Risk Factors Predicting Conversion to Laparoscopic Subtotal Cholecystectomy and Post-operative Outcomes from a High-Volume Centre

by

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Declaration

I, **Karien Booyse**, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Risk Factors Predicting Conversion to Laparoscopic Subtotal Cholecystectomy and Post-operative Outcomes from a High-Volume Centre

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Abstract

Background*:* Laparoscopic subtotal cholecystectomy (LSC) is utilized as a safe and feasible alternative for difficult cholecystectomies to avoid bile duct injury and can aid in avoiding conversion to open surgery. This study assesses the risk factors and outcomes of patients who underwent LSC.

Methods: A retrospective analysis was conducted of patients undergoing LSC from September 2019 to August 2021. Relative clinical and operative factors as well as post-operative outcomes were analysed.

Results: There were 631 consecutive cholecystectomies included, 53 of which required LSC. Nine (16.9%) used the reconstituting technique and 43 (81.8%) were fenestrating LSC, one procedure not specified. High BMI (26.4%) and previous endoscopic retrograde cholangiopancreatography (ERCP) (18.9%) were the most common indicators for expected difficulty. Severe inflammation (58.5%) followed by extensive adhesions (52.8%) were the leading causes for conversion to LSC. Aberrant biliary anatomy was the strongest predictor of conversion, and an emergency operation was more likely to require a LSC. The presence of a contracted gallbladder, severe inflammation, gallbladder empyema and extensive adhesions were all independently associated with LSC (all $p < 0.05$). Postoperative complications were recorded in 26.4% of patients. Fifteen percent of patients had post-operative bile leaks; five resolved spontaneously while three required intervention with ERCP. There were eight Clavien-Dindo Grade III complications, three (5.7%) required ERCPs and five (9.4%) required relook laparotomies. There was one mortality.

Conclusions: LSC is a safe alternative that should be utilized in the management of complex gallbladder pathology. Post-operative bile leak was not a major clinical issue in our setting.

Introduction

Laparoscopic cholecystectomy (LC) has become the mainstay treatment for gallstone disease. The incidence of bile duct injury (BDI) increased dramatically after the introduction of LC.(1-8) BDI results in serious morbidity, increased cost, and the risk of litigation for the injuring surgeon. A major BDI during LC is a serious concern for patients, surgeons, healthcare providers and employers and is associated with long-term health related quality of life impairment with repercussions lasting years after repair. Technical errors and misidentification of the anatomy are the main causes. Pre-operative reasons for expected difficulty include male sex, elderly age, obesity, recurrent cholecystitis, and the need for endoscopic retrograde cholangiopancreatography (ERCP). Intra-operative factors such as aberrant anatomy, bleeding, contracted gallbladder, gallbladder empyema and extensive adhesions contribute to challenging conditions that increase the risk of BDI.(9-11) The critical view of safety (CVS) is widely accepted as the best method for avoiding BDI during LC.(12, 13) There are several surgical strategies that one can pursue when a CVS cannot be achieved.(14, 15) For more than a decade subtotal cholecystectomy has been utilized as such a procedure (16) but was poorly understood due to confusing terminology.(9, 17) In 2016 as part of the Society of American Gastrointestinal and Endoscopic Surgeons Safe Cholecystectomy effort, two different terms of subtotal cholecystectomy were described, namely fenestrating and reconstituting.(18) In a fenestrating subtotal cholecystectomy, the remaining gallbladder is left open to the peritoneum, while in a reconstituting subtotal cholecystectomy the lower end of the gallbladder is closed, creating a remnant gallbladder.(18) The remnant gallbladder may become symptomatic and require excision in a second operation. Laparoscopic subtotal cholecystectomy (LSC) is gaining momentum after being novel earlier on in the laparoscopic era. It is utilized as a safe and feasible alternative for difficult cholecystectomies to avoid BDI and can aid in avoiding conversion to open surgery.(19) Although subtotal cholecystectomy may help to reduce the incidence of BDI, postoperative morbidity is not insignificant and subtotal cholecystectomy is associated with a relatively high incidence of postoperative bile leak.(20)

There is a paucity of literature evaluating the risk factors for the conversion to LSC as well as for the outcomes after LSC in South Africa.(21) The aim of this study is to assess the results of the procedure across a healthcare sector in a large metropolitan area with an estimated population of 3 700 000.

Methods

A retrospective review of a prospectively maintained ethics approved database was performed (HREC: R040/2019). The database includes all patients undergoing intended LC within the Cape Metro West region. All patients who underwent LC were included over a two-year period between 1 September 2019 and 31 August 2021. Relevant patient characteristics, clinical information such as urgency of operation, indication, duration of symptoms, preoperative investigations, intraoperative details, and type of LSC performed were retrieved. Thirty-day post-operative outcomes including length of stay, type and severity of complications using the Clavien-Dindo Classification system (22), readmissions and need for additional procedures were included in the analysis. Research ethics board approval for this study was obtained from the Faculty of Health Sciences Human Ethics and Research Committee (HREC: 266/2021).

