COMPLICATIONS OF ILEOSTOMY CLOSURE AND THEIR RISK FACTORS

by

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DECLARATION

I, Deepanjali Banerjee, 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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PART A:

RESEARCH PROTOCOL

COMPLICATIONS OF ILEOSTOMY CLOSURE: THE SOUTH AFRICAN EXPERIENCE

Introduction

Ileostomy closure is associated with considerable morbidity and mortality.

Research Question

To determine the complications of ileostomy closure and compare the rates of complications, at a tertiary teaching hospital in South Africa with that worldwide.

Literature Review

An elective loop ileostomy is commonly constructed to protect a distal anastomosis when there is a high risk of anastomotic leakage such as following low anterior resection and restorative proctocolectomy or for diversion purposes during emergency surgical procedures.

Ileostomy closure is associated with significant morbidity. Most of the data concerning the complications following ileostomy closure come from a small number of reviews done in USA, Spain, Turkey and Europe. Reported morbidity rates are between 3-30% and mortality rate of 0-4%. It is only recently that a study demonstrated a major complication rate of 9.3% and a mortality rate of 0.6% among a total of 5,401 patients[1].

A recent study demonstrated the association between pre-operative hypoalbuminaemia and anaemia and a higher complication rate following ileostomy closure.[2] The literature has also shown that there are no differences in complication rates whether a trainee or consultant performed the closure [3], however, there are lower rates of bowel obstruction and anastomotic leakage noted in patients with stapled anastomosis compared to hand sewn anastomosis[4]. There seems to be a higher complication rate following a longer interval between stoma formation and closure[5]. Neoadjuvant chemotherapy does not seem to predict the incidence of complications seen post closure[1].

There are no studies done in South Africa demonstrating the complication rate following an ileostomy closure.

Aims and Objectives:

Previous literature pertaining to complications following ileostomy closure and possible risk factors associated with ileostomy closure have been seen derived largely from developed countries. South Africa has its own unique patient population dynamics with regards to the colorectal disease burden including the, time and age at presentation, genetic variability, access to health care facilities, financial security,

varying levels of social security and differences in sociocultural health seeking behaviour patterns. It would therefore be interesting to evaluate whether the type of complications seen at a tertiary teaching hospital in South Africa are comparable to that seen worldwide.

Aim: To determine the complication rate after an ileostomy closure at Groote Schuur Hospital (GSH) between January 2008 and December 2012.

Specific Objectives:

- To determine if there are any surgical factors that may contribute to development of complications seen.
- To determine if the technique of ileostomy closure has any influence on the complications seen.
- To determine if the indication for the ileostomy has any association with the complications seen.
- To determine if there are certain patient factors that may predispose to development of complications seen.

Materials and Methods:

A retrospective review of patients who underwent ileostomy closure at the colorectal unit, Groote Schuur Hospital, from January 2008 to December 2012 will be undertaken.

The data will be collected from patient's hospital folders.

The type of data to be collected is as follows in **Table 1** below:

PARAMETERS	AGE	SEX	BMI	DURATION OF STOMA	DURATION OF SURGERY	LENGTH OF HOSPITAL STAY	TIME TAKEN TO ACHIEVE BOWEL MOVEMENT	YES	NO
1.Indication:									
Cancer									
IBD									
Emergency diversion									
2.Comorbidity:									
Diabetes									
Hypertension									
Renal impairment									
COPD									
3.Smoking									
4.Performance Status:									
ASA 1									
ASA 2									
ASA 3									
ASA 4									
5.Type of closure:									
Hand sewn									
Stapled									
6.Experience level of surgeon:									
Junior Consultant									
Registrar									
7.Type of wound closure:									
Stapled									
Hand sewn									
8. Pre-op chemo/radio therapy									
9.Complications									
(A) Major:									
Anastomotic Leak									
Fistula									
Bowel Obstruction									
Stricture									
Incisional hernia									
(B) Medical:									
Pneumonia									
UTI									
DVT									
Line Sepsis									
Cardiac complications									
Renal Failure									
(C) Minor:									
Wound Infection									
Stitch Granuloma									
PR bleeding									
(D) Death									
(E) Clavien-Dindo classification									
I									
II									
III									
IV									
V									

Table 1: Data Collection Sheet

Data analysis and management

The chi squared test, Student's t-test, ANOVA and their non-parametric equivalents will be used for tests of hypothesis where appropriate. Data will be collected and entered directly into an excel spreadsheet. The data will be coded and double entered into the spreadsheet. Data will then be analysed and managed in the statistical software package, Stata version 12.1. Means, standard deviations, ranges and histograms will be used to describe continuous data while medians, interquartile ranges, pi-charts and bar-graphs will be utilised for categorical data.

