents n=2, bicycle accidents n=2, go-kart injury n=1, train accident n=1). Ninety-six (90%) patients were treated at the trauma centre within 24 hours of the injury. Thirty-five (33%) patients were in shock (systolic blood pressure <90mm Hg) on admission to hospital despite paramedical resuscitation while in transit (Table 2).

The diagnosis of a grade III pancreatic injury was established at laparotomy in the 69 patients with penetrating injuries who had either bullet or stab wounds of the abdomen and required an urgent laparotomy. Nine patients who had sustained blunt abdominal trauma and were initially treated non-operatively, presented subsequently with a CT confirmed pancreatic injury and a pseudocyst not amenable to ultrasound-guided endoscopic drainage and had a distal pancreatectomy and splenectomy. Four additional patients with blunt abdominal injuries had an urgent laparotomy and suction drainage of a pancreatic injury and subsequently required a distal pancreatectomy and splenectomy for a necrotic distal pancreas (n=2) or a complicated pseudocyst

(n=2). In the remaining 25 patients who had blunt abdominal trauma, a major pancreatic injury was established at laparotomy and each had a distal pancreatectomy and splenectomy. An abdominal CT scan was used to pre-operatively identify the pancreatic injury in 9 patients. Diagnostic ERCP was performed in 4 patients to confirm a main pancreatic duct injury before operation.

16.3.1 Anatomical site and severity of injury

Eleven patients had an injury of the neck of the pancreas, 54 injuries involved the body and 42 the tail of the pancreas. All patients had AAST grade III pancreatic injuries (Table 2).

16.3.2 Surgical management

All 107 patients underwent a laparotomy. The median time to surgery after admission to hospital was 3 (range 0.1–80) hours. Forty four of the 107 patients also had extra-abdominal wounds which involved limbs, chest, neck and head. Splenectomy was done in 92 (86%) and the spleen was preserved in 15 patients (14%). An additional procedure for associated injuries was necessary in 88 patients (82%) (Table 2). The extent of the pancreatic resection ranged from lesser resection for distal body and tail injuries, to major resections of the neck, body and tail for injuries at the pancreatic neck over the SMV-PV confluence.

Table 2 Clinical data of 107 patients undergoing distal pancreatectomy for trauma

	Total (n=107)	Blunt (n=38)	GSW (n=63)	Stab (n=6)
Male	94	29	59	6
Female	13	9	4	0
Age				
Median (range)	26 (15-64)	30 (15-54)	25 (15-64)	27 (21-33)
RTS				
< 7.8 (range)	38 (3.3-7.5)	10 (4.6-7.5)	25 (3.3-7.5)	3 (5.1-7.1)
>7.8	69	28	38	3
Shock on admission	35	9	23	3
Patients transfused	85	24	56	5
Blood transfusion				
Median units (Range)	7 (1-124)	5 (2-58)	7 (1-124)	8 (4-16)
DCS	13	2	10	1
Pancreatic Injury Site				
Neck of pancreas	11	8	2	1
Body of pancreas	54	19	32	3
Tail of pancreas	42	11	29	2
Associated Abdominal Injuries				
Nil (isolated injury)	19	19	0	0
1 or 2 organs injured	39	16	18	5
3 or more injured	49	3	45	1
Associated injured organs				
Spleen	47	10	34	3
Liver	45	8	36	1
Kidney	39	5	33	1
Stomach	37	1	35	1
Diaphragm	29	1	23	5
Colon	28	5	22	1
Duodenum	5	1	4	0
Associated vascular injuries	14	4	8	2
Repeat laparotomy	47	11	33	3
Days in Hospital				
Median (range)	16 (1-255)	16 (1-92)	17 (1-255)	11 (7-149)
ICU Admission	57	21	34	2
Days in ICU				
Median (range)	8 (1-153)	6 (1-40)	14 (1-153)	4 & 30 respectively
Complications				
Systemic	66	19	42	5
Complications				
Intra-abdominal	39	8	30	1
Complications Pancreatic	26	10	13	3
Outcome				
Died	13	3	10	0

16.3.4 Associated organ injuries

Nineteen (18%) patients had an isolated pancreatic injury, all of whom had blunt abdominal trauma. The remaining 88 (82%) patients had a total of 238 associated intra-abdominal injuries involving predominantly spleen (n=47, 44%), liver (n=45, 42%), kidney (n=39, 36%) stomach (n=34, 45.3%), diaphragm (n=29, 27%), colon (n=28, 26%) and duodenum (n=5, 5%). Thirty nine (36%) of the 107 patients had one or two associated injuries while 49 (46%) had three or more associated intra-abdominal injuries (Table 2). Gunshot injuries had significantly more associated abdominal injuries than blunt or stab injuries (p<0.01). Concurrent extra-abdominal trauma involving chest (n=32), spine (n=13), limbs (n=12), head (n=4) and neck (n=1) occurred in 10 patients after blunt trauma and 34 patients with penetrating trauma.

16.3.5 Associated vascular injuries

Fourteen (13%) of the 107 patients had 1 or more associated vascular injuries involving IVC (n=5, 4.7%), renal artery (n=3, 2.8%) left gastric artery (n=2, 1.9%), splenic artery (n=2, 1.9%), superior mesenteric artery (n=2, 1.9%), aorta (n=1, 0.9%), portal vein (n=1, 0.9%), renal vein (n=1, 0.9%).

16.3.6 Damage Control Surgery

Initial damage control surgery (DCS) was necessary in 13 patients who had complex pancreatic and associated injuries aggravated by major blood loss, coagulopathy, acidosis, and hypothermia. These patients had a median RTS of 6.8 (range 3.3–7.8) and received a median of 8 (range 5-89) units of blood. Eleven of the 13 patients were shocked on admission to hospital. Five patients

had associated vascular injuries and 11 had three or more associated adjacent organ injuries. During the damage control laparotomy, all 13 patients had initial control of bleeding followed by a distal pancreatectomy and splenectomy (n=11) or packing (n=2). Ten had relook laparotomies. Four of the 13 (31%) died. Gunshot injuries required significantly more associated damage control operations and repeat laparotomies than blunt or stab injuries ($p<0.01$) (Table 2).

Five patients (4.6%) had injuries involving both pancreas and duodenum. After the distal pancreatectomy, the duodenal injuries were managed by primary duodenal repair with intraluminal duodenal tube drainage, feeding jejunostomy and closed suction drainage of the pancreas.

Fifty seven (53%) patients required intensive care unit (ICU) admission. Median ICU and total hospital stay (range) were 8 (1–153) and 16 (1–255) days respectively. Gunshot injuries required a significantly longer ICU stay than blunt or stab injuries ($p<0.01$).

16.3.7 Morbidity

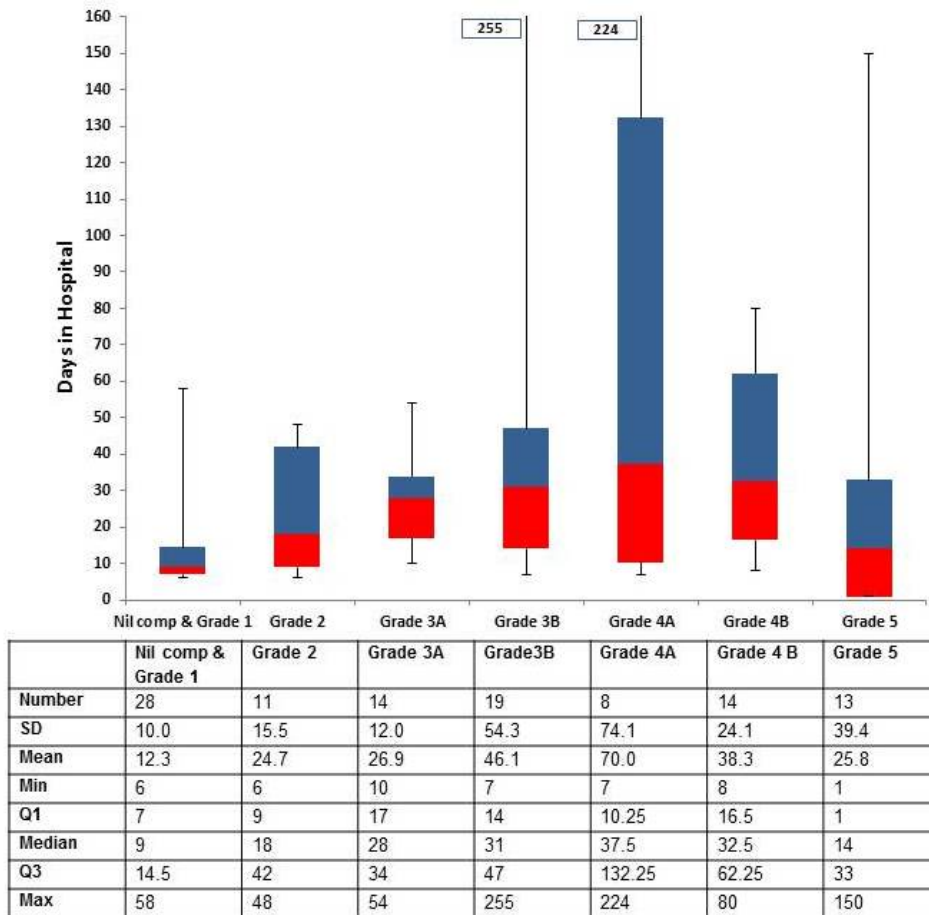
Twenty seven (25%) patients had no postoperative complications and had a median hospital stay of 8 days, range 6-58 days. One patient required in hospital rehabilitation for 58 days for an associated spinal injury. Sixty six (75%) of the remaining 80 patients had systemic complications, 39 had intra-abdominal complications and 26 had pancreas-specific complications. The 66 systemic complications included pneumonia (n=20) acute respiratory distress syndrome (n=27), pleural effusion (n=8), atelectasis (n=7), sepsis (n=15), renal

failure (n=13), disseminated intravascular coagulopathy (n=11), bleeding (n=12). The 39 intra-abdominal complications included intra-abdominal and subphrenic abscess (n=32), anastomotic leak (n=5), enterocutaneous fistula (n=10), bowel obstruction (n=3), bile leak (n=3), gastric outlet obstruction (n=2), wound sepsis (n=6) and abdominal compartment syndrome. Forty seven (44%) patients required a relaparotomy with intra-abdominal sepsis the most frequent indication for reoperation (Table 2). Median hospital stay for patients with complications was 24 (1–255) days which was significantly longer than those without complications ($p < 0.05$, Table 2).

Twenty six patients had pancreas-specific complications. Eighteen patients (17%) developed a clinically obvious pancreatic fistula after the distal pancreatectomy, and 8 had a contained fluid collection. Median maximum daily fistula volume was 375 mL (IQR, 135–570 mL). All were initially treated conservatively. Twelve pancreatic fistulae resolved spontaneously on conservative management alone after a median of 24 (IQR 14–46) days. Six persistent fistulae required endoscopic intervention with retrograde cholangiopancreatography and pancreatic duct sphincterotomy and resolved within 14 days after intervention. The remaining eight patients had symptomatic localised peri-pancreatic fluid collections identified on CT scan which were treated with percutaneous ultrasound-guided 8 Fr catheter drainage. Six resolved and two required surgical drainage for persistent multi-locular collections despite percutaneous drainage. One patient presented subsequently after discharge with a symptomatic pancreatic pseudocyst which was treated with endoscopic transgastric 10 Fr pigtail stent pseudocyst drainage.

In the 79 (74%) patients with at least one significant (grade II-V) postoperative complication, the Clavien–Dindo grades were as follows: 11 (13.8%) patients had grade II complications, 14 (17.5%) had grade IIIa, 19 (23.8%) had grade IIIb, 8 (10%) had grade IVa, 14 (17.5%) had grade IVb and 13 (16.3%) had grade V complications (Figure 1). The median length of the postoperative stay in patients with no or grade I complications was 9 ± 10 days; in grade II, 18 ± 15.5 days; in grade IIIa, 28 ± 12 ; in grade IIIb, 31 ± 54.3 ; in grade IVa; 37.5 ± 74.1 in grade IVb 32.5 ± 24.1 , and in grade V the length of postoperative stay was 14 ± 39.4 days. The length of hospitalization in patients with grade II-IV injuries was significantly greater compared to those with no or grade I complications ($P < 0.05$).

Figure 1 Box and whiskers plot demonstrating the relationship between the duration of hospital stay and the Clavien-Dindo postoperative complication grade. Boxes represent the interquartile ranges and the lines in each box show the median values. The whiskers represent extreme values.



16.3.8 Mortality

Thirteen (12%) patients (median RTS 7.1, range 3.3-7.8) died at a median of 14 (range 1-150) days after the distal pancreatectomy after receiving a median total blood transfusion of 28 (0-102) units. Mortality for gunshot injuries was 16% and 8% for blunt trauma. There were no deaths in patients who had a distal pancreatectomy for stab wounds. Ten of the 13 patients who died were

shocked on admission. Six had associated major vascular injuries and four underwent an initial damage control operation before definitive surgery. Analysis showed that four patients died of bleeding or disseminated intravascular coagulopathy within 24 hours of the resection after receiving a median of 27 units of blood. All had associated vascular injuries and three or more associated adjacent organ injuries. Nine patients died between 5 and 150 days after the pancreatic injury of multi-organ failure (n=5), sepsis (n=3) and an infarcted right ventricle (n=1) after blunt cardiac trauma. Only one death was considered attributable to the pancreatic injury and occurred in a patient who developed pancreatic necrosis with renal and respiratory failure complicated by intra-abdominal sepsis. The median number of operations and complications in this group was 3 (range 1-8) and 4 (range 1-7). The overall mortality rate for patients arriving at the referral centre in shock was 29% (10 of 35) compared to 4% (3 of 72) ($P<0.05$) for patients who had a systolic blood pressure greater than 90mm Hg.

16.4 Discussion

The present study evaluated both morbidity and mortality associated with distal pancreatectomy for trauma and examined in particular the severity grade and management of pancreas-specific postoperative complications using internationally accepted graded classification systems. The data confirm the findings of others that pancreatic injuries are seldom isolated and the principal cause of early death after major pancreatic trauma is the severity and number of associated injuries (Timberlake 1997, Mayer, Tomczak et al. 2002, Krige, Beningfield et al. 2005). In the present study is the largest series to date of

consecutive patients undergoing a distal pancreatectomy for trauma, associated injuries were common, with more than 80% of patients having one or more associated injuries. The spleen and liver were the most frequently injured organs which is consistent with the findings of others (Cogbill, Moore et al. 1991, Degiannis, Levy et al. 1995). The mortality in this series was 12% which compares favorably with results reported by other investigators where mortality ranged from 12% (Cogbill, Moore et al. 1991) to 20% (Mayer, Tomczak et al. 2002). There was a close correlation between mortality, associated injuries and the number of intra-abdominal organs injured when compared to survivors. Most early deaths were due to associated vascular injuries. Pancreas-related deaths were uncommon, occurred late, and were due to sepsis and multi-organ failure. The data in this study show that the presence of shock is significantly related to early mortality rate. The current concept of damage control surgery has been increasingly accepted. There is consensus that patients who remain unstable due to persistent or unmanageable bleeding, hypothermia, acidosis or coagulopathy should undergo a damage control procedure with abdominal packing and subsequent re-exploration (Chrysos, Athanasakis et al. 2002, Seamon, Pieri et al. 2007, Wang, Li et al. 2007, Nicol, Navsaria et al. 2010). However, despite applying the principles of damage control surgery in 13 patients in this study, mortality was 31% in this high risk cohort.

The reported incidence of overall complications following distal pancreatic resection for trauma ranges from 30 to 60% and is mainly the result of severe trauma with higher AAST grades, associated injuries, diagnostic delay exceeding 24 hours and inadequate or inappropriate initial treatment (Malgras,

Douard et al. 2011). There is neither consensus nor consistency on how to quantify or report morbidity after resection for major pancreatic injuries. The absence of a globally acknowledged classification system to report postoperative complications following abdominal trauma has led to inconsistent documentation of the results of trauma, the inability to accurately evaluate various series, and the lack of a robust risk adjusted stratification classification to assess surgical outcomes. In this study we adapted a previously described classification of postoperative complications to a cohort of patients undergoing distal pancreatectomy in a level I trauma centre in order to rank each complication category by severity (Dindo, Demartines et al. 2004). The most widely used grading system used to evaluate postoperative complications is the Clavien-Dindo classification which was developed as a simple, objective and reproducible system to grade complications and was validated initially in a large cohort of patients undergoing general surgery (Clavien, Barkun et al. 2009) and more recently following elective pancreatic surgery (DeOliveira, Winter et al. 2006). This system discriminates complication severity on the basis of whether or not a patient requires medical treatment (Clavien grade I or II), an invasive intervention without general anaesthesia (grade IIIa), a procedure in the operating room under general anaesthesia (grade IIIb) to manage the complication, or whether the patient has a life-threatening event associated with the complication (grade IV) or death as a result of the complication (grade V) (Baker, Sherman et al. 2013). This is the first major study to evaluate the usefulness of the Clavien-Dindo classification to grade the severity of postoperative complications after distal pancreatectomy for trauma. This study found that patients with no or grade I postoperative complications had a

significantly shorter hospital stay than patients with grade II to grade IV complications, confirming that the Clavien–Dindo classification is a useful tool to determine the grades of severity of complications after pancreatic trauma.