Patient management

Written informed consent was obtained from all patients undergoing intended LC and a standardized operative note was completed before their inclusion in the prospective database. Evaluation included pre-operative imaging studies and serum liver function tests. From 1 September 2019 a change in practice at participating hospitals was implemented that included a standardized operative checklist, doublet photography and documentation of the CVS with confirmation of the assistant's agreement. The intra-operative dissection checklist and photo documentation as well as confirmation with the assistant of achievement of the CVS prior to dividing the cystic artery and duct were used for the duration of this study. Aberrant biliary anatomy was defined intra-operatively with a cholangiogram.

Complications and re-admissions at 30-days were determined by following up with each individual hospital, confirming whether any lab tests were done for the patient during the 30-day follow up period on the National Health Laboratory Service TrakCare website and searching the Electronic Continuity of Care Record, the Western Cape Government Health website displaying admissions and discharges.

Statistical Analysis

Data were summarised as median with interquartile range or frequency and percent for non-parametric continuous data and categorical data, respectively. The Mann Whitney-U and Fisher's exact tests were used as appropriate. A multivariate logistic regression was

conducted to estimate the odds ratio (OR) of conversion to LSC with 95% confidence intervals. Statistically significant variables on univariate analysis were included in the multivariate logistic regression analysis. Statistical analysis was performed using SPSS version 28.0.1.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY). A p-value < 0.05 was considered statistically significant.

Results

Patient Demographic and Clinical Characteristics

Six-hundred and thirty-one patients who underwent cholecystectomy during the study period were analysed and 53 (8.4%) of these patients required a LSC. Four (0.63%) underwent conversion to open cholecystectomy. One of the four patients was converted to open due to difficult access to the abdomen resulting from multiple previous upper abdominal surgeries. The second conversion was due to an intra-operative finding of a cholecysto-duodenal fistula and the remaining two conversions where due to failure to achieve the CVS.

Patient demographic and clinical characteristics are summarized in Table 1. Nine (16.9%) patients underwent a reconstituting LSC, while 43 (81.1%) underwent a fenestrating LSC and one patient's procedure was not specified. Thirty-seven (70%) patients had at least one comorbidity. Cardiovascular comorbidities were most common (n=19, 35.8%) and included hypertension, ischaemic heart disease and atrial fibrillation. Diabetes mellitus was the second most common (n=9, 17%). The most common American Society of Anaesthesiologists (ASA) classification was physical status II with (n=21, 39.6%) patients, and there were no patients with ASA IV or V status.

The urgency of the operation and indication for the intended LC as well as level of hospital at which the LSC was performed are summarized in Table 2. In 28 patients (52.8%) LSC were performed as an urgent operation during the index hospital admission. The majority had acute cholecystitis (n=33, 66.2%), with concurrent choledocholithiasis present in 13 (24.5%), and two (3.8%) had gallstone pancreatitis. More than half (n=30, 56.6) of the operations were performed at an academic hospital.

Pre-operative risk factors associated with an expected difficult cholecystectomy were identified and are summarized in Table 3. A BMI of more than 35 (n=14, 26.4%) and previous endoscopic retrograde pancreatography (ERCP) (n=10, 18.9%) were the two most

common risk factors. Four patients (7.5%) required pre-operative management with a cholecystostomy tube. Complicated cholecystitis on imaging revealing a perforated, emphysematous, contracted, thick walled or oedematous gallbladder were all regarded as predictors of difficulty.

Intraoperative findings

Intraoperative findings are listed in Table 4. The main reasons for not achieving the CVS were due to severe inflammation (n=31, 58.5%), followed closely by extensive adhesions (n=28, 52.8%). Other factors such as difficulty grasping the gallbladder (n=17 32.1%), a contracted gallbladder (n=15, 28.3%) and gallbladder empyema (n=15, 28.3%) were identified. There were two patients who had aberrant biliary anatomy, both identified with an intra-operative cholangiogram. Intra-operative bleeding ranged from mild (n=25, 47.1%), quantified as < 100 ml, to moderate (n=22, 41.5%; 100-500 ml), with no instances of severe (> 500ml) blood loss. In total, operative drains were placed in 49 patients (92.5%). The median length of stay for patients undergoing LSC was 4.5 days (IQR 2-5).