Ethics approval

Ethics approval will be sought from the University of Cape Town Human Research Ethics Committee and the Groote Schuur Surgery Departmental Research Committee.

Work Plan

- February 2013- March 2013: Ethics and Departmental Research Committee approval and literature review.
- March 2013- April 2013: Data collection and analysis.
- April 2013-May 2013: Write up and submission of first draft.

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PART B:

LITERATURE REVIEW

A.CONSTRUCTION OF ILEOSTOMY

INTRODUCTION

The construction of an ileostomy is used increasingly to reduce the risk of pelvic sepsis after very low rectal anastomosis. The actual benefit from a defunctioning stoma will depend on the successful reversal of the stoma being associated with minimal risk. Although closure of ileostomy is regarded as a fairly minor procedure, it is still associated with significant morbidity and mortality. This review of the literature examines the morbidity and mortality associated with closure of an ileostomy.

DEFINITION

Ileostomy is derived from 2 Greek words, *eilos* (twisted bowel) (1) and *stoma* (mouth) (2), literally translated to mean a hole in the twisted part of the bowel, i.e. the ileum. The more refined definition of an ileostomy being the surgical creation of an opening in the ileum through the abdominal wall to allow for preferential drainage of the intestinal contents.

HISTORY AND EVOLUTION OF ILEOSTOMIES

There have been numerous advances and developments in the creation of both ileostomies and colostomies as we know them today (3). Various Greek scholars including Hippocrates (460-377BC) and Claudius Galen (131-201AD) recognised that injuries to the bowel were life threatening, but did not know the reason behind this or how to treat them (3). With the discovery and use of guns in the 14th century, gunshot wounds became common, and there was an associated increase in bowel injuries which resulted in a high morbidity and mortality. Most injuries were managed expectantly as little was known about how to fix them. Those pioneering surgeons who dared to fix them ended up with exceptionally high rates of peritonitis, anastomotic leaks and death. The patients who survived these injuries did so despite the surgeons' skills and knowledge, and ended up with enterocutaneous fistulae. The Swiss Alchemist and physician, Theophrastus Bombastus Von Honenheim (1493-1541) noted that patients got better after creation of an intestinal fistula (3).

The first documented stoma creation was performed by the British surgeon, William Cheselden (1688-1752) on a 73 year old woman who had a strangulated umbilical hernia with 55cm of dead bowel, for which he carried out a resection and brought out

a piece of her intestine onto the abdominal wall. She survived several years post operatively despite limitations in wound and ostomy care (3).

Since then numerous surgeons performed ileostomies with disastrous complications and death. Some of these complications were related to poor aseptic techniques, inadequate anaesthesia, anastomotic leaks, peritonitis and poor wound care. As anaesthesia and aseptic techniques improved from the mid-19th –20th century more operations were performed successfully. The German Surgeon, Baum has been credited for performing the first documented ileostomy in 1879 (3).

The most morbid complication was noted to be a high stoma output termed "ileostomy dysfunction" (2). This entity was noted by Crile & Turnbull (1954) to be as a result of serositis secondary to the exposed serosa of the ileostomy on the abdominal wall. They rectified this problem by excising the seromuscular layer of the exposed portion of the bowel, everting the mucosa and submucosal layers of the bowel wall over the ileostomy and suturing it to the abdominal wall (4). The commonly performed Brooke ileostomy done today, involves evagination of the full thickness of the bowel wall and suturing the edge to the abdominal wall (5). It was first described by Bryan Brooke in 1952 and has the advantage of preventing skin excoriation, allows better fitting of the stoma bag at the base of the ileostomy and hence prevents leakage (6).