Pancreatic leaks remain the Achilles heel of pancreatic resection (Jensen, Portschy et al. 2013) and were the most common complication in this study, occurring in 17% of patients. The reported incidence of pancreatic fistula after distal pancreatectomy for trauma varies widely ranging from 8 to 69% (Cogbill, Moore et al. 1991, Degiannis, Levy et al. 1995, Fahy, Frey et al. 2002) in part due to inconsistencies in the criteria used to define a pancreatic fistula. Previous studies have used different laboratory levels of amylase in fistula fluid, fluid volumes, techniques of recognition and postoperative time frames for description. The inconsistent rates of pancreatic fistula described stems largely from the variable definitions of a pancreatic leak (Seamon, Kim et al. 2009). In the present series, conservative management was used in all patients and included intra-operatively placed drains and additional percutaneous drains when necessary. Previously reports have shown that more than 90% of traumatic pancreatic fistulas close spontaneously within eight weeks on conservative management (Goh, Tan et al. 2008, Ahmed and Vernick 2009, Sharpe, Magnotti et al. 2012).

The best method of dealing with the divided pancreatic duct and the resection margin after distal pancreatectomy for trauma is unresolved (Kao, Bulger et al. 2003). In this study the standard method of treatment was ligation of the pancreatic duct at the transection margin with a transfixing suture and closure of the distal pancreatic resection margin with interrupted absorbable sutures to

achieve haemostasis and minimise fistula formation as described previously (Farrell, Krige et al. 1996, Krige, Beningfield et al. 2005, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012). Over the last decade, a variety of resection and closure techniques have been proposed and evaluated for the pancreatic remnant during elective surgery following left sided pancreas resection in order to minimize complications, especially pancreatic fistulas (Kleeff, Diener et al. 2007). These techniques have used hand-sewn suture and stapled closure methods, or a combination of both (Kajiyama, Tsurumaru et al. 1996, Fahy, Frey et al. 2002, Sheehan, Beck et al. 2002, Bilimoria, Cormier et al. 2003, Takeuchi, Tsuzuki et al. 2003, Balzano, Zerbi et al. 2005) ultrasonic dissection tools (Suzuki, Fujino et al. 1999), pancreaticojejunal anastomosis (Adam, Makowiec et al. 2001), mesh application, seromuscular and gastric serosal patches (Moriura, Kimura et al. 1995, Kluger, Alfici et al. 1997), or fibrin glue sealant (Ohwada, Ogawa et al. 1998, Bilimoria, Cormier et al. 2003, Knaebel, Diener et al. 2005). Despite a wide selection of techniques for stump closure, none have reproducibly been able to reduce fistula rates in a meaningful way, and no technique has been identified as consistently superior to others (Jensen, Portschy et al. 2013). While transection and closure of the pancreatic remnant with a stapler is favoured by some, this technique resulted in reported fistula rate as high as 22.9 per cent in a recent meta-analysis (Knaebel, Diener et al. 2005). While few reports are available after pancreatic resection for trauma, neither Cogbil (Cogbill, Moore et al. 1991) nor Fitzgibbons (Fitzgibbons, Yellin et al. 1982) found a difference in the pancreatic leak rates in trauma patients whose pancreatic stumps were either sutured or stapled after distal pancreatectomy. Others have recommended a Roux-en-Y

pancreatojejunostomy to encompass and drain the resection margin to reduce the risk of a fistula (Yellin, Vecchione et al. 1972). Operative techniques which preserve pancreatic tissue are technically more demanding than a distal pancreatic resection alone and a Roux-en-Y jejunal loop creates additional enteric anastomoses. In patients with multiple injuries, the additional hazard of an anastomotic leak is not justified and none of these elaborate options are appropriate and are not recommended or warranted in severely injured patients. A meta-analysis of 6 studies reported a cumulative fistula rate of 32% after elective resection and found no significant relationship between the pancreatic remnant closure technique and the pancreatic leak rate (Knaebel, Diener et al. 2005). Stapling or carefully oversewing the transected end of the pancreas and using simple techniques such as an omental patch or fibrin glue to buttress and seal the cut margin are usually sufficient, and have not led to increased fistula formation.

Although this study represents the largest series of distal pancreatectomies for trauma to date, there are several limitations that should be considered when interpreting these results. The most important is that this is a retrospective analysis of outcomes in a longitudinal cohort study and not a randomized controlled trial or a matched cohort study. An additional substantive limitation is that this is a single centre study at a tertiary referral centre and although these data are likely to be similar to other major academic institutions, it is not applicable to community-based hospitals. While the retrospective nature may have led to treatment bias, the study design minimized possible biases that may arise from patient selection, referral policies and local variations in treatment

strategies. Unlike other studies which included non-consecutive patients or incomplete follow-up, this study design avoided these pitfalls by excluding non-measurable biases. In order to achieve a homogenous and clinically sound study population, consecutive patients were evaluated without exclusions and using complications and death as the main outcomes, provided consistent and objective end-points in the study. Because this study evaluated patients over a long duration, improvements in supportive care invariably would have occurred. A major strength of this study is that it was conducted in a single centre in a defined and homogenous population of consecutive patients and was supervised by the same group of senior investigators during the study period. Specific strengths of the current study and of the analysis include the large size of the cohort and the application of validated ISGPS definitions and the internationally accepted Clavien–Dindo classification for postoperative complications, providing consistent and robust data and allowing reliable comparison.

In conclusion, this study shows that although mortality after distal pancreatectomy for trauma is substantial, most deaths are unrelated to the pancreatic injury and are due to associated injuries. The foremost risk factors for death were shock on admission to hospital, a major vascular injury and three or more associated adjacent organ injuries. The study demonstrated that mortality was highest in patients who had sustained a gunshot injury and this cohort required significantly more associated damage control operations and repeat laparotomies than blunt or stab injuries of the pancreas. Postoperative morbidity in this study was considerable and an increasing complication severity

grade, when measured by the Clavien-Dindo method, led to the need for escalating intervention and prolonged hospitalization. Nearly one half of patients required a relaparotomy, the most frequent indication for reoperation being intra-abdominal sepsis. While one in six patients developed a pancreatic fistula after the distal pancreatectomy, most fistulae resolved spontaneously on conservative management alone. Persistent fistulae resolved after endoscopic intervention with retrograde cholangiopancreatography and pancreatic duct sphincterotomy. This study demonstrates that surgical simplicity is key in grade III injuries involving the pancreatic body and tail. Stable patients should be treated with a distal resection without the addition of unnecessary pancreaticoenteric anastomoses as a primary procedure during the acute injury in patients with multiple associated injuries. A damage control operation is a prudent alternative if the patient is unstable. The pancreatic duct at the resection margin should be identified and sutured. In this study the technique of attempting to identify and suture-ligate the pancreatic duct and closure of the transected end of the pancreas with interrupted sutures with reinforcement using omentum to seal the resection margin resulted in a reasonable pancreatic fistula rate.

CHAPTER 17

Endoscopic and operative treatment of delayed complications after pancreatic trauma: an analysis of 27 civilians treated in an academic Level 1 Trauma Centre

17.1 Introduction

Injuries to the pancreas occur infrequently but may result in significant morbidity and mortality if the main pancreatic duct or adjacent viscera and vasculature are damaged (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005). Early mortality is most commonly due to uncontrolled bleeding from large visceral veins in close proximity to the pancreas or major injuries to nearby solid organs (Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008). Late mortality is generally due to infection or multiple organ failure (Kao, Bulger et al. 2003, Hwang and Choi 2008, Antonacci, Di Saverio et al. 2011). Neglect of a major ductal injury with retroperitoneal extravasation of pancreatic enzymes predisposes to delayed local complications, the most serious of which are pancreatic pseudocysts, persistent fistulae, intra-abdominal sepsis or secondary haemorrhage from major vessels adjacent to the pancreas (Wang, Li et al. 2007, Stawicki and Schwab 2008, Seamon, Kim et al. 2009).

While the management of acute pancreatic injuries is well documented, only limited data are available detailing the consequences of delayed complications following a severe pancreatic injury. Endoscopic intervention has no role in severely injured patients with acute pancreatic trauma but may be useful in haemodynamically stable patients who present later with complications related

to the pancreatic trauma. On the basis of previously published clinical experience from the unit the hypothesis of this study was that delayed local pancreatic complications which occur after a major pancreatic injury are likely to be due to main pancreatic duct damage and could thus theoretically be managed effectively by non-operative endotherapeutic methods such as pancreatic duct stenting or pseudocyst drainage (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994, Farrell, Krige et al. 1996, Beckingham, Krige et al. 1999, Apostolou, Krige et al. 2006, Thomson, Krige et al. 2014). To test this hypothesis the present study critically evaluated the efficacy of endotherapeutic pancreatic duct stenting and transmural cyst drainage in the management of delayed complications after a major pancreatic injury in a cohort of consecutive patients using robust and reliable methodology with objective and reproducible end-points.

17.2 Methods

17.2.1 Study design

After approval by the University of Cape Town Human Research Ethics Committee, an analysis was done of consecutive patients who, beyond 6 weeks after the pancreatic injury, either developed a local complication (e.g. pseudocyst) or had a non-resolving complication (e.g. pancreatic fistula) related to a pancreatic duct injury between January 1990 and December 2013.

17.2.2 Study population and data collection

Details of the study population, data collection and variables recorded for each patient are outlined in the methodology section in Chapter 3.

17.2.3 Definitions

Details of definitions applied are provided in the study methodology in Chapter 3.

17.2.4 Initial and operative management of pancreatic injuries

Details of initial and operative management of pancreatic injuries and damage control laparotomy are given in the study methodology in Chapter 3.

17.2.5 Management of delayed pancreas specific complications

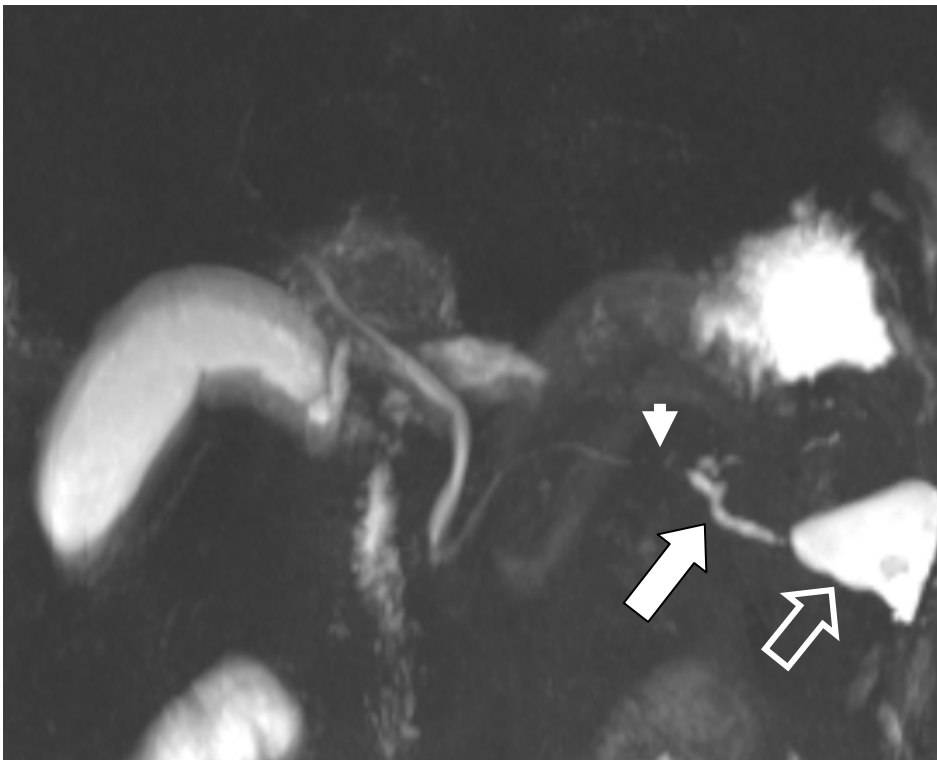
The diagnosis of a pancreatic duct fistula or stricture or pseudocyst was based on review of the original operative and clinical findings, fluid amylase levels, ultrasound and CT scan findings (Thomson, Krige et al. 2014). The site of the pancreatic duct fistula (head, neck, body or tail) was noted on MRCP and ERP (Fig 1). The number and size of the pseudocyst(s) was measured in cm in 2 dimensions and location, relationship and proximity to stomach and duodenal wall recorded (Fig 2). The degree and extent of the main pancreatic duct injury was assessed using the Cape Town pancreatographic grading system for pancreatic injuries modified from the original classification by Takishima et al. (Table I).

Table 1 The Cape Town pancreatographic grading system for pancreatic injuries modified from the original classification by Takishima

Classification of Injury	ERP/MRCP Findings
Grade 1	Normal pancreatic duct.
Grade 2	Main pancreatic duct intact. Injury to a branch of the pancreatic duct
A	Contrast contained within the pancreatic parenchyma
B	Contrast leak beyond the pancreatic parenchyma into the retroperitoneal space.
Grade 3	Injury to main pancreatic duct. Duct continuity present
A	Injury to main pancreatic duct in body or tail with duct continuity *
B	Injury to main pancreatic duct in the head with duct continuity
Grade 4	Complete main pancreatic duct division with no duct continuity
A	Complete main pancreatic duct division in body or tail with no duct continuity *
B	Complete main pancreatic duct division in the pancreatic head with no duct continuity *
C	Complete main pancreatic duct division with a leak or pseudocyst after resection of distal/proximal damaged pancreas *

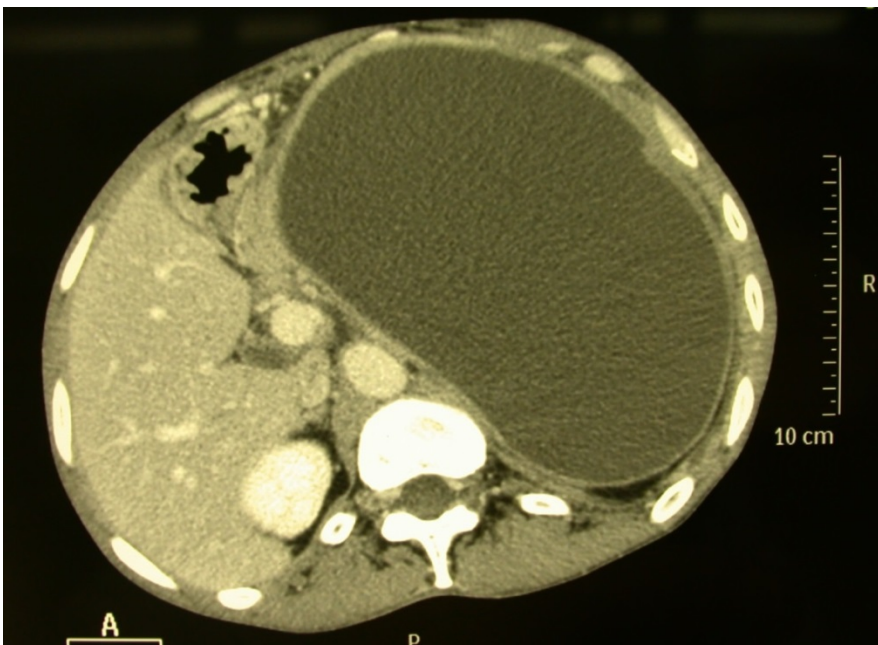
* Line to discriminate between grades 3a, 3b, 4a and 4b is the right margin of the superior mesenteric vein

Figure 1



MRCP showing a stricture (arrow head) in the mid main pancreatic duct with a fistula (white arrow) and a fluid collection (open arrow)

Figure 2



CT scan demonstrating post-traumatic pseudocyst

17.2.5.1 ERP technique

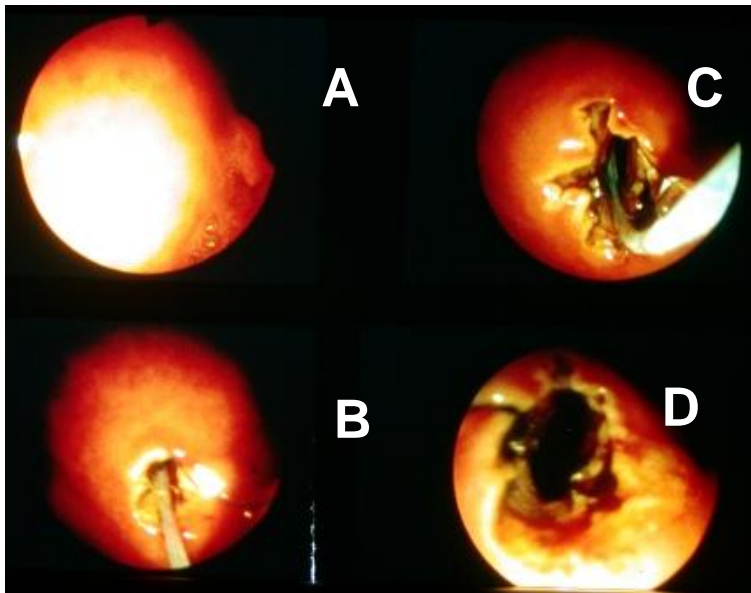
ERP was performed in a dedicated ERCP endoscopy suite and supervised by hepatobiliary surgeons experienced in interventional endoscopy (Thomson, Krige et al. 2014). Blood was taken for coagulation screen before the procedure and patients were fasted overnight. Intravenous ampicillin and gentamycin were administered for antibiotic prophylaxis. Endoscopic retrograde cholangiopancreatography (ERCP) was performed using a side-viewing duodenoscope (TJF 145 or TJF 160, Olympus Optical Co. Ltd., Tokyo, Japan) under conscious sedation with intravenous midazolam and pethidine. The pancreatic duct was selectively cannulated under direct endoscopic vision via the ampulla. A pancreatogram was obtained to define the site and extent of the ductal injury. This information was recorded and used to determine the therapeutic strategy of either endoscopic transpapillary sphincterotomy with or without pancreatic duct stenting, or transmural pseudocyst drainage or surgery (Thomson, Krige et al. 2014). When endoscopic stenting or pseudocyst drainage was not feasible technically or if the pseudocyst recurred after initial endoscopic management, patients were referred for surgery.