Complications and re-interventions

There was a total of 21 postoperative complications that occurred in 14 patients (26.4%), (Table 5). There were eight Clavien-Dindo Grade III complications that required intervention. Three (5.7%) required ERCP and five (9.4%) requiring intervention under general anaesthesia. There was one mortality (Grade V).

Three patients underwent re-operation before discharge. The first for intra-abdominal bleeding for which an exploratory laparotomy with haematoma washout, removal of a residual gallstone and placement of a drain was performed. The second required laparoscopic washout and drainage of a subhepatic collection for a bile leak with a concomitant wound infection. The third patient had biliary peritonitis and a supra-umbilical port site infection and underwent a laparotomy; a washout was performed for the disseminated biliary collections and a free intra-abdominal gallstone was identified and removed. This patient underwent ERCP three days later which demonstrated a bile leak from the gallbladder remnant and an endoscopic common bile duct (CBD) stent was placed.

There were eight (15%) patients who developed post-operative bile leaks, all had undergone a fenestrating LSC. Five leaks resolved spontaneously while three required intervention with ERCP, one as previously described following a re-look laparotomy and another for

postoperative biliary colic and worsening liver function tests. The ERCP showed two residual CBD stones and sludge which was extracted with an endoscopic balloon. Cholangiogram relieved a leak from the cystic duct and a plastic stent was placed. The third ERCP was for a persistent bile leak, which was controlled with an endoscopically placed stent. This patient also had an intra-abdominal collection and underwent a fluoroscopy guided percutaneous drain on post-operative day six. This was the only patient who required percutaneous drainage of a collection.

Two patients (3.8%) were readmitted to the hospital within 30 days. One was readmitted three days post discharge with an acute abdomen. An exploratory laparotomy was performed during which a transverse colon perforation with significant contamination was identified and a right hemicolectomy was performed. The single mortality was a patient who was readmitted day one post discharge in septic shock secondary to a bile leak. The patient underwent an exploratory laparotomy and died less than 12 hours post operatively. No bile duct injuries occurred for the duration of the study.

Adjusted Analysis

All statistically significant pre-operative (Table 6) and intra-operative (Table 7) clinical factors from the univariate analyses were included in a multivariate logistic regression analysis (Table 8.) Aberrant biliary anatomy was the strongest predictor of conversion to LSC (OR 100, 95% CI 9.14-1094.06, $p < 0.01$). Patients who required an operation during the same admission as their initial presentation were (OR 3.24, 95% CI 1.26-8.30, $p = 0.01$) more likely to require conversion to LSC. Similarly, patients who presented with acute cholecystitis were also more likely to require conversion (OR 3.58, 95% CI 1.15-11.18, $p = 0.03$). The presence of a contracted gallbladder, severe inflammation, gallbladder empyema and extensive adhesions were all independently associated with conversion to LSC (all $p < 0.05$). Moderate blood loss (100-500 mL) was another a predictor of conversion (OR 6.0, 95% CI 2.15-16.76, $p <0.01$). In addition, younger patients (OR 1.04, 95% CI 1.01-1.08, $p = 0.01$), presented with a higher risk.

Table 1. Demographic characteristics of patients undergoing laparoscopic subtotal cholecystectomy in the Cape Metro West Region from September 1, 2019 through August 31, 2021.

Variables	**Laparoscopic subtotal cholecystectomy n = 53 (%)**
Demographics	
Female sex	30 (56.6)
Age in years, median (IQR)	56 (45 - 65)
BMI, median (IQR)	30 (29 - 34)
C**omorbidities**	
Cardiovascular	19 (35.8)
Respiratory	3 (5.7)
Liver	1 (1.9)
Diabetes mellitus	9 (17)
Retroviral disease*	1 (1.9)
Other (total)	**5 (9.4)**
Gastroesophageal reflux disease	2 (3.8)
Rheumatoid arthritis	1 (1.9)
Hypothyroidism	1 (1.9)
Hyperthyroidism	1 (1.9)
ASA Class	
ASA I	19 (35.8)
ASA II	21 (39.6)
ASA III	4 (7.5)

*24 patients with unknown HIV status at the time of LSC

IQR - interquartile range, BMI – body mass index, ASA – American Society of Anaesthesiologists, HIV – Human Immunodeficiency Virus, LSC – laparoscopic subtotal cholecystectomy

Table 2. Urgency, indication and location of patients undergoing laparoscopic subtotal cholecystectomy in the Cape Metro West Region from September 1, 2019 through August 31, 2021.