Turnbull & Weakley first described the loop ileostomy in 1971 (7)-(9). Prior to this all ileostomies constructed were end stomas (10).

INDICATIONS

(a)Indications for a temporary ileostomy

The following are indications for the formation of a temporary loop ileostomy (10):

- To protect complex anastomoses such as following an ileoanal anastomosis or a low anterior resection for rectal cancer.
- To defunction an ileoanal pouch anastomosis (IAPA) following proctocolectomy in patients with Ulcerative colitis (UC), Familial Adenomatous Polyposis(FAP) & Hereditary Non Polyposis Coli Colorectal Cancer (HNPCC).
- To defunction patients who have severe perianal fistula disease due to Crohn's disease.
- To divert the faecal stream away from a vulnerable distal bowel anastomosis done as an emergency procedure in a heavily contaminated acute abdomen secondary to bowel perforation or trauma.
- For management of an anastomotic leak.
- Management of perianal/perineal sepsis.

- To divert and allow healing in cases of complex rectovaginal, rectourethral or pouch vaginal fistulae.
- To manage obstetric complications.
- Patients with radiation proctitis
- Patients with anal stenosis.

(b)Indications for a permanent ileostomy

Indications for permanent end ileostomies include:

- To relieve distal obstruction due to unresectable pelvic malignancy (10).
- To provide a permanent defunctioning solution in patients in whom a restorative procedure is not possible e.g. Total proctocolectomy in Crohn's disease or patients with FAP, and a low lying rectal cancer involving the anal sphincter complex.
- As a last line of therapy for patients with intractable idiopathic constipation (11).
- Paraplegic patients.
- Patients with faecal incontinence unresponsive to other forms of treatment (10).

(c)Ileostomy Versus Colostomy debate

The main reason for performing a defunctioning ileostomy or colostomy is to divert the intestinal content away from a distal anastomosis to allow it to heal adequately and to reduce the rate of leakage related re-interventions (12). This can be done with either a colostomy or an ileostomy.

The ileostomy versus colostomy debate has raged for many years and there is still no consensus as to which is superior. A recent met-analysis and systematic review conducted by Rondelli et al (2009) (12) looked at 5 RCTs and 12 comparative studies and concluded that the rate of sepsis and prolapse were lower in patients with loop ileostomies (LI) compared to those with loop transverse colostomies (LC). However, they also reported a lower incidence of bowel obstruction after closure of LC compared to LI, but this was only significant in those patients with rectal cancer.

A met-analysis done by Güenaga et al (2008)(13) and Lertsithichai (2004) (14) arrived at the conclusion that stoma prolapse occurs more commonly in LC than with LI but could not make any recommendations as to which of the two techniques was better as the sample sizes of the analysed RCTs were too small.

These met-analyses contained very heterogeneous patient populations. In an attempt to rectify this problem, a retrospective review of 462 patients done by Rullier et al (2001) (15) on a more homogenous group of patients (rectal cancer patients only with similar demographics) showed that the complication rate was significantly higher in LC (34%) compared to LI (12%). The risk of intervening post stoma

construction and closure was significantly higher in LC (22%) compared to LI (9%). Thus it would appear that LI is better than LC in patients with rectal cancer.

Only 2 small RCTs (Gooszen 1998 (16) & Law 2002 (17)) have so far favoured LC over LI. With the current evidence leaning in favour of loop ileostomies albeit from small RCTs, retrospective studies, systematic reviews and met analyses, larger, well designed RCTs are required to provide a better answer as to which transitory stoma is indeed better.

(d)Ileostomy in patients with low rectal cancer

Colorectal cancer is the third most common cancer in men and second most common in women worldwide (18). It is the third most common cancer in the world and the fourth most common cause of death (19). Colorectal cancer surgery has evolved remarkably over the last decade. Anterior resection with total mesorectal excision (TME) has become the standard operation for resectable middle and lower third rectal cancers that do not involve the anal sphincter complex.