17.2.5.2 Transmural pseudocyst drainage

The pseudocyst was confirmed to be in close proximity to the gastric or duodenal wall by first evaluating a recent computed tomogram (CT). Endoscopic drainage was performed using a side-viewing duodenoscope. The pseudocyst was identified as a distinct intraluminal bulge in the posterior wall of the stomach or the first part of the duodenum. A needle knife papillotome was passed through a 10-Fr coaxial catheter to puncture the cyst wall at the site of

maximal prominence using blended diathermy (Fig. 3). The co-axial catheter and a 0.89 mm x 450 cm guide wire (Jagwire[®], Boston Scientific Corporation, Natick, MA 01760-1537, USA) were advanced into the cavity to secure the tract and maintain endoscopic access. The incision in the mucosa and the deeper layers was extended to approximately 10mm in size using a needle-knife or standard papillotome (Fig 3). In patients who had a thick pseudocyst wall or those with evidence of infection in the pseudocyst, one or two 7Fr or 10Fr double pigtail stents (Fig 4) were placed across the cystenteric tract to ensure patency and adequate pseudocyst drainage (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994). Antibiotic therapy was given for 48 h after drainage and repeat imaging was done during the same hospital admission to gauge response and assess adequacy of drainage (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994).

Figure 3



Endoscopic cystgastrostomy sequence using a blended current bowed hot-wire sphincterotome. Panel A: Pseudocyst bulge evident in the stomach; Panel B: Penetration into the pseudocyst with a needle-knife to establish a tract; Panel C: Endoscopic cystgastrostomy created with a sphincterotome; Panel D: Completed cystgastrostomy

Figure 4



Endoscopic plastic stent drainage of a post-traumatic pseudocyst

17.2.5.3 Transpapillary drainage

Pancreatic duct cannulation was attempted first using a floppy tip guide-wire. If duct access was not achieved, a small volume of contrast was injected via the catheter to identify and define the main pancreatic duct. After successful deep cannulation, more contrast was injected to confirm either pancreatic duct integrity or a stricture or disruption of the duct. Pancreatic duct disruption was regarded as complete if the main duct upstream to the stricture or disruption could not be filled with contrast or was considered to be partial when contrast entered and opacified the main duct upstream from the point of disruption. Duct stenting was done using a 0.89 mm hydrophilic guide wire (Jagwire[®], Boston Scientific Corporation) positioned in the main pancreatic duct and a 7-Fr

transpapillary pancreatic stent was advanced over the guidewire into the pancreatic duct.

17.2.6 Data analysis

The data were analysed using Stata version 11 (*StataCorp. 2009. Stata: Release 11. Statistical Software. College Station, TX: StataCorp LP*). Statistical analysis was performed using the Fischer exact test and 2-tailed Student t test. A p value less than 0.05 was considered statistically significant.

17.3 Results

During the study period 432 patients were treated for pancreatic injuries of whom 27 (20 men, 7 women, median age 31, range 15-68 years) presented with delayed complications related to the initial pancreatic injury and were referred to the HPB unit for definitive management. The mechanism of injury was blunt abdominal trauma in 16 (assault n=13, passenger motor vehicle accident n=1, sport injury n=1, fall from a height n=1), low velocity abdominal gunshot (n=6) and abdominal stab wound (n=5). Sixteen patients had isolated injuries of the pancreas and 11 had associated collateral damage to one or more adjacent organs (1 associated organ injury n=5, 2 organs n=4, 3 organs n=1, 5 organs n=1). Thirteen patients were initially managed non-operatively while 14 (gunshot n=6, stab wounds n=5, blunt injury n=3) underwent an urgent laparotomy and subsequently developed a pancreatic-related complication and presented weeks or months after the index operation. Three of the 14 patients had isolated injuries of the pancreas and 11 had one or more injuries as indicated above. Four of the 14 had associated major vascular injuries and

required a median transfusion of 14 (range 8-47) units of blood in the peri-operative period. Eight of the 14 recovered with no complications while 6 patients had significant complications (respiratory n=6, bleeding/DIC n=3, sepsis n=3, intra-abdominal collection n=2, adhesive bowel obstruction n=1, enterocutaneous fistula n=1). None of the 27 patients in this study died.

17.3.1 Anatomic site and severity of injury

Ten patients had proximal pancreatic injuries (head n=2, neck n= 8). Fourteen patients had an injury involving the body of the pancreas, and 3 had injuries which involved the pancreatic tail. The 27 patients had grade 2a (n=1), 3a (n=6), 3b (n=4), 4a (n=6), 4b (n=7) and grade 4c (n=3) ductal injuries (Table 1).

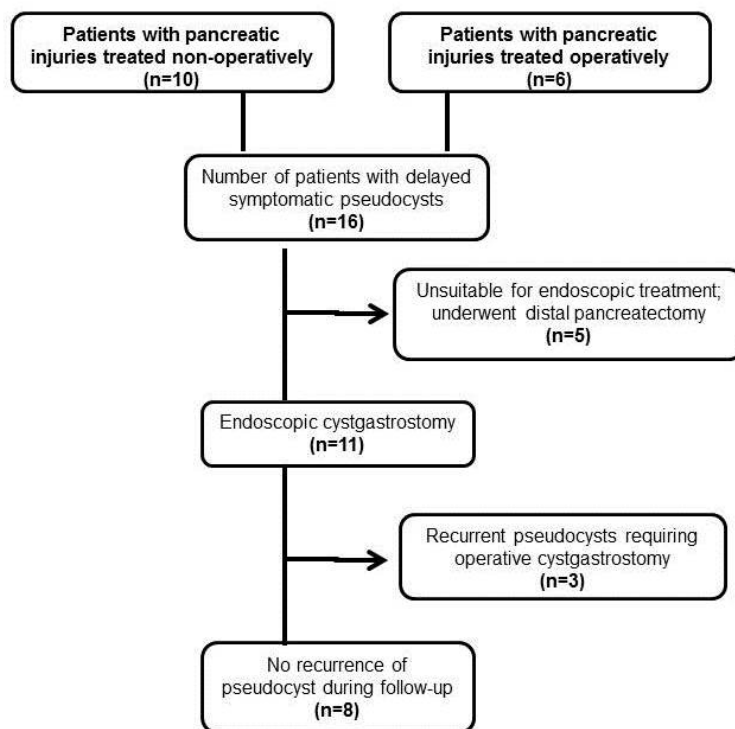
17.3.2 Delayed presentation of post-traumatic pseudocysts

Sixteen patients had non-resolving symptomatic pancreatic pseudocysts (median diameter 10cm, range 6-19cm) and presented between 6 weeks and 8 months after the pancreatic injury. Ten patients had initially sustained blunt abdominal trauma and had been managed non-operatively while 6 patients had previously undergone a laparotomy for abdominal trauma and had either a distal pancreatectomy and splenectomy (n=1) or external sump drainage of the pancreatic injury (n=5) (Fig 5).

After detailed CT and ERP evaluation, 5 patients who had complete main duct division and grade 4a (n=2) and 4b (n=3) ductal injuries and pseudocysts were not drained endoscopically because there was no close apposition with the posterior stomach wall or drainage was regarded as high risk due to splenic

vein thrombosis and the presence of large intramural gastric varices and all 5 underwent a distal pancreatectomy (Fig 5). Eleven patients underwent endoscopic transmural cystgastrostomy with double pigtail stent drainage (n=5) or endoscopic cystgastrostomy using a sphincterotome to cut an opening in the stomach wall (n=3) or by transpapillary stenting (n=3). The pseudocysts recurred in all 3 transpapillary stent patients who had grade 4a n=2, 4b n=1 ductal injuries and were restented and recurred again. All 3 subsequently underwent a successful operative cystgastrostomy. In the remaining 8 patients (grade 2a ductal injuries n=1, grade 3a injuries n=4, 3b n=2, 4c n=1) there was no recurrence of the pseudocyst on follow-up of 18 to 60 months after removal of the endoscopic stents.

Figure 5 Patients with delayed presentation of complicated post-traumatic pancreatic pseudocysts



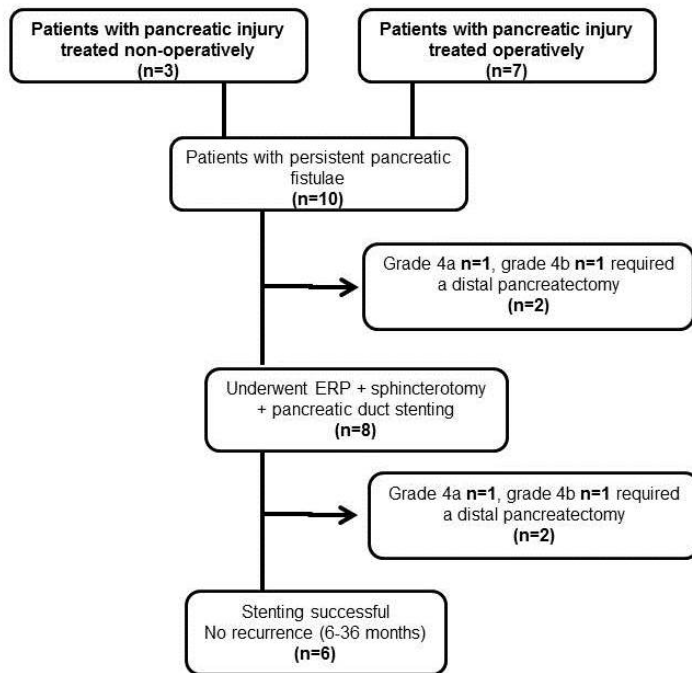
17.3.3 Persistent post-traumatic pancreatic fistulae

Ten patients were referred with persistent high-output (median 320ml/day, range 250-475ml/day) pancreatic fistulae 6-20 weeks after a pancreatic injury (Fig 6). Three patients with blunt trauma had been managed non-operatively and developed peripancreatic fluid collections which were treated by ultrasound-guided percutaneous catheter drainage but did not resolve. Seven patients had undergone operative management of abdominal trauma and had either a distal pancreatectomy and splenectomy (n=2) or external drainage (n=5) of the pancreatic injury. All 10 underwent an ERCP and sphincterotomy and attempted ductal stenting (Fig 6). Stent placement was unsuccessful in 2 patients who had complete pancreatic duct disruption (grade 4a n=1, 4b=1) at the pancreatic neck and body and both had an elective distal pancreatectomy. The remaining 8 patients were stented. In 2 patients with complete duct disruption (grade 4a/b ductal injuries) non-bridging 7-Fr stents were placed for pancreatic neck and proximal body injuries but there was no resolution of the external pancreatic fistulae after 6 weeks of drainage and both were treated surgically with a distal pancreatectomy. The remaining 6 patients had either bridging 7-Fr stents placed for grade 3b ductal injuries of the proximal body ducts (n=2) or stents placed for injuries in the distal body (3a n=2, 4c=2) and are well after stent removal with no recurrence after endoscopic management during follow-up (6-36 months).

One patient with a grade 4b complete main pancreatic duct obstruction at the pancreatic neck and painful upstream obstructive pancreatopathy had unsuccessful stenting and required surgical intervention.

In summary, all 14 patients who had either grade 2a, 3a, 3b or 4c ductal injuries resolved after endoscopic intervention. Thirteen patients with grade 4a and 4b ductal injuries all required surgery.

Figure 6 Outcome of intervention in patients with persistent post-traumatic pancreatic fistulae



17.3.4 Complications

The 27 patients underwent a total of 49 endoscopic procedures (47 elective, 2 emergency). Complications occurred in 4 patients after endoscopic stent placement. All complications resolved on either endoscopic re-intervention (n=2) or on conservative management (n=2). Stent migration occurred in 1 patient and a new stent was placed. One patient had bleeding from the sphincterotomy site which was controlled with endoscopic injection and 2 patients had self-limiting pancreatitis. Two patients who required a distal pancreatectomy for a pancreatic pseudocyst after unsuccessful endoscopic

drainage, developed a low output pancreatic fistula, both of which resolved on conservative therapy.

17.4 Discussion

Major injuries to the pancreas remain an important cause of morbidity and mortality even when treated in contemporary high volume specialist trauma centres (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005, Subramanian, Dente et al. 2007, Stawicki and Schwab 2008, Recinos, DuBose et al. 2009). Overall reported morbidity rates following major pancreatic injuries range from 30% to 70% and are primarily related to either delayed or inappropriate intervention or substantial collateral damage from associated vascular, hepatic and bowel injuries due to the close proximity of adjacent organs and critical vascular structures (Stawicki and Schwab 2008, Recinos, DuBose et al. 2009). The most frequently reported pancreas-specific complications are fistulae and pseudocysts which commonly manifest in the first weeks after the injury (Stawicki and Schwab 2008).

Limited data are available on the management of delayed complications after pancreatic injuries (Carr, Cairns et al. 1989, Coelho, Ardengh et al. 2011). Most complications manifest early and are treated using either percutaneous ultrasound drainage of amylase-rich fluid or infected collections, or endoscopic or operative intervention. This study is novel on two accounts. The degree of pancreatic duct injury was graded using a new modified grading system and the study then assessed endoscopic therapeutic outcome according to the grade of injury. Previous classifications of pancreatic pseudocysts were based on features found in chronic pancreatitis and are not relevant or applicable in

pancreatic trauma (D'Egidio and Schein 1991, Nealon and Walser 2002). In this study, a modified grading classification was used for the degree of main pancreatic duct injury which was adapted from the classification originally proposed by Takashima. The current classification is more comprehensive and makes allowance for main duct injury with or without duct continuity and also incorporates leaks and pseudocysts which occur after pancreatic resection, both factors which were not included in the original Takashima classification (Takishima, Hirata et al. 2000).

Optimal management of traumatic pancreatic pseudocysts depends on the patient's symptoms, cyst size, location, degree of main duct injury and the maturity of the pseudocyst wall (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994). Previous studies from our group found that while traumatic pancreatic pseudocysts which occur as a consequence of side duct injuries with an intact main pancreatic duct generally resolve spontaneously, large persistent or symptomatic pseudocysts that result from proximal main duct injuries require intervention utilising either endoscopic or surgical drainage (Lewis, Krige et al. 1993, Thomson, Krige et al. 2014). We have reported previously that although endoscopic drainage of selected traumatic pancreatic pseudocysts is practical and safe, the procedure may not be technically possible in all pseudocysts and that those in whom safe access is not feasible or who recur despite endoscopic drainage, operative drainage is required (Lewis, Krige et al. 1993, Funnell, Bornman et al. 1994, Thomson, Krige et al. 2014). In this study 14 patients with grade 2a, 3a, 3b and 4c pancreatic main duct injuries were successfully treated endoscopically with pancreatic duct stenting or pseudocyst drainage while 13

patients with grade 4a and 4b duct injuries who had complete duct division and the “disconnected duct syndrome” failed endoscopic management and required surgical intervention.

Despite increasing global experience, the published results of endoscopic pseudocyst drainage and sphincterotomy and duct stenting for the complications of pancreatic trauma are limited (Bhasin, Rana et al. 2009) and vary widely due to differences in patient selection, extent and degree of duct damage and endoscopic tools and techniques used. In a study from San Francisco General Hospital ERCP was performed in 26 patients at a mean of 19 days after the injury. Using endoscopic intervention and treatment of the ductal injury ERCP was able to avoid an operation or reduce the extent of surgical intervention in 11 of the 26 (42%) patients (Rogers, Cello et al. 2010). In a small retrospective study from India 11 patients had endoscopic therapy after pancreatic trauma. Seven patients were treated for a symptomatic pseudocyst and 4 patients had a persistent external pancreatic fistula. Eight were successfully treated with either cystogastrostomy or bridging pancreatic stent or nasopancreatic drain. In patients with complete duct disruption non-bridging stents did not resolve the pseudocysts and these required surgery. The authors concluded that complications related to pancreatic trauma in selected patients can be effectively treated endoscopically (Bhasin, Rana et al. 2012).

In a multicentre study from Brazil, outcome was analyzed after endoscopic treatment in 51 symptomatic patients who had persistent traumatic pseudocysts (Coelho, Ardengh et al. 2011). Endoscopic retrograde pancreatography

(ERCP) graded the extent of main pancreatic duct damage according to the original Takishima classification. Treatment was selected as either transpapillary drainage (Takishima 2 and 3 without bulging), transmural (type 1), or combined (type 2 or 3 with bulging). ERCP was successful in 47 (90%) of 51 patients. Thirteen patients had transmural drainage, 10 had transpapillary and 24 had combined drainage. The success rate was 94% and recurrence rate was 8%. There were no procedure-related deaths but 9 patients had complications. The authors concluded that endoscopic treatment of traumatic pancreatic pseudocysts could be considered a safe and effective alternative to surgical treatment and that ERCP and the Takishima classification were useful in determining the best endoscopic approach (Coelho, Ardengh et al. 2011).