Variables	**Laparoscopic subtotal cholecystectomy n = 53 (%)**
Urgency of operation	
Same admission	28 (52.8)
Elective	25 (47.1)
Indication	
Biliary Colic	3 (5.7)
Acute Cholecystitis	33 (66.2)
Choledocholithiasis	13 (24.5)
Gallstone pancreatitis	2 (3.8))
Other	2 (3.8)
Recurrent biliary sepsis Recurrent cholecystitis	1 (1.9) 1 (1.9)
Hospital	
Secondary level	23 (43.4)
Tertiary level	30 (56.6)

Table 3. Pre-operative risk factors associated with an expected difficult laparoscopic cholecystectomy of patients undergoing laparoscopic subtotal cholecystectomy in the Cape Metro West Region from September 1, 2019 through August 31, 2021.

Variable	**Laparoscopic subtotal cholecystectomy n = 53 (%)**
BMI > 35	14 (26.4)
Previous surgery	3 (5.7)
Liver disease	2 (3.8)
Percutaneous drain	4 (7.5)
ERCP	10 (18.9)
Pancreatitis	4 (7.5)
Other	**14 (26.4)**
Delayed presentation	1 (1.9)
Recurrent cholecystitis	4 (7.4)
Thick wall on ultrasound	1 (1.9)
Emphysematous gallbladder	2 (3.8)
Male sex	3 (5.7)
Contracted gallbladder	1 (1.9)
Perforated gallbladder	1 (1.9)
Oedematous gallbladder	1 (1.9)

BMI – body mass index, ERCP – endoscopic retrograde cholangiopancreatography

Table 4. Intraoperative findings recorded in operative notes from patients undergoing laparoscopic cholecystectomy converted to laparoscopic subtotal cholecystectomy in the Cape Metro West from September 1, 2019 through August 31, 2021.

Variable	**Laparoscopic subtotal cholecystectomy n = 53 (%)**
Bleeding	7 (13.2)
Aberrant biliary anatomy	2 (3.8)
Aberrant arterial anatomy	1 (1.9)
Equipment problems	1 (1.9)
No progress	5 (9.4)
Fatty liver	3 (5.7)
Difficulty grasping	17 (32.1)
Contracted gallbladder	15 (28.3)
Intrahepatic gallbladder	5 (9.4)
Severe inflammation	31 (58.5)
Gallbladder empyema	15 (28.3)
Extensive adhesions	28 (52.8)
Necrotic gallbladder	2 (3.8)
Severity of bleeding	
Mild	25 (47.1)
Moderate	22 (41.5)

Table 5. Thirty-day complications and severity score from patients undergoing laparoscopic cholecystectomy converted to laparoscopic subtotal cholecystectomy in the Cape Metro West from September 1 2019 through August 31 2021.

Surgical complications	**Clavien-Dindo Classification, n = 53 (%)**							
	I	**II**	**IIIa**	**IIIb**	**IVa**	**IVb**	**V**	**Total**
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n
Biliary								**16**
Bile Leak	4 (7.5)	-	1 (1.9)	2 (3.8)	-	-	1 (1.9)	8
Bowel injury	-	-	-	1 (1.9)	-	-	-	1
Jaundice	-	-	1 (1.9)	-	-	-	-	1
Intra-abdominal collection	-	-	1 (1.9)	1 (1.9)	-	-	-	2
Intra-abdominal bleed	-	1 (1.9)	-	1 (1.9)	-	-	-	2
Postoperative ileus	1 (1.9)	-	-	-	-	-	-	1
Postoperative pain	1 (1.9)	-	-	-	-	-	-	1
Wound								**2**
Infection	1 (1.9)	-	-	-	-	-	-	2
Nonsurgical complications								**3**
Acute kidney injury	1 (1.9)	-	-	-	-	-	-	1
Nonsurgical infection	2 (3.8)	-	-	-	-	-	-	2
Total	10 (18.9)	1(1.9)	3 (5.7)	5 (9.4)	-	-	1 (1.9)	21

Table 6. Univariate analysis of pre-operative clinical factors for patients undergoing laparoscopic cholecystectomy compared to patients who required conversion to laparoscopic subtotal cholecystectomy.

Variable	Laparoscopic cholecystectomy n = 571 (%)	Laparoscopic subtotal cholecystectomy n = 53 (%)	p-value
Sex, male	87 (15.2)	23 (43.4)	< 0.01
Age, years	44 (34.8-57)	40 (31-40)	< 0.01
BMI	31.9 (27.1-37.2)	31.1 (26.9-36.6)	0.31
Elective operation	394 (69.0)	25 (47.2)	0.01
Indication			
Biliary colic	178 (31.1)	3 (5.7)	< 0.01
Acute cholecystitis	178 (31.1)	32 (60.4)	< 0.01
Choledocholithiasis	100 (17.5)	13 (24.5)	0.20
Gallstone pancreatitis	98 (17.2)	2 (3.8)	0.01
Other *	17 (3.0)	2 (3.8)	0.67
Comorbidities			
Cardiovascular	131 (22.9)	19 (35.8)	0.04
Respiratory	28 (4.9)	3 (5.7)	0.74
Liver	6 (1.1)	1 (1.9)	0.46
Diabetes mellitus	46 (8.1)	9 (17.0)	0.04
Other ^	84 (14.7)	8 (15.1)	1.00
≥1 comorbidity $	321 (56.2)	37 (69.8)	0.06
HIV status			
Positive	40 (7.0)	1 (1.9)	0.21
Negative	227 (39.8)	14 (26.4)	
Unknown	235 (41.2)	24 (45.3)	
ASA status			
ASA 1	218 (38.2)	19 (35.8)	0.56
ASA 2	235 (41.2)	21 (39.6)	
ASA 3	27 (4.7)	4 (7.5)	
Difficult gallbladder	308 (53.9)	46 (86.8)	< 0.01