Many surgeons prefer to defunction the primary coloanal anastomosis using a covering loop ileostomy while others do not. There are several factors which influence this decision. These include surgeon preference, the presence of comorbidities, recent radiotherapy, technically challenging operation, steroid therapy, severe contamination during the surgery, incomplete circular stapler doughnuts, failed hydro pneumatic leak test and height of the anastomosis (10), (20). For low lying rectal lesions (i.e. between 2cm and 5cm) the leak rates are significantly high if there is no diverting ileostomy (44.4% versus 12.7% respectively) (21). These leak rates are thought to occur either secondary to devascularisation of the rectal stump or large area created by the TME and is compounded by poor anastomotic healing post neoadjuvant radiotherapy (12).

Chronic medical conditions like renal dysfunction, diabetes mellitus and chronic liver disease all result in chronic malnutrition and poor wound healing and are indications for a covering loop ileostomy. Radiotherapy and steroid therapy similarly cause delayed wound healing and high rates of anastomotic leaks thereby mandating formation of a loop ileostomy.

TECHNIQUE OF ILEOSTOMY CONSTRUCTION

Ileostomies can be performed open or may be performed using standard laparoscopic techniques or through single incision laparoscopic procedures (22).

The open technique of loop ileostomy construction involves the following steps: (**See Figure 1**)

- A circular incision is made over a premarked stoma site on the patient's abdomen.

- Dissection is carried down to the rectus sheath and the sheath is incised in a cruciate manner, the muscle layer retracted away and the peritoneal cavity entered.
- A loop of small bowel about 20-30cm from the terminal ileum is brought out through the trephine hole onto the skin using Babcock forceps or a Jacques catheter ensuring there are no twists in the bowel.
- The proximal end is marked with a suture. An enterotomy involving 80% of the circumference is made on the antimesenteric side of the ileum.
- The proximal end of the ileostomy is spouted while the distal end is sutured flush with the skin using vicryl 2/0.

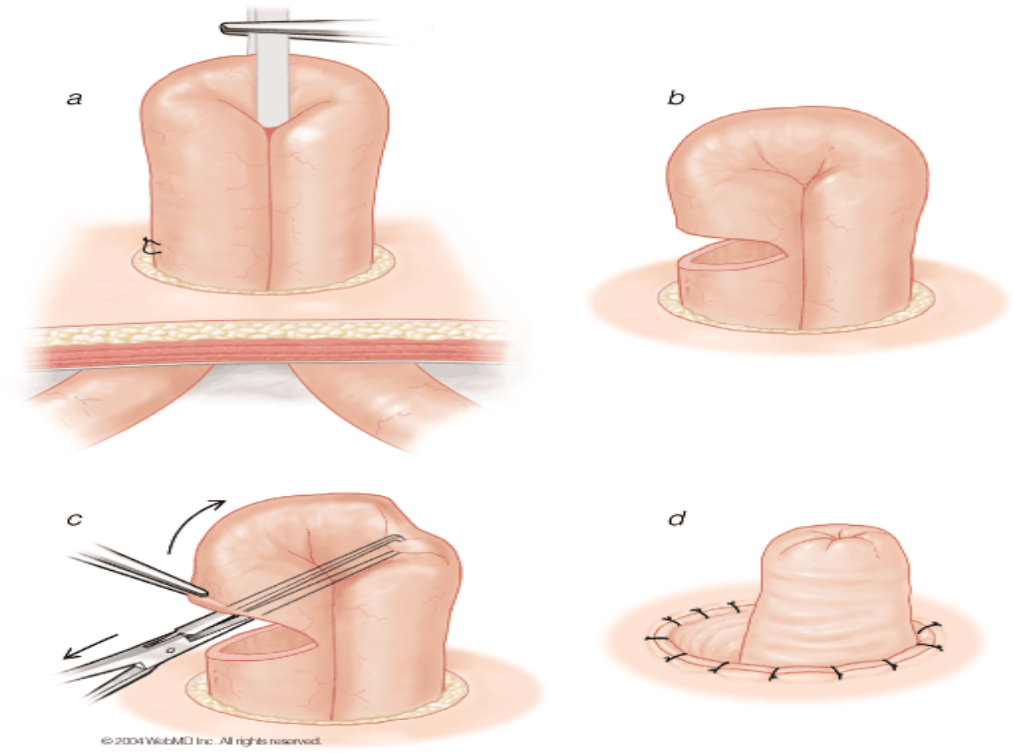

Figure 1: Construction of a loop ileostomy (23)

COMPLICATIONS OF ILEOSTOMY CONSTRUCTION

Ileostomy formation has its own complications and these can be classified as early or late, physiological, functional or psychological (22).