EUS guided drainage has replaced conventional endoscopic guided drainage and is now accepted as the standard of care in the management of symptomatic pseudocysts in most major centres (Song and Lee 2014). EUS has significant advantages over non-EUS-guided transmural drainage and includes the identification and safe drainage of non-bulging pseudocysts and those with a small anatomic window for safe drainage and detection and avoidance of intramural vascular collaterals as occurs in splenic vein thrombosis (Song and Lee 2014). Two randomized trials have compared EUS-guided PPC drainage and conventional endoscopy-guided PPC drainage. Varadarajulu *et al.* found that all 14 EUS drainages were successful while only five of 15 patients randomized to EGD drainage were successful, and all 10 EGD failures had a successful outcome after cross-over to EUS drainage (Varadarajulu, Christein et al. 2008). Similar results were found in the study by

Park *et al.* in which all patients had eventual successful drainage after 8 patients with no bulge crossed over to successful EUS drainage (Park, Lee *et al.* 2009). In a subsequent study Fockens *et al.* showed that EUS changed management in more than one third of patients who had pseudocyst drainage (Fockens, Johnson *et al.* 1997).

Although there have been substantial improvements in both the tools and the techniques used in interventional endoscopy, decisions regarding the optimal type, size, and number of stents for pseudocyst drainage are unresolved. Most endoscopists have used multiple double pigtail plastic stents for transmural drainage with a nasocystic drain added for irrigation if viscous debris is present (Larsen and Kozarek 2014, Song and Lee 2014). Recently, purpose-designed short fully covered self-expandable metal stents with a large lumen and double collars to prevent stent migration have been tested (Song and Lee 2014). The larger stent lumen facilitates drainage in pseudocysts with thick debris and decreases the need for repeated endoscopic procedures while increasing the success rate and reducing time to resolution. While most of the endoscopic experience has been obtained in patients with pancreatitis, the results of endoscopic management of the “disconnected duct syndrome” (DDS) due to complications after acute pancreatitis may not be directly comparable to duct disruption seen after pancreatic trauma (Fischer, Gutman *et al.* 2014, Larsen and Kozarek 2014). In a series of 31 patients with DDS after acute pancreatitis who underwent endoscopic treatment 12 required surgery (Pelaez-Luna, Vege *et al.* 2008), while in another series Varadarajulu *et al.* described 33 patients with DDS of whom 8 required salvage surgery and 22 were successfully treated

with transmural drainage with prolonged stenting (Varadarajulu and Wilcox 2011).

There are several important limitations and caveats to consider in the interpretation of the results of this analysis. Despite the fact that the study group was drawn from a high volume tertiary academic centre with one of the largest existing translational pancreatic trauma databases which is maintained and managed by trained full-time staff, the number of patients with delayed complications are small and may reflect an inherent referral and treatment bias. The analysis is based on a select surgical cohort treated in a centre with constant access to specialist multidisciplinary HPB care which is not representative of or applicable to lesser resourced hospitals where such facilities may not be freely available. Also, the patient population studied comprises a heterogenous group in which most patients had complex pancreatic injuries and severe associated intra-abdominal injuries. An important consideration is that, patients were accumulated over two decades during which the technique of endoscopic intervention has evolved substantially. Initially endoscopic pseudocyst drainage was only possible when an obvious intraluminal bulge was visible. The introduction of EUS has allowed pseudocysts without an obvious intraluminal bulge to be drained safely. In addition the endoscopic drainage technique has changed since the original description and the initial endoscopic cystgastrostomy method is now seldom applied and has been replaced with safer and more effective multiple plastic stents and more recently with partially covered SEMS (Song and Lee 2014).

In conclusion, endotherapy for established pancreatic complications after trauma is generally safe with a low incidence of adverse events and is likely to be effective in half of those with persistent pseudocysts or leaks. All the patients in this study who had either grade 2a, 3a, 3b or 4c pancreatic ductal injuries resolved after endoscopic intervention and those with grade 4a or 4b ductal injuries uniformly required surgery. In this analysis the new proposed Cape Town pancreatic ductal injury grading classification showed a close correlation with outcome after endoscopic and operative intervention. It is important, however, that the validity of these data and the new grading system for pancreatic duct injuries be confirmed in future prospective studies.

CHAPTER 18

Isolated pancreatic injuries: an analysis of 49 consecutive patients treated at a Level 1 Trauma Centre

18.1 Introduction

Isolated injuries of the pancreas are uncommon and occur in less than 1% of patients with abdominal trauma (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005). Serious sequelae may follow if the magnitude of the pancreatic injury is underestimated or inappropriately treated (Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008). Neglect of a main pancreatic duct injury invariably leads to major complications which include pseudocysts, fistulas, intra-abdominal sepsis and delayed secondary haemorrhage. Although several substantial reports detailing the management of pancreatic injuries have been published in the past, few series have specifically assessed outcome after isolated injuries of the pancreas (Lochan, Sen et al. 2009).

A feature of previous publications assessing pancreatic injuries is the frequency of associated collateral visceral and vascular injuries which profoundly influence outcome and hamper accurate comparative studies (Kao, Bulger et al. 2003, Hwang and Choi 2008, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014). A further limitation of previous reports is the relatively small number of patients included and the absence of a detailed and precise subgroup analysis of isolated pancreatic injuries. Based on our previously published clinical experience (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012, Krige, Kotze et al. 2014, Krige, Kotze et al. 2014) the hypothesis of this study is that much of the morbidity and mortality that occurs as a

consequence of a major pancreatic injury is due to collateral damage to adjacent vital organs and in their absence, isolated pancreatic injuries should have a significantly lower complication and death rate. To test this hypothesis this study used a large, high-quality surgical outcomes database in a cohort of consecutive patients using robust and reliable methodology with objective and reproducible end-points to assess outcome and injury-specific factors associated with morbidity and mortality after an isolated pancreatic injury.

18.2 Methods

Study population and data collection

Details of the study population, data collection and variables recorded are outlined in the methodology section in Chapter 3.

18.2.1 Definitions

Details of definitions applied are provided in the study methodology in Chapter 3.

18.2.2 Initial and operative management of pancreatic injuries

Details of initial and operative management of pancreatic injuries and damage control laparotomy are given in the study methodology in Chapter 3.

18.2.3 Endoscopic management of pancreatic pseudocysts

The diagnosis of a pseudocyst or pancreatic duct fistula was based on review of the original operative and clinical findings, fluid amylase levels, ultrasound, CT scan, MRI, MRCP, ERP and EUS findings (Thomson, Krige et al. 2014). The site of the pancreatic duct fistula (head, neck, body or tail) was noted and the

size of the pseudocyst was measured in cm in 2 dimensions and location, relationship and proximity to stomach and duodenal wall recorded. The degree and extent of the main pancreatic duct injury was assessed using the Cape Town pancreatographic grading system for pancreatic injuries (Table 1), modified from the original classification by Takishima et al. (Takishima, Hirata et al. 2000).

Table 1 The Cape Town pancreatographic grading system for pancreatic injuries modified from the original classification by Takishima et al.

Classification of Injury	ERP Findings
Grade 1	Normal pancreatic duct as evident on ERP
Grade 2	Main pancreatic duct intact. Injury to branches of pancreatic duct on ERP
A	Contrast contained within the pancreatic parenchyma
B	Contrast leaks beyond the pancreatic parenchyma into the retroperitoneal space
Grade 3	Injury to main pancreatic duct on ERP. Duct continuity present
A	Injury to main pancreatic duct in body or tail with duct continuity *
B	Injury to main pancreatic duct in the head with duct continuity
Grade 4	Complete main pancreatic duct division with no duct continuity
A	Complete main pancreatic duct division in body or tail with no duct continuity *
B	Complete main pancreatic duct division in the pancreatic head with no duct continuity *
C	Complete main pancreatic duct division with no duct continuity due to resection of damaged pancreas *

* Line to discriminate between grades 3A and 3B, 4A and 4B is the right margin of the superior mesenteric vein

18.2.3.1 ERP technique

ERP was performed or supervised by hepatobiliary surgeons experienced in interventional endoscopy and performed in a dedicated ERCP endoscopy suite using a side-viewing duodenoscope (TJF 145 or TJF 160, Olympus Optical Co.

Ltd., Tokyo, Japan) under conscious sedation (Thomson, Krige et al. 2014). Transmural endoscopic pseudocyst drainage was accomplished using a needle knife papillotome passed through a 10-Fr coaxial catheter to puncture the cyst wall at the site of maximal prominence using blended diathermy. A co-axial catheter and a hydrophilic 0.89 mm x 450 cm guide wire (Jagwire[®], Boston Scientific Corporation, Natick, MA 01760-1537, USA) were advanced into the cavity to secure the tract and maintain endoscopic access. In patients who had a thick pseudocyst wall or those with evidence of infection in the pseudocyst, one or two 7Fr or 10Fr double pigtail stents were placed across the tract to ensure patency and adequate pseudocyst drainage. Patients in whom EUS did not identify safe transmural access, transpapillary drainage and duct stenting was performed using a 0.89 mm hydrophilic guide wire (Jagwire[®], Boston Scientific Corporation) positioned in the main pancreatic duct and a 7-Fr transpapillary pancreatic stent was advanced over the guidewire into the pancreatic duct. When neither endoscopic stenting nor endoscopic pseudocyst drainage were technically feasible, patients were referred for surgery.

18.2.4 Statistical analysis

Pearson's chi-square test was used for analysis of categorical variables, and odds ratios (ORs) with 95 per cent confidence intervals (CI) were calculated. Statistical analysis was performed using non-parametric Mann–Whitney, or Student's *t*-test when appropriate. $P < 0.05$ was considered statistically significant. The data were analysed using Stata version 11 (*StataCorp LP, College Station, Texas, USA*).

18.3 Results

During the period under review 448 consecutive patients were treated for pancreatic injuries (GSW 245, blunt 122 and stab wounds 81), 49 of whom had an isolated pancreatic injury. Median age of the 49 patients was 30 (range 13–68) years, 41 (83.7%) were male and 8 female. Forty three patients sustained blunt injuries (assault n=28, motor vehicle accidents: 3 pedestrians, one driver and 2 passengers, falls from a height n=4, sport injuries n=4 and a go-kart injury n=1. Six patients had penetrating stab wounds. The pancreatic head was injured in 3 patients, the neck in 10 patients, the pancreatic body in 30 and tail injuries occurred in 6 patients. Concurrent extra-abdominal trauma involving chest (n=4), limbs (n=4), and head (n=1) occurred in 4 patients after blunt trauma and in one patient who had penetrating trauma due to a stab wound.

Thirty four (69.4%) patients underwent urgent surgery after resuscitation and 15 patients who were initially treated non-operatively after blunt abdominal trauma presented 6 weeks to 4 months later with a non-resolving symptomatic pancreatic pseudocyst or fistula and were managed with endoscopic intervention. In the 34 patients who underwent an urgent laparotomy two clear patterns of surgical intervention were evident. Those with major pancreatic injuries and clear division of the pancreatic parenchyma and an evident injury to the main pancreatic duct (n=20) underwent definitive resection of the injured pancreas. Those who had lesser pancreatic injuries combined with other serious extra-abdominal injuries had external drainage only (n=14) of the pancreatic injury. The details of these two categories are presented below.

18.3.1 Definitive pancreatic surgery (n=20)

Twenty of the 34 patients who presented with an acute abdomen and were found at laparotomy to have a grade 3 or 4 pancreatic injury had either a distal pancreatectomy and splenectomy (n=14) or a splenic-preserving distal pancreatectomy (n=6). Significant morbidity occurred in 14 of the 20 patients (Table 2). Post-operatively 7 of the 20 patients developed a pancreatic fistula. Five fistulas resolved on conservative treatment (grade A), one patient required endoscopic pancreatic duct stent drainage (grade B) and one patient with a persistent pancreatico-colo-cutaneous fistula underwent operative closure (grade C). One patient required ultrasound-guided drainage of a pancreatic fluid collection, and two patients required TPN for enterocutaneous fistulas. Other complications included pneumonia and a pleural effusion (n=5), intra-abdominal sepsis (n=4), adhesive obstruction (n=1) which required surgery and adhesiolysis, systemic sepsis (n=1) and one patient had retroperitoneal bleeding and was packed after a distal pancreatectomy. There was no mortality in this group. Median hospital stay for those who had a pancreatic resection was significantly longer than those who did not ($p<0.05$, Table 2) while patients who had complications similarly had significantly longer hospital stays [36 (7–92) vs 14 (8–31)] days ($p<0.05$).

Table 2 Demographic and clinical details of patients with isolated pancreatic injuries

	Surgical resection n=20	Surgical drainage n=14	Delayed presentation n=15	
Males	18	10	13	
Females	2	4	2	
Age (range)	29 (13-49)	29 (15-56)	31 (18-68)	
AAST				
Grade 1	-	4	-	
Grade 2	-	4	-	
Grade 3	16	6	13	
Grade 4	4	-	2	
Site				
Head	-	-	3	
Neck	7	-	3	
Body	11	9	9	
Tail	2	4	-	
Extra-abdominal injuries	1	4	0	
Dindo-Clavien grading	n=20	n=14	n=5	10 pts in this group had no surgery
0	6	5	-	
1	1	-	2	
2	2	2	-	
3	3	4	-	
4	8	1	-	
5	-	-	-	
6	-	2	-	
Pancreatic fistula grade				
A	5	1	1	
B	1	5	-	
C	1	-	-	
Mortality	0	2	0	
Days in hospital (range)	29 (8-92)	16 (2-90)	16 (8-65)	

18.3.2 External pancreatic drainage (n=14)

Fourteen of the 34 patients had an acute abdomen and underwent an emergency laparotomy. Eight patients were assessed intra-operatively to have either AAST grade 1 or 2 pancreatic injuries which were treated by external *PenSil* drainage placed close to the injury site and 6 had uneventful recoveries. Six patients had AAST grade 3 injuries which were treated by drainage alone because other extra-abdominal collateral injuries took precedence. All six

developed a pancreatic fistula which required endoscopic intervention with ERP and transpapillary pancreatic duct stenting with 7Fr Teflon stents for resolution. One patient also required ultrasound-guided drainage of a pancreatic fluid collection. Four patients had additional postoperative complications which included DIC, renal failure and septic shock, wound infection, pneumonia and renal failure. Duration of hospitalisation ranged from 2-90 days (median 16 days).

Two of the 14 patients in this cohort died. A 28 year old man was admitted to hospital shocked with a RTS of 5.1 after blunt head, thoracic and abdominal trauma. A grade 1 pancreatic injury was drained at laparotomy but he died of his head injury 24 hours later. The second death was a 34 year old man who had sustained multiple fractures of ribs, arms, legs and pelvis and a traumatic leg amputation. A grade 1 pancreatic tail laceration was drained and he died of DIC, renal failure and septic shock. In neither patient was the pancreatic injury the cause of death. Duration of hospitalisation in this group was 7 to 65 days, median 29 days. Seven patients required admission to ICU for a median of 5 days, range 1 to 7 days.

18.3.3 Delayed presentation of post-traumatic pancreatic complications

Fifteen patients who had sustained blunt abdominal trauma and had been managed non-operatively, presented with pancreatic related complications 6 weeks to 4 months after the pancreatic injury. Fourteen patients had non-resolving symptomatic pancreatic pseudocysts (median diameter 10cm, range 6-19cm) and one patient had a persistent external pancreatic fistula. After detailed CT, MRCP and ERP evaluation, 4 patients who had pseudocysts and

complete main pancreatic duct division with a disconnected duct syndrome (grade 4A and 4B ductal injuries) could not be drained endoscopically because there was no close cyst apposition with the posterior stomach wall and drainage was regarded as high risk due to splenic vein thrombosis and the presence of large intramural gastric varices. All 4 underwent operative pancreatic pseudocyst drainage (cyst-gastrostomy n=3, cyst-jejunostomy n=1). The fifth patient had a persistent external pancreatic fistula due to complete main pancreatic duct division (grade 4A ductal injury) which was not amenable to endoscopic stenting and he underwent a pancreaticojejunostomy. One patient developed post-operative abdominal sepsis and a prolonged ileus (Table 2).

The remaining 10 patients (grade 3A ductal injuries n=4, grade 3B injuries n=6) underwent endoscopic transmural pseudocyst drainage. One patient recurred and had a further endoscopic procedure with no recurrence of the pseudocyst. These 10 patients underwent a total of 21 endoscopic procedures. Complications occurred in 2 patients after endoscopic stent placement. Both complications resolved on either endoscopic re-intervention or on conservative management. Stent migration occurred in 1 patient and a new stent was placed. One patient had self-limiting pancreatitis. All 10 patients are asymptomatic with no pseudocyst recurrence on follow-up of 18 to 48 months after removal of the endoscopic stents.

18.4 Discussion

Pancreatic injuries seldom occur in isolation and the principal cause of early death after a major pancreatic injury is the severity and the aggregate of associated vascular, solid organ and gastro-intestinal injuries (Chryso,

Athanasakis et al. 2002, Krige, Beningfield et al. 2005, Subramanian, Dente et al. 2007, Degiannis, Glapa et al. 2008). This report represents the largest series to date of consecutive patients with isolated injuries of the pancreas and is characterized by several distinctive features. This study confirms that isolated injuries are uncommon and occurred in only 49 of the 448 patients registered on a large comprehensive pancreatic injury database. Most isolated injuries in this series were the consequence of blunt abdominal trauma although penetrating injuries predominate in the database. The mortality of isolated injuries of the pancreas in our series was 4% which is in accordance with the only two other publications on the same topic (Buccimazza, Thomson et al. 2006, Lochan, Sen et al. 2009). These figures are significantly less than the published data on overall mortality in pancreatic trauma and is due to the inherent selection bias of this specific type of injury. Forty per cent of the patients in this study had a definitive pancreatic resection at the index presentation with zero mortality. Although 31% of patients presented with delayed pancreas-specific complications, two-thirds of the pseudocysts and fistulas were successfully treated endoscopically.