* Other indications included concern for malignancy (n=1), cholangitis (n=3), gallbladder polyps (n=4), Mirizzi syndrome (n=3), gallbladder empyema (n=3), chronic cholecystitis (n=1), previous cholecystitis (n=2), recurrent cholecystitis (n=2), cholecystoduodenal fistula (n=1)

^ Other comorbidities included GERD (n = 9), thyroid disease (n=9), renal dysfunction (n=5), pregnancy (n=5), malignancy (n=4), current smoker (n=4), hypercholesterolaemia (n=4), osteoarthritis (n=4), epilepsy (n=2), vascular dementia (n=2), haematological disorders (n=2), previous cerebrovascular accident (n=2), previous intracranial haemorrhage (n=1), previous deep venous thrombosis (n=1), peripheral vascular disease (n=1), multiple sclerosis (n=1), Previous COVID (n=1), glaucoma (n=1), hepatitis B virus (n=1), other comorbidity not recorded (n=2)

$ Comorbidities tabulated in the one or more comorbidity calculation included HIV positive status and a BMI greater than 35.

Table 7. Univariate analysis of intra-operative clinical factors for patients undergoing laparoscopic cholecystectomy compared to patients who required conversion to laparoscopic subtotal cholecystectomy.

Variable	Laparoscopic cholecystectomy n = 571 (%)	Laparoscopic subtotal cholecystectomy n = 53 (%)	p-value
No intraoperative difficulty	191 (33.5)	2 (3.8)	< 0.01
Intra-operative complications			
Bleeding	30 (5.3)	7 (13.2)	0.03
Aberrant biliary anatomy	2 (0.4)	2 (3.8)	0.04
Aberrant arterial anatomy	21 (3.7)	1 (1.9)	1.00
Equipment problems	10 (1.8)	1 (1.9)	1.00
No progress	-	5 (9.4)	< 0.01
Hepatomegaly	7 (1.2)	-	1.00
Fatty liver	9 (1.6)	3 (5.7)	0.07
Difficulty grasping gallbladder	65 (11.4)	17 (32.1)	< 0.01
Contracted gallbladder	20 (3.5)	15 (46.9)	< 0.01
Intrahepatic gallbladder	11 (1.9)	5 (9.4)	0.01
Severe inflammation	56 (9.8)	31 (58.5)	< 0.01
Gallbladder empyema	15 (2.6)	15 (28.3)	< 0.01
Extensive adhesions	39 (6.8)	28 (52.8)	< 0.01
Other*	29 (5.1)	10 (18.9)	< 0.01
Intraoperative cholangiogram	92 (16.1)	6 (11.3)	0.43
Estimated blood loss			
Minimal	482 (84.4)	25 (47.2)	< 0.01
Moderate	40 (7.0)	22 (41.5)	< 0.01

* Other intra-operative complications included avulsed cystic artery (n=4), difficult dissection (n=3), necrotic gallbladder (n=5), obstructed view (n=1), oedematous gallbladder (n=1), perforated gallbladder (n=3), short cystic duct (n=2), obliterated Calots triangle (n=2).
Minimal blood loss was defined as <100mL and moderate blood loss was defined as 100-500mL.

Table 8. Multivariate logistic regression analysis of clinical factors influencing conversion to laparoscopic subtotal cholecystectomy.

Variable	p-value	Odds ratio	95% CI
Age	0.02	1.04	1.01-1.08
Sex, male	0.31	1.63	0.63-4.22
Timing, same admission	0.01	3.28	1.27-8.44
Biliary Colic	0.96	1.05	0.17-6.51
Acute cholecystitis	0.03	3.58	1.15-11.18
Gallstone pancreatitis	0.13	0.21	0.03-1.59
Cardiovascular disease	0.79	1.16	0.41- 3.29
Diabetes mellitus	0.42	1.68	0.47-5.96
Bleeding	0.22	0.36	0.07-1.83
Aberrant biliary anatomy	< 0.01	96.55	8.77-1062.45
Difficulty grasping gallbladder	0.43	0.63	0.20-1.99
Contracted gallbladder	< 0.01	6.59	1.85-23.42
Intrahepatic gallbladder	0.59	1.58	0.30-8.19
Severe inflammation	0.02	3.23	1.18-8.87
Gallbladder empyema	0.04	4.31	1.08-17.23
extensive adhesions	< 0.01	7.24	2.74-19.14
Estimated blood loss, moderate	< 0.01	6.0	2.15-16.80

Discussion

In this study, 53 patients underwent LSC, the majority of which were of the fenestrating type. There were four conversions to open completion cholecystectomy, but no conversion to open subtotal cholecystectomy. No BDI occurred during our study period. LSC provides the advantage of maintaining the benefits of minimally invasive surgery, while decreasing the risk of BDI. Postoperative morbidity, specifically bile leaks, increased after LSC. Five patients required re-exploration, with one mortality due to a bile peritonitis recorded in our series.

Commonly described reasons for conversion to LSC include dense fibrotic adhesions within the hepatocystic triangle, a fibrotic gallbladder, gallbladder empyema and a gangrenous gallbladder, all of which lead to unclear anatomy and a difficult dissection.(23) Several of these factors were present in our patients. Of the predictive factors for conversion to LSC, the most common in this study was found to be severe inflammation (58.5%), followed by extensive adhesions in 52.8%. Other commonly reported predictive factors included difficulty grasping the gallbladder, a contracted gallbladder, empyema of the gallbladder and a necrotic gallbladder. Tornqvist et al. reported that increased levels of inflammation, as graded by the Tokyo Guidelines, are associated with higher biliary injury rates.(24) It is suggested that in difficult operating conditions where the CVS cannot safely be achieved, LSC is preferable to persisting with total cholecystectomy to minimize the likelihood of BDI.(25)

In a fenestrating LSC the gallbladder is opened along its long axis and emptied of stones, including removal of stones in the lumen of the gallbladder neck and cystic duct if possible.(19) The bottom of the GB lumen remains open, and the cystic duct may be sutured from the inside, although this is often not possible.(19) Depending on the extent of contamination the area should be carefully drained with 1 or 2 closed suction drains. Patients require close monitoring for bile leak-related events and recurrent symptoms. Secondary interventions are required in more than one-third of subtotal patients whose cystic duct is not safely identified and ligated.(17) Improper technique, drainage and retained stones can lead to serious complications as seen in our cohort where two of the relooks had residual stones and one patient with improper drainage died.

Subtotal cholecystectomy can be performed laparoscopically or open, although laparoscopic is the preferred method if the surgeon’s skill allows. A meta-analysis by Elshaer et al. favoured LSC with less risk of stone retention, wound infection, subhepatic collection,

reoperation, postoperative pain and a shorter hospital stay, smaller risk of incisional hernia and mortality.(19, 20)

Although LSC avoids common BDI, postoperative morbidity, specifically bile leak, is not insignificant.(13) A higher incidence of bile leak from the gallbladder stump is described in the literature, with most studies suggesting that bile leak is usually a minor complication, with a few leaks resolving spontaneously (19) although endoscopic intervention can be required in up to 10% of patients.(17) Previous meta-analyses have recorded bile leaks with an incidence of 10.6% to 18.0%. The incidence of bile leak is considered to vary depending on the type of subtotal cholecystectomy performed, and the rate decreases when the cystic duct and/or gallbladder stump is closed.(14, 26) LeCompte et al. reported a biliary fistula in eight of 30 patients (26%) who underwent subtotal cholecystectomy, all managed successfully by early postoperative ERCP.(27) We recorded a 15.1% incidence of bile leak in LSC group. Of the patients with bile leaks in this study, only three (5.7%) required intervention with ERCP while the remainder resolved spontaneously with persistent non suction drainage.

Complications such as subphrenic collections and postoperative intra-abdominal collections have also been reported.(28) In another study by Harilingam et al., the postoperative readmission rate for intra-abdominal collections was 1.5% and the reported postoperative collection rate was 3.8%; one patient underwent a laparoscopic washout and one needed percutaneous drainage.(29) This lower rate compared to other studies may be due to a smaller cohort and a shorter time period. In our study we recorded a 3.8% incidence of intra-abdominal collections, and the 30-day readmission rate was 3.8%.