Morbidity in this series was substantial both in the incidence of pancreatic-specific complications presenting as complex non-resolving fistulas and pseudocysts and in overall morbidity. The reported incidence of a pancreatic fistula after distal pancreatectomy for trauma varies widely and ranges from 3 to 24% due in part to inconsistencies in the diagnostic criteria used and the variable definitions of a pancreatic leak (Goh, Tan et al. 2008, Sharpe, Magnotti et al. 2012). In this study, an adapted definition for pancreatic fistula was used

as proposed by the International Study Group on Pancreatic Fistula (ISGPF) that was designed for pancreatic resections (Bassi, Dervenis et al. 2005). Twenty-five of 39 patients (64%) had Dindo-Clavien grade 1-6 complications and a clinically significant pancreatic fistula occurred in 29% of patients. Conservative management was used initially in all patients in the present series and most pancreatic fistulas closed spontaneously as is the experience of other authors (Goh, Tan et al. 2008, Sharpe, Magnotti et al. 2012). Patients who had refractory pancreatic fistulas underwent endoscopic sphincterotomy and pancreatic duct stenting to decompress the pancreatic duct and promote antegrade flow of pancreatic fluid (Malleo, Pulvirenti et al. 2014). In this study four patients had a traumatic “disconnected duct syndrome” due to complete transection of the main pancreatic duct with the resultant isolated upstream pancreatic segment no longer in communication with the papilla (Larsen and Kozarek 2014). The ensuing fistula is seldom amenable to transpapillary stenting as the isolated pancreatic segment is not accessible from the papilla (Nadkarni, Kotwal et al. 2015) and the defect cannot be bridged endoscopically and all four patients underwent operative pancreatic pseudocyst drainage.

Ideally, in order to minimise or eliminate a postoperative pancreatic fistula, a reliable technique that prevents leakage from the severed duct or parenchymal margin should be used. However, the optimal management of the divided pancreatic duct and the resection margin after distal pancreatectomy for trauma remains unresolved and the choice of technique is often dictated by intraoperative findings and the extent of the pancreatic injury (Krige, Kotze et al. 2014). Several surgical resection and closure techniques have been utilized to

seal the pancreatic remnant to reduce complications and in particular pancreatic fistulas. These methods include hand-sewn suture techniques, stapled closure techniques, or a combination of both ultrasonic dissection devices, pancreatocentric anastomosis, application of meshes, seromuscular and gastric serosal patches, or sealing with fibrin glue. While stapler transection and stapler closure of the pancreatic remnant is favoured by some surgeons, this technique resulted in a fistula rate of 22.9 per cent in a recent meta-analysis (Knaebel, Diener et al. 2005). Other surgeons have advocated the use of a Roux-en-Y pancreatojejunostomy to incorporate and drain the resection margin to reduce this risk (Yellin, Vecchione et al. 1972). Even in patients without multiple injuries, the added risk of an anastomotic leak is not warranted and this procedure is not recommended. Most trauma surgeons oversew or staple the transected end of the pancreas and use simple methods to buttress or seal the cut margin. Procedures designed to preserve pancreatic tissue are technically more complex than a distal pancreatectomy and are a potential site for anastomotic leaks and resultant sepsis (Yellin, Vecchione et al. 1972). In this series distal pancreatectomy with splenic preservation was achieved in one third of patients in whom the spleen was not injured. As noted by previous authors (Cogbill, Moore et al. 1991), the data in this study suggest that a distal pancreatectomy with splenic preservation can be achieved in selected haemodynamically stable patients who have few associated injuries.

In most modern well equipped gastro-intestinal units, endoscopic procedures now play an increasing role in the management of complex pancreatic fluid collections and duct leaks (Larsen and Kozarek 2014). However, despite

increasing global experience, the published results of endoscopic pseudocyst drainage and endoscopic sphincterotomy and duct stenting for the complications of pancreatic trauma are limited and vary widely due to differences in patient selection, extent and degree of duct damage and endoscopic tools and techniques used (Bhasin, Rana et al. 2009, Coelho, Ardengh et al. 2011). EUS guided drainage has replaced conventional endoscopic guided drainage and is now accepted as the standard of care in the management of symptomatic pseudocysts in most major centres (Coelho, Ardengh et al. 2011). EUS has significant advantages over non-EUS-guided transmural drainage and includes the identification and safe drainage of non-bulging pseudocysts and those with a small anatomic window for safe drainage and detection and avoidance of intramural vascular collaterals as occurs in splenic vein thrombosis (Bhasin, Rana et al. 2009). In two-thirds of patients with non-resolving pseudocysts in this study, endoscopic intervention was successful.

Published data focussing on isolated pancreatic injuries are scant. There are only two papers which specifically address this topic. Eleven patients (7 men, 4 women, median age 30, range 13-51 years) were treated in Newcastle upon Tyne by Lochan and colleagues (Lochan, Sen et al. 2009). All 11 sustained blunt abdominal trauma and 10 were initially treated conservatively. In two patients, primary treatment with somatostatin analogues resulted in early resolution of symptoms and signs. Six patients underwent surgery at various stages post-injury, some as long as 4 and 6 years after the injury. Eight patients were asymptomatic after a median follow-up of 58 months (range 22-

106 months), but two patients had chronic pain following distal pancreatectomy and one patient had occasional discomfort. In a study from Durban, 16 patients (13 men, 3 women, age range 4 - 46 years) had isolated pancreatic injuries due to blunt trauma (n=14) or stab wounds (n=2) (Buccimazza, Thomson et al. 2006). Nine patients were managed in the acute phase: 6 by splenic-preserving distal pancreatectomy and 2 by distal pancreatico-enteric anastomosis; 1 was drained. Delayed presentation occurred in 7 patients, 6 with pseudocysts and 1 with infected pancreatic necrosis who subsequently died. The six patients with pseudocysts were managed endoscopically, four of whom resolved and two subsequently required an operation, one had a pancreaticojejunostomy and the other a distal pancreatectomy. These authors conclude that in the acute situation, resection or distal pancreatico-enteric anastomoses are attainable with a low morbidity in patients with isolated pancreatic injuries (Buccimazza, Thomson et al. 2006).

A strength of the current study lies in the use of the generally accepted ISGPS definitions and the Clavien–Dindo classification for postoperative complications, which makes comparative data analysis more reliable. However, several important limitations of this study should be considered in the interpretation of the data. Although the study group was drawn from a high volume tertiary academic centre with one of the largest existing translational pancreatic trauma databases maintained by trained full-time staff, the sample size of patients with isolated pancreatic injuries is relatively small which increases the possibility of type II errors. The analysis is based on a selected patient cohort treated in a major academic centre which has constant access to specialist multidisciplinary

and surgical HPB care which may not be representative of smaller or lesser resourced hospitals. Also, the study cohort comprises a heterogenous group of complex pancreatic injuries which reflects the inherent referral and treatment bias found in major academic centre.

18.5 Conclusion

In conclusion, this analysis has shown that isolated pancreatic injuries in the absence of other major extra-abdominal injuries have a good outcome with low mortality rates. Two thirds of patients with isolated pancreatic injuries required operative intervention. One third of patients who were stable after abdominal trauma without clinical evidence of shock, peritonitis or an abdominal injury requiring operative intervention were managed conservatively but in retrospect clearly had an underlying but occult pancreatic injury and presented subsequently with a pseudocyst. With careful intra-operative evaluation of the injury, most pancreatic injuries can be managed by either distal resection or drainage without the need for complex enteric diversions or pancreaticoenteric anastomoses as a primary procedure during the acute injury phase.

Delayed complications invariably have a major duct injury component but with detailed imaging and evaluation most patients can be effectively treated with endoscopic stent placement or pseudocyst drainage. The data in this study support the contention that the modern management of major pancreatic injuries requires an integrated multidisciplinary approach with trauma and pancreatic surgeons, interventional endoscopists, radiologists and intensivists working in tandem for the benefit of patients who often have complex injuries and considerable postoperative morbidity.

CHAPTER 19

An analysis of predictors of morbidity after stab wounds of the pancreas in 78 consecutive injuries

19.1 Introduction

Injuries of the pancreas are infrequently encountered and occur in less than 5% of penetrating abdominal trauma but may result in substantial morbidity and mortality rates when treatment is delayed or inappropriate (Vasquez, Coimbra et al. 2001, Chrysos, Athanasakis et al. 2002, Subramanian, Dente et al. 2007). Pancreatic injuries seldom occur in isolation because of the intimate relationship to surrounding organs. The anatomic proximity of the portal and superior mesenteric veins and inferior vena cava to the head and neck of the pancreas make these structures particularly vulnerable to penetrating injuries of the proximal pancreas (Chinnery, Krige et al. 2012). Outcome is determined by the cause and grade of the pancreatic injury, the number and severity of associated injuries and the speed and quality of surgical intervention (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005). Previous reports have suggested that associated organ injury is a more important predictor of outcome than the severity of injury to the pancreas (Young, Meredith et al. 1998). Overall morbidity rates exceed 30% especially when the liver, duodenum, colon and major visceral veins are involved (Al-Ahmadi and Ahmed 2008, Ankouz, Elbouhadouti et al. 2010). Mortality may reach 46% and is highest in the elderly and those who are haemodynamically unstable and correlates closely with the number of associated injuries which are detrimental to outcome (Scollay, Yip et al. 2006).

The absence of a universally acceptable classification has prevented accurate comparisons between series (Chrysos, Athanasakis et al. 2002). Because pancreatic injuries are uncommon and most series have small numbers, some studies include all patients with blunt and penetrating pancreatic injuries (Kao, Bulger et al. 2003, Scollay, Yip et al. 2006, Al-Ahmadi and Ahmed 2008), while others combine gunshot and stab wounds of the pancreas (Ivatury, Nallathambi et al. 1990, Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001). Several substantial reports detailing pancreatic injuries have been published in the past, including from our own institution (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012), but none have explicitly evaluated the consequences of stab wounds of the pancreas (Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001, Krige, Kotze et al. 2011). This study therefore examined the factors associated with morbidity and mortality of stab wounds of the pancreas in a high volume academic trauma referral centre.

19.2 Methods

19.2.1 Study population and data collection

Details of the study population, data collection and variables recorded are outlined in the methodology section in Chapter 3.

19.2.3 Definitions

Details of definitions applied are provided in the study methodology in Chapter 3.

19.2.4 Initial and operative management of pancreatic injuries

Details of initial and operative management of pancreatic injuries and damage control laparotomy are given in the study methodology in Chapter 3.

19.2.5 Statistical analysis

Analysis of categorical variables used Pearson's χ^2 test and odds ratios (ORs) with 95 per cent confidence intervals (CI) were calculated. When the Shapiro-Wilk test indicated that numerical variables were not normally distributed, the non-parametric Wilcoxon rank sum test was used. Statistical analysis was performed using non-parametric Mann-Whitney or Student's *t*-test, when appropriate. Statistically significant variables which were potential risk factors were incorporated in the model for logistic regression analysis. $P < 0.05$ was considered statistically significant. The data were analysed using Stata version 11 (*StataCorp LP, College Station, Texas, USA*).

19.3 Results

During the study period, 417 patients were treated for pancreatic injuries, of whom 78 had stab wounds which involved the pancreas. Median age of the 78 patients was 26 (range 16–62) years, 74 (95%) were men and the median RTS was 7.8 (range 2.0–7.8). Twenty-two (28.2%) patients were in shock (systolic blood pressure < 90 mm Hg) on admission to hospital.

19.3.1 Anatomical site and severity of injury

Eighteen patients had injuries of the proximal pancreas involving either the head, neck or uncinate process of the pancreas, 36 had an injury of the body of the pancreas and 24 injuries involved the tail of the pancreas. Sixty-five (83%)

patients had AAST grade I or II pancreatic injuries, and 13 (17%) patients had grade III, IV or V pancreatic injuries (Table 1).

Table 1 AAST grade of pancreatic injury and associated morbidity, pancreas related morbidity and vascular injuries

AAST	n	No. of associated abdominal injuries			No. of associated vascular injuries		Systemic complications		Intra-abdominal complications		Pancreatic complications	
		0	1, 2	3+	n	%	n	%	n	%	n	%
1	43	2*	34	7	5	11.6	8	18.6	3	6.9	2	4.6
2	22	2*	15	5	10	45.5	13	59	4	18.2	3	13.6
3	10	0	8	2	1	10	5	50	6	60	10	100
4	2	0	1	1	1	50	2	100	1	50	0	-
5	1	0	0	1	1	100	1	100	1	100	0	-

*4 isolated pancreatic injuries

19.3.2 Surgical management

Each of the 78 patients underwent a laparotomy. Median time to operation after admission to the Trauma centre was 3 (range 0.1–80) hours. Eight patients (10.3%) underwent urgent surgery for an acute abdomen or shock not responding to fluid resuscitation. Seventy patients were stable after the initial resuscitation, 17 of whom had stab wounds which involved limbs, chest, neck and head, and underwent additional imaging before laparotomy.

19.3.3 Associated injuries to other organs

Only 4 (5%) patients had an isolated pancreatic injury. Seventy four patients had 98 associated intra-abdominal injuries involving liver (n=34, 45.3%), stomach (n=34, 45.3%), diaphragm (n=24, 32%), spleen (n=13, 17.3%), colon (n=12, 16%), duodenum (n=7, 9.3%), kidney (n=4, 5.1%). Fifty eight (78.4%) of

the 74 patients had one or two associated injuries while 16 (21.6%) had three or more associated intra-abdominal injuries (Table 1).

19.3.4 Associated vascular injuries

Eighteen (24%) of the 75 patients had associated vascular injuries involving IVC (n=7, 9.3%), left gastric artery (n=2), splenic artery (n=2), mesenteric vein (n=2), middle hepatic vein (n=1), aorta (n=1), portal vein (n=1), renal artery (n=1), renal vein (n=1). An associated vascular injury did not correlate significantly with morbidity ($p < 0.063$).

19.3.5 Surgery

The 78 patients had a total of 81 laparotomies to treat the pancreatic injuries. Eight (10.3%) patients with major pancreatic and associated injuries had an initial damage control operation necessitated by major blood loss, acidosis, coagulopathy and hypothermia. Sixty nine patients (84.6%) had drainage of the pancreas after haemostasis and four had a distal pancreatectomy as the primary procedure. Three patients underwent a secondary pancreatic procedure once stable which included a Whipple resection, a distal pancreatectomy and splenectomy and a distal pancreatectomy alone.

The 8 patients who underwent a damage control surgery (DCS) had a median RTS of 5.4 (range 2.0–7.8) and received a median of 17 (range 4-32) units of blood. Seven of the 8 patients were shocked on admission to hospital. Five patients also had associated vascular injuries and 3 had three or more adjacent organ injuries. During the damage control laparotomy, all 8 patients had control of bleeding and drainage only. During a subsequent laparotomy one patient

with an AAST grade V pancreatoduodenal injury required a pancreatoduodenectomy. In the DCS group 2 of the 4 survivors underwent one repeat laparotomy each. The four survivors each received a median of 16 (range 4-28) units of blood.

Seven patients (9%) had injuries involving both pancreas and duodenum. Two patients had AAST grade I pancreatic injuries, 3 patients had grade II pancreatic injuries, 1 had a grade IV pancreatic injury and 1 had a grade V pancreatic injury. One patient mentioned previously required a pancreatoduodenectomy and in the remaining 6 patients the pancreatoduodenal injuries were treated with primary duodenal repair, intraluminal duodenal tube drainage, a feeding jejunostomy and closed suction drainage of the pancreas.

19.3.6 Morbidity

Eighteen patients (23.1%) required intensive care unit (ICU) admission. Median ICU and total hospital stay (range) were 4 (1–41) and 8 (1–149) days respectively. Forty one patients (52.6%) did not have postoperative complications and had a median hospital stay of 6 (range 4-11) days. Of the remaining 37 patients (47.4%), 29 had systemic complications, 15 intra-abdominal complications and 15 pancreas specific complications. The 29 systemic complications included pneumonia (n=9) acute respiratory distress syndrome (n=3), pleural effusion (n=3), atelectasis (n=7), sepsis (n=4), renal failure (n=2), disseminated intravascular coagulopathy (n=3), bleeding (n=3). The 15 intra-abdominal complications included subphrenic abscess (n=8), anastomotic leak (n=2), enterocutaneous fistula (n=3), bowel obstruction (n=2),

bile leak (n=3), gastric outlet obstruction (n=2) and wound sepsis (n=2). Median hospital stay for patients with complications was 13 (1–149) days which was significantly longer than those without complications ($p < 0.05$, Table 2). There was no significant difference between the site of the pancreatic injury (head and neck *versus* body *versus* tail) with regard to general complications ($p = 0.673$). In contrast the pancreatic injury grade, had a significant influence on the development of general complications (AAST grade I–II *versus* grade III–V injuries; $p < 0.001$) (Table 2).

Eight patients (10.2 per cent) developed a pancreatic fistula as a complication of the pancreatic injury. Five pancreatic fistulae resolved spontaneously on conservative management alone after a median of 4.4 (range 1–6) weeks. Three persistent fistulae required endoscopic intervention with retrograde cholangiopancreatography, pancreatic duct sphincterotomy and pancreatic duct stenting with placement of a 7Fr pancreatic duct stent and resolved within 10 days. Three patients had symptomatic pancreatic fluid collections identified on CT scan which resolved after treatment with percutaneous ultrasound catheter drainage. Three patients presented subsequently after discharge with a symptomatic pancreatic pseudocyst which was treated with endoscopic pseudocyst drainage. Most pancreas-related complications occurred in patients with AAST grade III injuries (Table 2).

Table 2 Univariable analysis of factors associated with overall morbidity

	Total no. of patients	Patients who developed Complications	Patients with no complications	<i>p-value</i>	OR	95% CI
	n=78	n=37	n=41			
Gender						
Male	74	34 (91.9%)	40 (97.6%)	0.257	0.28	0.03-2.85
Female	4	3 (8.1%)	1 (2.4%)			
Age (years)						
Mean (SD)	28.36 (8.97)	27.76 (7.22)	28.90 (10.36)	0.996	---	---
Median (range)	26.5 (16-62)	26 (18-49)	27 (16-62)			
Revised Trauma Score (RTS)						
2.0 – 7.2	17	13 (35.1%)	4 (9.8%)	0.007	5.01	1.46-17.19
7.8	61	24 (64.9%)	37 (90.2%)			
Presence of Shock						
Yes	22	15 (40.5%)	7 (17.1%)	0.022	3.31	1.16-9.42
No	56	22 (59.5%)	34 (82.9%)			
Patients transfused						
Yes	35	25 (67.6%)	10 (24.4%)	<0.001	6.46	2.40-17.40
No	43	12 (32.4%)	31 (75.6%)			
Blood Transfusion						
Median units (Range)	8 (1-32)	9 (2-32)	2.5 (1-8)	0.001	---	---
Damage Control Surgery						
Yes	8	6 (16.2%)	2 (4.9%)	0.099	3.77	0.71-20.02
No	70	31 (83.8%)	39 (95.1%)			
AAST grade						
1, 2	65	24 (64.9%)	41 (100%)	<0.001	<i>a</i>	-
3, 4, 5	13	13 (35.1%)	0			
Pancreatic Injury Site						
Head & Neck	18	9 (24.3%)	9 (21.9%)	1.0	1.0	0.29-3.39
Body	36	16 (43.2%)	20 (48.8%)	0.673	0.8	0.28-2.25
Tail	24	12 (32.4%)	12 (29.3%)	-	-	-
Associated Abdominal Injuries						
Nil ^b , 1 or 2 organs	62	27 (73%)	35 (85.4%)	0.176	2.16	0.70-6.69
3 or more organs	16	10 (27%)	6 (14.6%)			
Associated injured organs						
Liver	34	13 (35.1%)	21 (51.2%)	0.153	0.52	0.21-1.28
Stomach	34	15 (40.5%)	19 (46.3%)	0.606	0.79	0.32-1.94
Diaphragm	24	12 (32.4%)	12 (29.3%)	0.762	1.16	0.40-3.39
Spleen	13	9 (24.3%)	4 (9.8%)	0.085	2.97	0.83-10.65
Colon	12	7 (18.9%)	5 (12.2%)	0.411	1.68	0.48-5.84

Duodenum	7	4 (10.8%)	3 (7.3%)	0.590	1.53	0.32-7.36
Kidney	4	3 (8.1%)	1 (2.4%)	0.257	3.53	0.35-35.52
No of patients with associated vascular injuries						
Yes	18	12 (32.4%)	6 (14.6%)	0.063	2.8	0.93-8.46
No	60	25 (67.6%)	35 (85.3%)			
Patients who required a repeat laparotomy						
Yes	16	16 (43.2%)	0	<0.001	<i>a</i>	-
No	62	21 (56.8%)	41 (100%)			
Days in Hospital						
Median (range)	9 (1–149)	13 (1–149)	7 (4–11)	<0.001	--	--
ICU Admission						
Yes	18	14 (37.8%)	4 (9.8%)	0.003	5.63	1.65-19.21
No	60	23 (62.2%)	37 (90.2%)			
Days in ICU						
Median (range)	8.5 (1–41)	16 (1–41)	2.5 (1–4)	0.062	---	---
Outcome						
Alive	74	33 (89.2%)	41 (100%)	0.046	-	-
Died	4	4 (10.8%)	--			

^a Exact confidence levels not possible with zero count cells

^b Nil* = 4 patients had an isolated pancreatic injury

19.3.7 Factors associated with morbidity

Increasing RTS, presence of shock, the need for a blood transfusion and the volume of blood transfused, the AAST grade of injury and the need for a repeat laparotomy were significant predictors of morbidity on univariable analysis (Table 2). Surprisingly, neither the need for damage control surgery nor associated abdominal injuries nor vascular injuries were significantly associated with likelihood of morbidity. A likely explanation is that although there was a trend, the small numbers in the samples did not achieve statistical significance. Similarly, controlling for all confounders, the multivariate analysis did not show a significant association between the risk factors due to a lack of statistical power.

19.3.8 Mortality

Mortality rate correlated with pancreatic injury severity. Mortality for grade 1, 2 and 3 injuries was 1.3%, compared to 100% for grade 4 and 5 injuries. Four (5.1%) of the 78 patients died. All 4 (median RTS 4.9, range 2.0–7.8) had an initial DCS, 3 of whom were shocked on admission with a systolic BP <90mm Hg. In the first of the four deaths, a 19 year old man had repair of a right renal vein and inferior vena cava laceration during initial damage control surgery. He underwent a Whipple resection for a grade 5 pancreatic injury 4 days later but required further laparotomies for sepsis 6, 15 and 17 days later. He developed ARDS due to a multi-drug resistant *acinetobacter* and *pseudomonas* and died of multi-organ failure. The second, a 25 year old man, arrived shocked and hypothermic and had DCS to control bleeding from stab wounds to the inferior vena cava, liver, duodenum, and pancreas. Despite transfusion of 14 units blood and control of bleeding, he died of multi-organ failure. The third patient, a 30 year old man arrived intubated and ventilated with a gunshot injury to the head, chest and leg and an abdominal stab. He had a thoracotomy to control bleeding from the lung and a laparotomy to suture gastric perforations and drain a grade 2 laceration of the body of the pancreas. He died subsequently as a result of the gunshot injury to his head. The fourth death, a 30 year old man, was shocked on arrival at hospital. He had an initial DCS with pack control of a bleeding grade 4 liver injury, damage control of a grade 5 duodenal injury, a grade 4 pancreatic injury and a grade 4 colonic injury. Two days later the duodenum and colon were repaired and the pancreatic injury drained. He had 3 further laparotomies to drain sepsis 4, 10 and 13 days later but ultimately died

of multiple organ failure 17 days after the initial injury. Four of the eight patients who had damage control surgery died (range 1-20 days, mean 10 days, median 9.5 days).

19.4 Discussion

The data in this study reflect the largest single centre evaluation of the consequences of stab wounds of the pancreas. This study shows that while mortality was low, morbidity was high. This study also found that most stab wounds of the pancreas resulted in AAST grade 1 and 2 injuries which were minor whereas the minority had major AAST grades 3, 4 and 5 injuries. Almost all patients had associated intra-abdominal injuries due to the close anatomical relationship of surrounding organs and vital visceral veins and, as a consequence, we found that one fifth of patients had at least three associated intra-abdominal organ injuries. Complications associated with pancreatic trauma in this study increased exponentially as the grade of injury advanced. Other significant predictors of morbidity in this study were increasing revised trauma score, shock on admission to hospital, amount of blood loss, necessity for transfusion, blood volume transfused, and the requirement for a repeat laparotomy. Several investigators have reported an increased incidence of infectious complications following pancreatic trauma when associated with hollow viscus injuries, particularly colon injuries (Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001). All patients in the current series who developed wound infections or intra-abdominal abscesses had associated intestinal or liver injuries.

Previous studies have identified factors putative of increased morbidity in pancreatic injuries. Gram-negative sepsis resulted in two-thirds of the deaths in a Louisville, Kentucky study, mortality increasing significantly with a five unit or greater blood transfusion, the need for reoperation and four or more associated organ injuries (Heitsch, Knutson et al. 1976). In a subsequent analysis of 193 pancreatic injuries treated in Seattle, Washington, Kao et al reported an overall morbidity of 50% and a 22% prevalence of pancreas-related complications. Multivariate analysis demonstrated that the grade of pancreatic injury was an independent predictor of both pancreatic complications and mortality(Kao, Bulger et al. 2003). Similarly, an Italian study in 55 patients found AAST grade predictive of morbidity (Antonacci, Di Saverio et al. 2011). Overall morbidity in a Korean study was 49.3%. Surgical complexity and an initial base deficit of -5.8mM/L were predictors of morbidity while a greater than 12 unit transfusion and an initial base deficit of -11mM/L were predictors of mortality (Hwang and Choi 2008).

Although death directly attributed to the pancreatic injury itself is unusual and occurs in less than 3% of patients (Recinos, DuBose et al. 2009),overall mortality from pancreatic injuries remains significant (Smego, Richardson et al. 1985). Other studies have reported mortality rates of 12 to 46 per cent for pancreatic injuries (Smego, Richardson et al. 1985, Ivatury, Nallathambi et al. 1990, Young, Meredith et al. 1998, Kao, Bulger et al. 2003, Scollay, Yip et al. 2006, Hwang and Choi 2008). Factors reported to influence overall mortality are the location, grade and complexity of the pancreatic injury, the degree of preoperative shock, the presence of vascular injuries, and the number of

associated injuries (Chrysos, Athanasakis et al. 2002, Krige, Beningfield et al. 2005, Subramanian, Dente et al. 2007). In the present study the overall mortality rate was 5 per cent., and half the deaths were in patients who were shocked with major associated vascular injuries. Other investigators have reported major bleeding from associated vascular injuries to be a significant factor in early deaths (Ivatury, Nallathambi et al. 1990, Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001, Kao, Bulger et al. 2003). In this study one quarter of patients had vascular injuries compared with one-third of patients with associated vascular trauma in other studies (Ivatury, Nallathambi et al. 1990, Akhrass, Yaffe et al. 1997, Vasquez, Coimbra et al. 2001, Kao, Bulger et al. 2003, Hwang and Choi 2008). In this study, early mortality resulted from uncontrolled bleeding or severe neurological injury in contrast to late deaths which were due to sepsis and multi-organ failure. We found no significant difference in mortality when analysed by mechanism or grade of pancreatic injury suggesting that death usually results from associated injuries other than pancreatic trauma per se.

Morbidity directly related to the pancreas is reported to occur in 10-35% of patients (Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001, Al-Ahmadi and Ahmed 2008, Antonacci, Di Saverio et al. 2011). In this study the incidence of pancreas-related complications in the 74 patients who survived was 20%, which is less than published range of 21.8–38.5 per cent (Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001, Kao, Bulger et al. 2003, Hwang and Choi 2008, Antonacci, Di Saverio et al. 2011) probably because pancreatic stab injuries cause less ductal damage than gunshot or blunt pancreatic injuries as

demonstrated in 2 previous studies from the Cape Town unit. As anticipated, the two most common pancreatic complications in this and other series were post-traumatic pancreatic fistulae and pseudocysts (Lewis, Krige et al. 1993, Young, Meredith et al. 1998, Vasquez, Coimbra et al. 2001). Data on post-traumatic pancreatic fistulae in earlier studies lack credibility because of the want of a universally acceptable definition of a pancreatic fistula which made documentation and comparison of fistula rates in past series unreliable. This study used the definition proposed by the ISGPF (Bassi, Dervenis et al. 2005). Despite their frequency, most pancreatic fistulas are self-limiting and resolve spontaneously. In those fistulas which persist, endoscopic intervention has transformed management and surgery is now seldom necessary. All three persistent fistulas in this study were successfully treated by endoscopic sphincterotomy and temporary duct stenting. Similarly, the three patients with post-traumatic pseudocysts were treated with endoscopic transgastric stent drainage. Previous reports from Cape Town have found that endoscopic drainage of selected traumatic pancreatic pseudocysts is feasible and safe (Funnell, Bornman et al. 1994). As with surgical drainage, the success of endoscopic drainage is dependent on the close proximity and adherence of cyst to stomach wall. Ultrasonography and CT are useful in establishing the initial selection criteria but the ultimate decision and choice of the drainage site requires endoscopic visual assessment aided by endoscopic ultrasonography which enhances the accuracy and feasibility of endoscopic drainage.

The anatomic and physiologic complexities found in combined injuries of the pancreas and duodenum have prompted a selection of operative methods of

treatment ranging from simple closure and drainage to complex procedures involving attempts to defunction the duodenum (Jones 1978, Moore and Moore 1984, Ivatury, Nallathambi et al. 1990, Talving, Nicol et al. 2006). Because of the wide range of possible injuries, no one method or formula can be consistently applied to all pancreatoduodenal injuries (Moore and Moore 1984, Timaran, Martinez et al. 1999). Our data confirm that combined pancreatoduodenal injuries often occur in conjunction with multiple other intra-abdominal injuries. Because of the large number of injury permutations involving the pancreas and duodenum, no one form of therapy is appropriate for all patients (Feliciano, Martin et al. 1987, Krige 2006)¹. As shown in this study, the duodenal injuries were managed by careful tissue debridement, primary repair using a single layer of interrupted absorbable sutures and both intraluminal tube decompression and external drainage, thereby avoiding complex reconstructive procedures during the acute injury (Rickard, Brohi et al. 2005).

Several limitations are evident when interpreting these results of this study. Our analysis is based on a select high-risk surgical cohort at a single tertiary referral academic centre and are thus unlikely to be representative of admissions to community-based hospitals. Another concern is that intensive care management of patients who have had surgery for major pancreatic trauma has advanced substantially since the inception of this study. These changes should not, however, have influenced data analysis as this was a longitudinal cohort study. An additional substantive limitation is that although this study is the largest of its kind to date, the sample size of the group with AAST grade III-V

pancreatic injuries is relatively small, which increases the possibility of a type II error. A strength enhancing the robustness of the data is that the study was conducted in a single centre in a defined and homogenous population of consecutive patients using uniform entry criteria.

In conclusion, this analysis showed that although mortality was low after pancreatic stab wounds, morbidity was high. Significant predictors of morbidity in this study were an increasing AAST grade of pancreatic injury, a high revised trauma scale, shock on admission to hospital, the need for a blood transfusion and a repeat laparotomy. The majority of patients in this study had grade I or II pancreatic injuries with neither substantial tissue loss nor a main duct injury and after control of bleeding were effectively treated with external drainage alone. More advanced grade injuries of the body and tail were managed by resection. It should be stressed that these conclusions apply specifically to civilian stab wounds of the pancreas and cannot be extrapolated to other mechanisms of pancreatic injury.

CHAPTER 20

Pancreatoduodenectomy for trauma: applying novel reconstruction techniques

20.1 Introduction

Pancreatoduodenectomy and subsequent reconstruction after complicated pancreatic injuries in severely injured patients has in the past resulted in prohibitive mortality rates. Exsanguination due to collateral injuries involving the inferior vena cava, portal or superior mesenteric veins frequently result in hypothermia, coagulopathy and acidosis which compound the physiological derangement (Wang, Li et al. 2007, Krige, Navsaria et al. 2016). In addition, technical difficulties resecting and reconstructing complex pancreatic injuries require special surgical skills and expertise (Krige, Nicol et al. 2014, Krige, Navsaria et al. 2016). Although other reports (Chrysos, Athanasakis et al. 2002, Subramanian, Dente et al. 2007, Wang, Li et al. 2007) and from our own institution (Farrell, Krige et al. 1996, Krige, Kotze et al. 2011, Chinnery, Krige et al. 2012) have detailed aspects of the management of pancreatic injuries including the overall management of proximal (Krige 1997, Krige, Nicol et al. 2014) and distal resection (Krige, Kotze et al. 2014), no publications have specifically assessed the technical aspects of reconstruction after emergency pancreatoduodenectomy for complex injuries of the pancreas and duodenum. This study evaluated the outcome of pancreatic, biliary and gastric reconstruction methods after pancreatoduodenectomy for major pancreatic injuries in a cohort of consecutive patients treated at a level I academic trauma centre.

20.2 Methods

20.2.1 Study population and data collection

Details of the study population, data collection and patient variables recorded are outlined in the methodology section in Chapter 3.

20.2.2 Definitions

Details of definitions applied are provided in the study methodology in Chapter 3.