The main concern with reconstituting LSC is that the gallbladder remnant may become symptomatic and require a second operation for removal. This outcome has been noted in the literature and may occur in as many as 18% of reconstituting LSC. A retrospective multi-center study from The Netherlands comparing subtotal cholecystectomy vs total cholecystectomy reported a higher biliary event recurrence (15% vs 3%) in the subtotal group.(30) Lidsky et al. reported that 6.2% of reconstituting STC required a completion cholecystectomy a median of 11.5 months after their index operation for recurrent symptoms.(17) The reconstituting type however, is associated with a lower rate of postoperative bile leaks (16% vs 42%) compared to fenestrating LSC.(31) There were only

nine reconstituting LSC in this study and none of these patients developed a bile leak. The follow up period is too short to determine if any of these patients develop a symptomatic gallbladder remnant. A systematic review by Elshaer et al. reported zero cases of incidental GB cancer in the specimens removed or in the GB remnant.(19) In view of the rare incidence of developing GB cancer as well as STC being limited to a select group of patients it precludes the necessity of a completion cholecystectomy to prevent GB cancer.(19) In a study by LeCompte fenestrating cholecystectomy provided excellent control over a follow-up period of more than one year.(27). Long term follow up and quality of life of patients undergoing STC needs to be assessed and analysed. We plan to follow them up for a five-year period with a follow up study to address long term outcomes.

Our results show that inpatients with difficult severely diseased gallbladders, subtotal cholecystectomy provides a safe, minimally invasive surgical option with favourable outcomes over a short-term (30-day) follow-up period. There were no bile duct injuries and similar rates of postoperative complications compared to previously published studies. Most complications were related to bile leak highlighting the need for good surgical technique, removal of all residual stones and adequate drainage.(27)

Limitations

There are some limitations that should be considered for this study. The retrospective nature of this study, although, the data was extracted from a well-maintained prospective database is the first to be considered. A relatively small cohort of patients as well as the biases inherent to observational studies including selection, information and confounding biases are some of the other limitations. The study was performed during the COVID-19 pandemic. This resulted in a global reduction in LC as described in the CHOLECOVID study.(32) Restricted non-emergent theatre time during the pandemic resulted in a lower number of LC performed in our unit in 2020. Long term follow up (after 30-days) was also lacking.

The strengths of this study encompass including consecutive patients, data capture across a surgical hospital complex which included four hospitals, with all treatment modalities including interventional radiology and ERCP readily available if needed. There was complete follow-up at 30-days for all patients.

Conclusion

LSC is a safe and feasible alternative for difficult laparoscopic cholecystectomies where the critical view of safety cannot be achieved. Hazardous dissection and biliary injury due to distorted anatomy caused by severe inflammation, extensive fibrosis and dense adhesions can be prevented by this procedure. LSC is safe, prevents BDI and conversion to an open operation. Post-operative bile leak was not a major clinical issue in our setting. Ongoing participation in the registry is encouraged as it produces a wealth of data to examine with opportunities for further study and research to improve patient care. Ongoing research should focus on developing and refining predictive scores using pre- and intra-operative factors.

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Part D - Supporting documents

Addendum A: Abbreviation and acronyms

ASA	American society of Anaestesiologist
BDI	Bile duct injury
BM	Body mass index
CI	Confidence interval
CBD	Common bile duct
CV	Critical view of safety
ERCP	Endoscopic retrograde cholangiopancreatography
GERD	Gastro-oesophageal reflux disease
GB	Gallbladder
HREC	Human research ethics committee
HIV	Human Immunodeficiency Virus
IQR	Interquartile range,
LC	Laparoscopic cholecystectomy
LSC	L aparoscopic subtotal cholecystectomy
ML	Millilitre
OR	Odds ratio

Addendum B: Index of tables

Addendum C: Author guidelines of World Journal of Surgery

MANUSCRIPT PREPARATION AND ORGANIZATION

General instructions:

• Use a normal, plain font (e.g., 10-12 point Times Roman or Arial) for text
• Double-space the text
• Use italics for emphasis
• Include page numbers
• Do not use field functions
• Use tab stops or other commands for indents, not the space bar
• Use the table function, not spreadsheets, to make tables

Manuscript style and text formatting:

Styling and text formatting refers to the use of special effects to enhance the appearance of the published article. Please make note of the following "Dos and Don'ts" regarding styling:

• DO enter all lists as single column lists.
• DO use your word processing features to indicate bold, italic, superscript, and subscript text within a paragraph or heading.
• DO NOT center text for headings. All text should be justified left, with ragged (unjustified) right margins.
• DO NOT use italic, underline, or other type effects for the entire text of a heading.
• DO NOT use all capital letters for a heading; use initial caps instead.
• DO NOT use multiple spaces to set up columns or tables; use tabs instead.
• DO NOT use carriage returns at the end of each line of text (use the word wrap feature).