20.2.3 Initial and operative management of pancreatic injuries

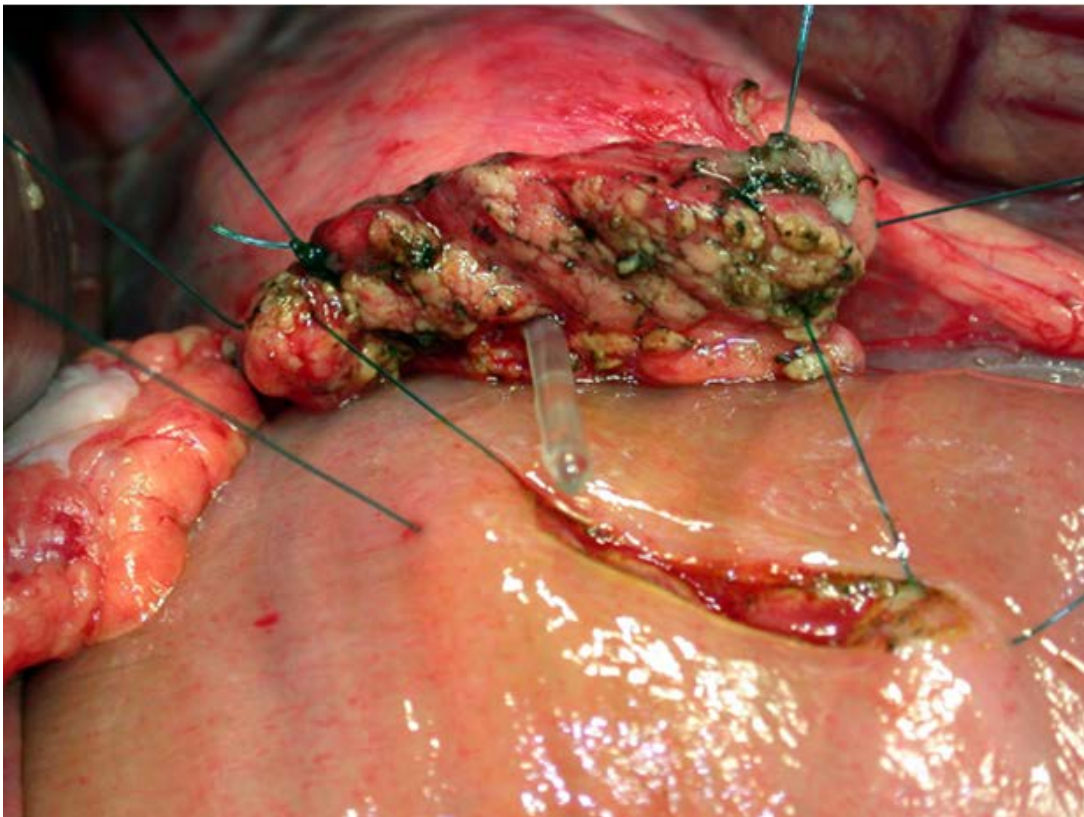
Details of initial management of pancreatic injuries and damage control laparotomy are given in the study methodology in Chapter 3.

20.2.4 Operative technique of pancreatic reconstruction

A pylorus preserving pancreatoduodenectomy (PPPD) was undertaken in all patients in whom the injury had not irretrievably damaged the pylorus. In those requiring a gastric resection a classic Whipple resection was done. The pancreatic remnant was mobilised for 2.5cm from the splenic and portal vein confluence to facilitate the pancreatic anastomosis (Fig 1). The end-to-side pancreatojejunostomy was constructed by placing the inferior row of interrupted 3/0 PDS sutures to include the edge of the pancreas and incorporate capsule and parenchyma as well as full thickness jejunal wall. In those in whom the pancreatic duct could be identified, the anastomosis was stented internally with an 8 cm 5Fr silastic paediatric feeding tube cut to size. 4 cm of stent were inserted into the pancreatic duct and the remaining 4 cm placed in the jejunum

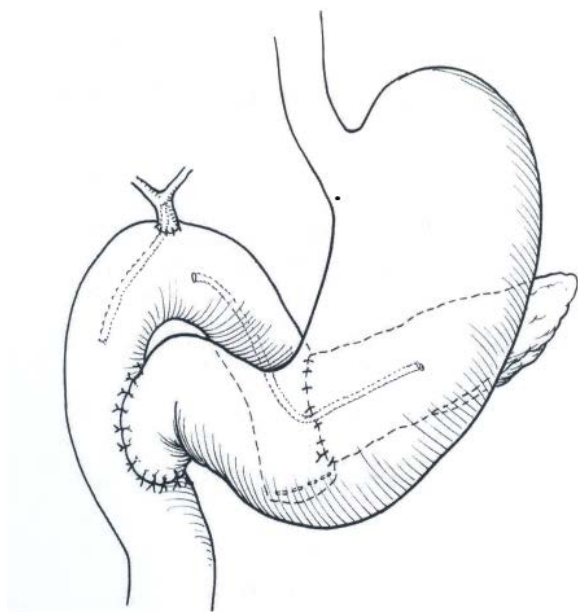
(Fig 2). The anterior layer pancreatic sutures were individually inserted first and then sequentially into the jejunal wall to complete the anastomosis. In patients in whom the jejunum was grossly oedematous after prolonged resuscitation and unsuitable for an anastomosis, the pancreatic stump was drained into the stomach. A 3cm oblique gastrostomy was made in the posterior wall of the stomach prior to placing interrupted 3/0 PDS sutures first through the edge of the superior surface of the pancreas, incorporating capsule and parenchyma, and then through the full thickness of the superior edge of the gastrostomy. The anastomosis was completed by suturing the posterior margin of the pancreas to the inferior margin of the gastrostomy in a similar manner.

Figure 1



Photograph of a stented end-to-side pancreatojejunostomy

Figure 2



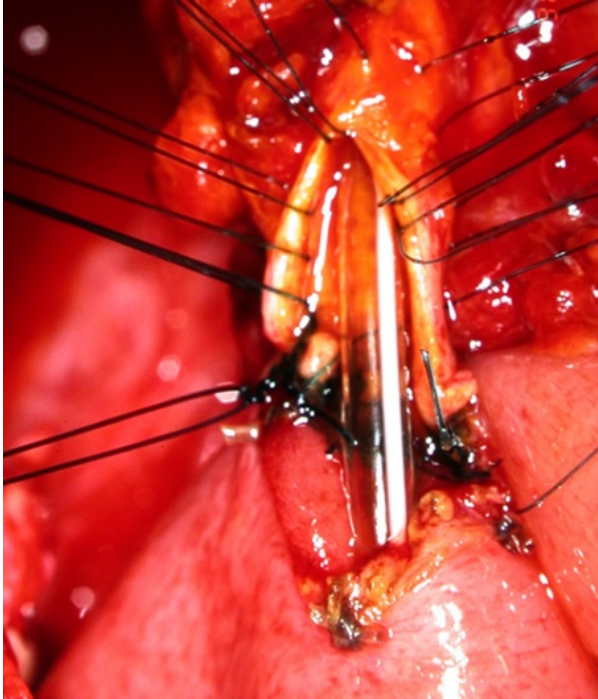
Pylorus preserving pancreatoduodenectomy with a distal duodenojejunostomy and stented pancreatic and biliary jejunal anastomoses

20.2.5 Operative technique of biliary reconstruction

The biliary anastomosis was a modification of the standard method used for bile duct reconstruction after iatrogenic injuries (Terblanche, Worthley et al. 1990, Hofmeyr, Krige et al. 2015). The duct was spatulated to increase anastomotic size using an anteriorvertical incision positioned to avoid the 3 and 9 o'clock bile duct arteries (Fig 3). All biliary anastomoses were stented with an 8 cm long 5Fr silastic paediatric feeding tube. In situations where the bile duct measured less than 3mm in width and gross oedema jeopardised the bile duct to jejunum anastomosis, the gall bladder was preserved and used as the conduit for the biliary-enteric anastomosis. In high-risk stented biliary anastomoses a modified Imanaga reconstruction technique (Fig 4) was used in which the

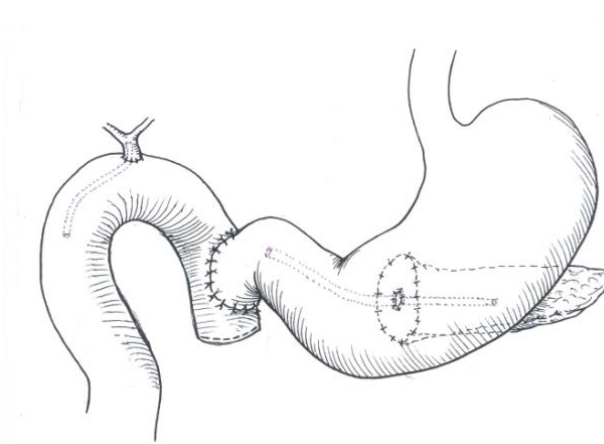
duodenojejunostomy was created end-to-side as the most proximal jejunal anastomosis to allow post-operative ERCP and biliary stent retrieval (Imanaga 1960).

Figure 3



Photograph of a spatulated and stented end-to-side hepaticojejunostomy

Figure 4



Pylorus preserving pancreatoduodenectomy and modified Imanago reconstruction with proximal duodenojejunostomy and pancreatogastrostomy

20.3 Results

Twenty (18 men, 2 women, median age 28 years, range 14 - 53 years) of 426 patients had AAST grade V injuries involving the head of the pancreas and duodenum which were not reconstructable and required a pancreaticoduodenectomy. Fourteen of the 20 had penetrating injuries (13 gunshot wounds, 1 stab wound) and 6 had sustained blunt abdominal injuries due to motor vehicle accidents. Ten of the 20 patients had 1 or more associated vascular injuries involving IVC (n=9), portal vein (n=2), superior mesenteric vein (n=2), renal veins (n=3) and lumbar veins (n=1). Concurrent extra-abdominal trauma occurred in three patients.

20.3.1 Surgery

20.3.1.1 Initial damage control surgery

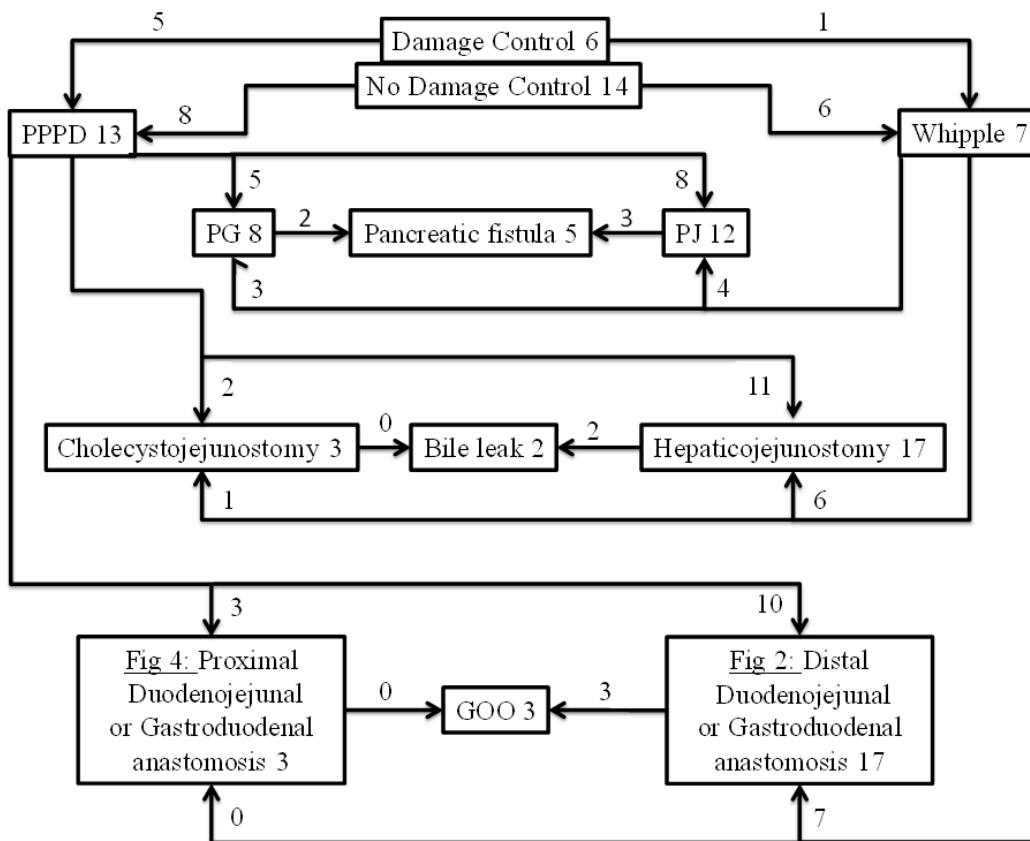
In 6 patients, the injury complex produced extreme physiological derangement, which mandated a damage control operation initially, and a subsequent pancreaticoduodenectomy and reconstruction. Five of the 6 were shocked on admission to hospital and five had associated vascular injuries. The pancreaticoduodenectomy was done at a median of 19 hours (range 11- 48 hours) after the initial damage control laparotomy in four patients or during a third laparotomy 48 and 96 hours later in two patients (Krige, Navsaria et al. 2016).

20.3.1.2 Pancreatoduodenal resection

Thirteen patients had a PPPD and seven a standard Whipple resection (Fig 5). In three patients the reconstruction used a modified Imanaga sequence of

anastomosis (Fig 4) to allow for a postoperative ERCP to be performed to access the biliary system for retrieval or replacement of a biliary stent placed because of an associated liver and intrahepatic ductal injury. In three patients the gallbladder was used as the conduit for biliary drainage into the jejunum. Eight patients had a pancreatogastrostomy and in 12 patients an end-to-side pancreatojejunostomy was used (Fig 5). The median duration of intensive care was 5 days (range 1-20 days). Seventeen patients survived. Median duration of hospital stay for survivors was 29 days, (range 14-94 days).

Figure 5



Pancreatoduodenectomy for trauma: operative management, reconstruction and complications

20.3.2 Morbidity

One patient had a Clavien–Dindo grade I complication, 7 (13.8%) patients had grade II complications, 2 (17.5%) had grade IIIa, 6 (10%) had grade IVa, and 3 (16.3%) had grade V complications and died. Two patients had an anastomotic leak, two had a bile leak and three had delayed gastric emptying (Fig 5). Five patients developed a pancreatic fistula after the pancreatoduodenectomy, three of twelve patients who had a pancreatojejunostomy and two of eight patients who had a pancreatogastrostomy (Fig 5). All five were grade B fistulas and were treated with fine-bore nasojejunal feeding and *octreotide* and all resolved after a median of 22 (IQR 12–38) days.

20.3.2.1 Late complications

One patient required hospitalization on three occasions with self-limiting alcohol-induced acute pancreatitis and one patient had symptomatic malabsorption which resolved on pancreatic replacement therapy. Three patients subsequently underwent further surgery. One patient had closure of a defunctioning colostomy 6 months after the pancreatoduodenectomy and two patients in whom the gallbladder had been preserved and used for biliary drainage returned 3 and 6 years after the pancreatoduodenectomy with cholangitis due to hepatic duct stones. Both had a cholecystectomy and a hepaticojejunostomy.

20.3.3 Mortality

Three of the 20 patients died. All three were profoundly shocked with major splanchnic venous injuries and had APACHE II scores on admission of 15, 18

and 18. Two died of MOF and disseminated intravascular coagulopathy within 48 hours after receiving a median of 27 units of blood during the damage control operation. The third patient died after 24 days of MOF due to resistant *acinetobacter* and *pseudomonas* intra-abdominal sepsis.

20.4 Discussion

This study reports the technical details and outcome of pancreatic, biliary and gastric reconstruction after a pancreatoduodenectomy for trauma. There is consensus that a pancreatoduodenectomy for trauma and the subsequent reconstruction is the most taxing of all pancreatic resections because the procedure is undertaken under adverse conditions with severe operative constraints. While some authors recommend that a pancreatoduodenectomy for trauma should be always performed as a two-stage procedure (Koniaris, Mandal et al. 2000, Wang, Li et al. 2007, Thompson, Shalhub et al. 2013) our data suggest otherwise. In this study all patients who were haemodynamically stable after intra-operative resuscitation underwent pancreatoduodenectomy and immediate reconstruction with survival of 13 of 14 patients. In contrast, a cohort of six other patients who remained hypotensive despite sustained resuscitation, had an initial damage control operation for haemostasis and staple closure of injured hollow viscera and external pancreatic and biliary drainage. The resection and anastomoses in this latter group were completed when the patient was stable at either the second or third operation.

When the trauma pancreatoduodenal resection has been accomplished, several critical decisions are necessary regarding the timing and method of reconstruction (Chrysos, Athanasakis et al. 2002). The key determinant of the

ultimate outcome is the integrity of the pancreatic anastomosis. As in elective resections, the pancreatic anastomosis following a trauma PD is the weakest link and pancreatic anastomotic failure is the most important factor responsible for the substantial postoperative morbidity and mortality. Even under elective circumstances the fistula rate is appreciable and is highest in those with a soft pancreas and a small duct (Yeo, Cameron et al. 1995). These risk factors pertain in the trauma situation and are compounded by a pancreas that is damaged and oedematous, as well as an oedematous bowel wall, making the situation even more unfavourable for a successful anastomosis (Krige 1997, Tajima, Kuroki et al. 2009, Krige and Thomson 2011).

In the elective setting a number of different methods have been proposed to reduce the incidence of post-operative pancreatic fistulas including the site of implantation (stomach or jejunum), anastomotic technique and pancreatic duct stenting (Madiba and Thomson 1995, McKay, Mackenzie et al. 2006, Lermite, Pessaux et al. 2007). These techniques need to be adapted to the prevailing operative circumstances. In this study the solution to overcoming these considerable technical difficulties was to use a stented single layer interrupted anastomosis with a pancreatic leak rate of 30% in survivors.

A pancreatogastrostomy (PG) was used in this study when profound shock, prolonged resuscitation and major vascular injuries resulted in an oedematous jejunum which jeopardised the anastomosis. Under these adverse circumstances there are several cogent practical and technical reasons for doing a PG in preference to a pancreatojejunostomy (Sikora and Posner 1995, Payne and Pain 2006). The posterior wall of the stomach is conveniently

positioned adjacent and anterior to the pancreatic remnant and the gastrostomy can be fashioned to the exact size required without any discrepancy in dimensions to allow a tension-free anastomosis. In addition, the stomach wall is thick, holds sutures well, has an abundant blood supply and is less likely than a jejunal loop to develop ischaemic complications (Delcore, Stauffer et al. 1994). Gastric and pancreatic secretions are easily removed via a nasogastric tube after PG and the pancreatic exocrine enzymes remain unactivated with a low pH and in the absence of enterokinase (Topal, Fieuws et al. 2013). As with the pancreatojejunostomy (PJ), this study used a single layer interrupted suture technique incorporating pancreatic capsule and parenchyma with a 5 Fr intraluminal duct stent rather than the more complex and time consuming duct to mucosa technique. PG and PJ each have their own advantages and limitations in elective resections but neither are universally applicable after major pancreatic trauma where oedema and tissue damage are crucial factors determining the use a particular anastomosis in the reconstruction. Current evidence suggests that it is technically more important to identify the subgroup of patients who may benefit from a specific technique (PG or PJ) than pursue a universal technique and attempt a “one size fits all” methodology. A recent meta-analysis of randomized controlled trials in patients who had either a PG or PJ after an elective pancreatoduodenectomy reported that the pancreatic fistula rate was significantly less in patients who had a PG while there were no differences in delayed gastric emptying, enteric or biliary fistulae, remnant pancreatitis or wound complications when comparing the two reconstruction methods (Que, Fang et al. 2015).

An end-to-side hepaticojejunostomy, using the high bile duct reconstruction technique with preplaced sutures (Terblanche, Worthley et al. 1990, Hofmeyr, Krige et al. 2015) is regarded as the gold standard for elective restoration of biliary-enteric continuity. The major risk factors for bile leaks and ultimately biliary strictures are the size of the bile duct and the adequacy of the blood supply of the bile duct (Northover and Terblanche 1979, Duconseil, Turrini et al. 2014). "Skinny" ducts have been shown to result in bile leaks in 4% of elective PD reconstructions (Duconseil, Turrini et al. 2014). Small size was a universal feature in this study which required a modified approach and biliary stenting. In patients who had labile vital signs and a small bile duct the gall bladder was used for the anastomosis after ligating the bile duct below the cystic duct insertion. However, two of the three required a revision 3 and 6 years later.

Unlike other reported series, a unique aspect of this study was the capability to do a pylorus preserving pancreatoduodenectomy in those injured patients in whom the pylorus was intact. Two immediate advantages of a pylorus preserving pancreatoduodenectomy were retention of the stomach thus allowing the full posterior gastric wall to be accessible for a pancreaticogastrostomy and the modified Imanaga sequence of reconstruction allowed postoperative endoscopic access through the duodenojejunal anastomosis to the biliary system for retrieval of biliary stents and balloon enhanced cholangiography which was important in those patients who had an associated bile leak due to a gunshot injury of the liver.

This analysis describes for the first time how techniques for pancreatic, biliary and gastric anastomoses need to be modified for reconstruction after a

pancreatoduodenectomy for trauma. Although a relevant limitation of this study is the small sample size, a robust feature of the data accrual and analysis is that morbidity was evaluated prospectively using internationally validated criteria to record outcome (Bassi, Dervenis et al. 2005, Clavien, Barkun et al. 2009). This study confirms that delayed resection and reconstruction after damage control is feasible with a reasonable prospect of survival. This study has demonstrated that a pylorus-preserving pancreatoduodenectomy is entirely appropriate and that a pylorogastric resection is only necessary when dictated by the extent of injury. A practical argument has been advanced that a pancreatogastrostomy may be a safer option than a pancreatojejunostomy when conventional anastomoses are high-risk due to oedematous tissues. These techniques do not need to be used in all pancreatoduodenal injuries requiring resection, but should be applied and adapted to the severity of the situation. This data emphasize that these are complex cases with significant postoperative morbidity and are best managed collaboratively by trauma and HPB surgical teams.

CHAPTER 21

Concluding summary and directions for future research

The optimal management of complex pancreatic injuries has until now remained undefined due to the lack of high quality evidence, the retrospective design of many studies and the risks of analysis bias. Despite a plethora of papers on pancreatic trauma, few have specifically addressed the full spectrum of complex injuries as patterns of injury have changed and methods of intervention have progressed. Earlier studies assessing outcome after pancreatic resections for major pancreatic injuries have applied unqualified primary endpoints with differing descriptions and definitions which consequently have resulted in flawed conclusions. These disparities and the weak data generated have hampered accurate comparisons and pooling of variable results across studies has hindered the establishment of clear benchmarks aimed at addressing and improving suboptimal outcomes.

To offset these deficiencies, this thesis analyzed relevant areas in pancreatic trauma by applying robust and reliable methodology and objective and reproducible endpoints in a large cohort of patients treated at an academic tertiary referral centre. Internationally accepted and validated definitions and grading scores were used to benchmark outcomes. Novel scoring systems such as the PIMS, a grading system for combined pancreatic and duodenal injuries and a pancreatographic classification of pancreatic ductal injuries were developed and introduced. The clinical studies in this thesis addressed twelve previously under-researched areas in the management of complex pancreatic

injuries and have advanced knowledge by identifying, investigating and resolving issues in treatment.

Each study has specific application in the assessment and therapy of major pancreatic injuries. The first study derived and validated the PIMS, a novel organ-specific risk prediction score calculated from five variables which predicts the likelihood of death in patients who have sustained a major pancreatic injury. The PIMS is simple, quick and easily understandable, accurately predicts post-operative mortality progressively across its range of scores, and can be used as a benchmark for survival. This model exploits variables readily available to trauma surgeons and is effective as a real-time score to predict outcome and to benchmark quality of surgical intervention and to aid in *post hoc* analysis of trauma research and comparative audit.

In the most comprehensive study yet, bivariate and multivariate logistic regression analyses was used to examine factors predicting complications and death in patients undergoing surgery for pancreatic trauma. In the logistic regression analysis model two variables, AAST grade of pancreatic injury and a repeat laparotomy were significant predictors of morbidity and using a similar stepwise regression analysis model five variables, age, shock, median number of units transfused and the presence of associated complications were significant factors associated with mortality.

Analysis in the following study showed that a pancreatoduodenectomy is life-saving and achievable in the cohort of stable patients with severe non-reconstructable pancreatic head injuries and that a pylorus-preserving pancreatoduodenectomy is technically feasible and safe in the acute trauma

situation. The current data however, emphasize that an emergency pancreatoduodenectomy for trauma is associated with significant post-operative morbidity and should be managed collaboratively by trauma and HPB surgical teams as the procedure is technically demanding and crucial procedural decisions must be made during resection and reconstruction.

The fourth study addressed three of the major unresolved issues in severe combined pancreatoduodenal injuries (CPDIs), namely, survival after initial damage-control surgery, outcomes after pancreatoduodenectomy for CPDI, and evaluation of predictive factors for morbidity and mortality using bivariate analysis of a new composite grading score for CPDI. Significantly more complications related to bleeding, disseminated intravascular coagulation, and hypovolaemic shock occurred in those patients who eventually died and significantly more abdominal sepsis and fistulas occurred in those who survived. Mortality was related to associated vascular injuries overall, major visceral venous injuries and the combination of vascular plus the total number of associated organs injured.

As there are no clear guidelines on the management of pancreatic injuries during damage control surgery, the fifth study evaluated the factors influencing mortality in patients who sustained pancreatic injuries and underwent DCS. Despite the magnitude of their combined injuries and the degree of physiological insult, DCS salvaged 45% of critically injured patients who later underwent definitive pancreatic surgery. Mortality correlated with associated vascular injuries overall, major visceral venous injuries and the combination of vascular plus the total number of associated organs injured.

To date there has not been any detailed evaluation of an initial damage control laparotomy followed by a proximal pancreatic resection in severe head of pancreas injuries, nor has there been a critical analysis of the timing of the pancreatoduodenectomy. In order to address this deficiency, the sixth study evaluated patient outcome after initial DCS and subsequent pancreatoduodenectomy and reconstruction to assess optimal operative sequencing. During the 20-year study period, 312 patients were treated for pancreatic injuries of whom 14 underwent a pancreatoduodenectomy. Six of the 14 patients were in extremis with exsanguinating venous bleeding and non-reconstructable AAST grade 5 pancreatoduodenal injuries and underwent DCS followed by delayed pancreatoduodenectomy and reconstruction when stable. Five of the six patients had a pylorus-preserving pancreatoduodenectomy and the reconstruction was modified to overcome the technical difficulties encountered with an oedematous jejunum and a small pancreatic and bile duct. Despite being near to death on arrival, four of the six patients survived.

The 6-scale Accordion Severity Grading System metrics was used for the first time in this study to benchmark the spectrum and severity of complications after pancreatic resection for trauma. Applying univariate logistic regression analysis, mechanism of injury, RTS <7.8, shock on admission, DCS, increasing AAST grade and type of pancreatic resection were significant variables for complications. Multivariate logistic regression analysis however showed that only age and the type of pancreatic resection were significant.

The eighth study showed that although mortality after distal pancreatectomy for trauma is substantial, most deaths were unrelated to the pancreatic injury and

were due to associated injuries. The foremost risk factors for death were shock on admission to hospital, a major vascular injury and three or more associated adjacent organ injuries. An increasing complication severity grade, when measured by the Clavien-Dindo method, led to the need for escalating intervention and prolonged hospitalization.

Endotherapy for established pancreatic complications after trauma is generally safe with a low incidence of adverse events and is likely to be effective in half of those with persistent pseudocysts or leaks. All the patients in this ninth study who had either grade 2a, 3a, 3b or 4c pancreatic ductal injuries resolved after endoscopic intervention and those with grade 4a or 4b ductal injuries uniformly required surgery. In this analysis the new Cape Town pancreatic ductal injury grading classification showed a close correlation with outcome after endoscopic and operative intervention.

In the analysis of the tenth study, isolated pancreatic injuries in the absence of other major extra-abdominal injuries had a good outcome with low mortality rates. Two-thirds of patients with isolated pancreatic injuries required operative intervention. One third of patients who were stable after abdominal trauma without clinical evidence of shock, peritonitis or an abdominal injury requiring operative intervention were managed conservatively but in retrospect clearly had an underlying but occult pancreatic injury and presented subsequently with a pseudocyst. With careful intra-operative evaluation of the injury, most pancreatic injuries can be managed by either distal resection or drainage without the need for complex enteric diversions or pancreato-enteric anastomoses as a primary procedure during the acute injury phase.

This study showed that although mortality was low after pancreatic stab wounds, morbidity was high. Significant predictors of morbidity were an increasing AAST grade of pancreatic injury, a high revised trauma scale, shock on admission to hospital, the need for a blood transfusion and a repeat laparotomy. The majority of patients had grade I or II pancreatic injuries with neither substantial tissue loss nor a main duct injury and after control of bleeding were effectively treated with external drainage alone. More advanced grade injuries of the body and tail were managed by resection.

In the final and twelfth study, an analysis evaluated for the first time how techniques for pancreatic, biliary and gastric anastomoses need to be modified for reconstruction after a pancreatoduodenectomy for trauma. This study demonstrated that a pylorus-preserving pancreatoduodenectomy is feasible in selected patients and that pylorogastric resection is only necessary when dictated by the extent of injury. The study showed that posterior gastric implantation is a safe option for an oedematous pancreas. These techniques do not need to be used in all pancreatoduodenal injuries requiring resection, but should be applied and adapted to the severity of the situation. The data emphasize that complex pancreatic injuries result in significant postoperative morbidity and are best managed collaboratively by trauma and HPB surgical teams.

The data presented in this thesis have been derived from a unique and dedicated pancreatic injury database which incorporates the full gamut of detailed granular data acquisition, including acute management, post-operative outcome and endoscopic, radiological and surgical treatment of post-injury

pancreas-specific complications. The twelve studies in the thesis span the spectrum of analysis, assessment and management and range from prognostic scoring and pancreatographic classification of ductal injuries to detailed surgical intervention for complex pancreatic injuries. Each of the studies advances existing knowledge in the treatment of pancreatic injuries with the intention that future application of this information will be to the benefit of all patients with complex injuries.

The database underpinning this thesis was established because comprehensive data with reliable patient information is often lacking in routine hospital discharge coding and is an essential requirement necessary to improve real world care. An important objective of registry data analysis is the improvement by reduction of inequity in trauma management across different health economies and the elimination of adverse variations in provision and outcome. In order to expand further research into pancreatic injuries, three broad areas of investigation and documentation need to be addressed in future research agendas. These include development of universally accepted pancreas-specific injury definitions, establishment of global pancreatic injury registries, a validated pancreatic injury classification and benchmarking of injury management with detailed outcome analysis.

Trauma remains an important public health problem and is listed by the World Health Organization as a leading cause of death and disability. However, no worldwide, standardised definitions exist for documenting, reporting and comparing data from patients with severe pancreatic injuries. Detailed definitions and comprehensive guidelines are crucial for optimal management of

pancreatic injuries and need to be developed and standardized before embarking on future research projects so that prospective international studies are meaningful and ensure valid comparisons in similar patients. To date, global comparisons of pancreatic injury management and outcome have not been documented systematically because inclusion criteria, data definitions, coding methods and protocols vary substantially and consequently patient selection and intervention are not comparable. Existing pancreatic injury classifications are inadequate and flawed. Few investigators have access to dedicated prospective pancreas-specific trauma databases. Most current clinical information banks lack the granular detail necessary to generate reliable data and obtain valid conclusions. Future studies will need to develop an internationally accepted and validated injury scoring and classification system to allow accurate comparative analyses. To assist in this initiative, the studies in this thesis have provided new methods of scoring severe pancreatic injuries which need to be applied in future comparative studies.

The purpose of a global pancreatic injury registry is improvement of care by benchmarking and research. Big data and detailed registries incorporating robust and validated systems are designed to provide capacity to facilitate research and analysis of important pancreatic injury subgroups. Ideally, detailed and comprehensive trauma registries generate survival prediction models to guide trauma system governance and benchmarking of hospital performance with robust outlier identification.

The development by consensus of the Utstein template for uniform reporting of data following major trauma has been a major advance and has allowed

international trauma auditing and benchmarking. A similar process should and can be developed and applied specifically for pancreatic injuries. A comprehensive global initiative will allow the establishment of detailed databases to improve the quality of clinical care, analysis and research. Regional, national and international registries require systematic continuous collection of pancreatic trauma data using specified inclusion criteria. All data should be anonymous, secure, and data input separate from routine hospital coding.

Three existing dominant databases exemplify the objectives proposed. The US Nationwide Inpatient Sample (NIS) is part of the Healthcare Cost and Utilization Project (HCUP) and is a national, all-payer discharge database containing information on a representative stratified sample of 20% of non-federal US community hospitals in participating states, including academic and specialty hospitals. However, the NIS is an administrative database and lacks important clinical variables, including patient factors such as injury severity score, imaging, laboratory values, operative data and long-term follow-up and readmission information. The NIS database also does not allow assessment of relevant peri-operative variables that influence the surgeon's decision to operate which results in selection bias.

Similarly, two databases in the United Kingdom provide data on pancreatic injuries but are limited by specific content and detail. The Trauma Audit and Research Network (TARN) database is a collaboration of hospitals from England, Wales and Northern Ireland and is the largest trauma database in Europe, with more than 350,000 records. The Scottish Trauma Audit Group

(STAG) database is a national audit across Scotland established with the intention of improving quality of care and long-term outcome. Data are prospectively recorded by medical and administrative staff before retrospective data cleaning by local audit coordinators. By modifying the above existing core datasets with grafting and bolt-on acquisition, these can be adapted to provide the necessary essentials for an international pancreatic injury research bank.

Detailed outcome analysis serves as a reference for future institutional and international comparisons. Benchmarking is not restricted to comparative analyses of outcome, but should serve as a mechanism for transforming surgical practice and enhancing quality of care. To further develop this, future studies should include the calculation of the total burden of multiple complications in individual patients by utilising the comprehensive complication index, a factor which is relevant in trauma patients with several injured organs. In order to strengthen research frontiers, academic trauma centres should pool data to overcome the paucity of robust information on complex pancreatic injuries. Standardizing data collection is crucial for success and both bridging and cross-linking will be necessary in future.

The management of major pancreatic injuries has become increasingly complex as reflected in the studies in this thesis. A key finding has been that previous studies have not provided definitive answers to important issues such as the management of complex grade 5 injuries of the pancreas. The application of modified surgical techniques used in elective pancreatic surgery to the treatment of complex pancreatic injuries has been an important development in HPB trauma surgery. The studies in this thesis strongly support close and

integrated collaboration between trauma and pancreatic surgeons in managing complex pancreatic injuries, a model which should be applied in modern trauma surgery.

CHAPTER 22

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Appendix

Appendix A Pancreatic Database Variables

Demographic Data

Gender

Age

Injury Specific Data

Injury Date

Injury Mechanism

 Penetrating gunshot wound

 Penetrating stab wound

 Blunt motor vehicle accident (driver)

 Blunt motor vehicle accident (passenger)

 Blunt motor vehicle accident (pedestrian)

 Blunt assault

 Blunt other

Delay from injury to hospital admission in hours

Delay from hospital admission to time of surgery in hours

Shock on admission

Revised Trauma Score

Pre-operative radiological investigations

 Lodox

 Ultrasound

 CT scan

 MRI/MRCP

Clavien-Dindo

Accordion

Pancreatic Complication Data

Pancreatic complication

Fluid collection

Fistula

Pseudocyst

Amylase (serum or fluid)

Lipase (serum or fluid)

Pancreatic complication treatment

ERCP

Endoscopic sphincterotomy

Endoscopic stent

Endoscopic cyst drainage

US catheter drainage

Surgery

Hospital Specific Data

Admission Date

Discharge Date / Date of Death

ICU Days

Readmission after discharge

Narrative/Notes (free text)