Manuscript organization:

Manuscripts should be organized and follow the sequence as indicated below:

TITLE PAGE: The title page should include:

• A concise and informative title
• The name(s) of the author(s) including the affiliation(s) and address(es) of each author. The complete name and address of the author to whom correspondence should be sent, as well as his/her phone number, fax number, and email address.
• A short title for use as a running head
• Keywords: 3-6 keywords relevant to the manuscript
• Trail registration number for randomized clinical trials (see “Types of Manuscripts: Original Scientific Reports” above)
• Grant support for the research reported
• Statements to comply with ethical requirements (see “Compliance with Ethical Requirements” below for more details):

- ♦ A statement for each author in the manuscript must be included declaring whether there are any conflicts of interest in the manuscript. Even if there is no conflict of interest, this should also be explicitly stated as none declared on the title page.
- ♦ Statement of informed consent should be included if individual participants are included in the study. For example: “Informed consent was obtained from all individual participants included in the study.”

- Statement of human and/or animal rights should be included (if applicable) stating that the study was approved by the appropriate institution and/or national research ethics committee

Manuscript word count of your submission

ABSTRACT (if applicable):
The abstract must appear between the title page and the Introduction section of the manuscript, even if it has been uploaded separately. Manuscripts that require an abstract should contain a structured abstract of not more than 250 words. It should be a factual description of the study performed organized with the headings of: *Background* (includes aims, hypotheses, or objectives), *Methods* (includes patient population, procedures, and data analysis), *Results*, and *Conclusions.*

The abstract should contain the data to support the key findings or conclusions of the study. The trial registration number for randomized clinical trials must be included at the end of the abstract. The first time an abbreviated term is used, spell it out in full and follow with the abbreviation in parentheses – for example: ultrasound (US).

TEXT:

Original Scientific Reports should be arranged in sections titled Introduction, Material and Methods, Results, and Discussion.
1. Introduction: conveys the background and purpose of the report
2. Material and Methods
3. Results & Discussion
When required by the nature of the report, manuscripts that do not follow this specific format may be accepted.

ACKNOWLEDGEMENTS:

A brief statement should acknowledge individuals, other than authors, who were of direct help in the reported work or if the work was supported by a federal or commercial grant. All acknowledged persons should give their written consent to being named in the manuscript. This consent is to be uploaded upon manuscript submission.

REFERENCES:

Reference citations in the text should be identified by numbers in brackets (e.g. [4]). Number the references in order of their first appearance in the text (not alphabetically). Once a reference is cited, all subsequent citations should be to the original number. References may not appear in your Reference List unless they have been cited in the text or tables. Manuscripts that have been accepted for publication or are in press may be listed as references, but the Journal does not reference unpublished data and personal communications. Use the form for references adopted by the U.S. National Library of Medicine, as in Index Medicus. For each reference, show inclusive page ranges (e.g., 7-19).

Addendum D: Departmental Research Committee approval

UNIVERSITY OF CAPE TOWN

Department of Surgery
Departmental Research Committee
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19 Apr 2021

Dr. K Booyse

Department of Surgery
University of Cape Town

Dear Dr. Booyse

RE: Project 2021/194

PROJECT TITLE: An Analysis Of Risk Factors Predicting Conversion To And Outcomes After Laparoscopic Subtotal Cholecystectomy Performed In The Cape Metro West Region.

The above protocol has been reviewed by the Department of Surgery Research Committee. I am pleased to inform you that the committee approved the scientific merit of the study, and endorse the protocol for submission to the relevant ethics committee.

Although this letter serves as confirmation that the above protocol has successfully passed through the surgical DRC, respective ethics committees still require DRC chair signature before submission.

Please use the above project number in all future correspondence,

Yours sincerely

A/PROF MARITZ LAUBSCHER
CHAIR SURGICAL DRC

Addendum E: Faculty Ethics Committee approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50- Old Main Building
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Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

30 April 2021

HREC REF: 266/2021

Dr C Kloppers
Department of General Surgery
F-26 NGSH
Email: christo.kloppers@uct.ac.za
Student: Karien_booyse@yahoo.com

Dear Dr Kloppers

PROJECT TITLE: AN ANALYSIS OF RISK FACTORS PREDICTING CONVERSION TO AND OUTCOMES AFTER LAPAROSCOPIC SUBTOTAL CHOLECYSTECTOMY PERFORMED IN THE CAPE METRO WEST REGION-MMED CANDIDATE-DR KARIEN BOOYSE-SUB-STUDY LINKED TO R040/2019

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

This approval is subject to strict adherence to the HREC recommendations regarding research involving human participants during COVID -19, dated 17 March 2020 & 06 July 2020.

Approval is granted for one year until the 30 April 2022.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Karien Booyse will also be involved in this study.

Please quote the HREC REF 266/2021 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.