Early complications (up to 30 days after the operation) include haemorrhage, stomal pain, retraction (17%) (22), ischaemic necrosis, detachment, early skin excoriation and peristomal abscess formation (10).

Late complications (more than 30 days after the operation) include stoma prolapse (<4%), parastomal herniation (1-3%), stenosis and up to 25 % patients develop small bowel obstruction post ileostomy formation (10). Peristomal fistula formation is also a complication of ileostomy formation and is seen most commonly in patients with Crohn's disease. The causes of fistulae include deep placement of a suture or mechanical causes such as leakage or injury from stoma appliances (10). In patients with Crohn's disease fistula formation around the ileostomy is a sign of disease recurrence until proven otherwise (10).

Other late complications include high output of the ileostomy, leading to dehydration and renal dysfunction, and peristomal skin problems such as dermatitis (23), ulceration, fungal infections and folliculitis (22). These peristomal conditions occur in 18.3-61% of patients with ileostomies. The incidence of dehydration in patients with ileostomies varies from zero to more than 70% (10). Ischaemia of an ileostomy is a rare (1-5%) complication but common in obese patients in whom the large abdominal pannus causes increased mesenteric tension and strangulation of the ileostomy (22). Complication rates of defunctioning ileostomies range between 5-100% (10). Of those patients who have ileostomies, between 10-70% of them will have a complication related to their stoma (22).

The other major complication of ileostomy formation which is often under stated in the literature is permanence of the stoma i.e. non-closure of stoma. The incidence of non-closure reported in the literature ranges from 0-19% (10). Some of the risk factors associated with non-closure in patients with colorectal cancer include occurrence of complications after the index surgery such as symptomatic anastomotic leaks, old age of the patient, advanced cancer disease and adjuvant chemotherapy (20). Non-closure has a serious impact on the quality of life of these patients affecting their psychosexual functioning, altered self-image, difficulties with long term stoma care, depression, social problems and financial repercussions (10),(24),(25). These patients often succumb to complications of long term depression and have a poor survival rate.

B. CLOSURE OF ILEOSTOMY

(1)TIMING OF CLOSURE

There is significant morbidity associated with loop ileostomy formation. The proponents of early closure argue that early closure will improve the quality of life of the patient, reduce ileostomy related morbidity and still protect a distal anastomosis.

Ileostomy closure is usually performed three months after the primary operation to allow for wound healing to occur and time to allow for the development of any

complications which may occur so that they can be dealt with appropriately prior to considering closure (26). In addition this time also allows the inflammation, induration and oedema within the abdomen and around the ostomy site to resolve. The intra-abdominal adhesions also become less vascular and fibrotic. Closure after 8.5 weeks has been reported to be associated with lower postoperative complications (27).

Several prospective, non-randomised studies have suggested that early closure of ileostomies i.e. within two weeks, is possible in a select group of patients (27), (28), (29). However, there is currently no consensus over which selection criteria should be used for these patients. Some proposed criteria include patients with normal stoma function, absence of signs of local and systemic infection, absence of a demonstrable leak on water soluble contrast studies done on 7th postoperative day and patients who are not on any steroid therapy (28).

A randomised controlled trial (RCT) by Alves et al (30) allocated a select group of patients to either early closure (EC) on day 8, or late closure (LC) on day 60. The overall morbidity was similar (31% in EC and 38% in LC group). Furthermore overall surgical complications and reoperation rates were similar in both groups. However wound complication rates were higher in the EC group. Small bowel obstruction (16% vs. 3%) and medical complications (15% vs. 5%) were higher in the LC group compared to the EC group.

Delayed closure is considered to be closure beyond 12 weeks (10). The main reasons for this include the presence of a symptomatic anastomotic leak, enterocutaneous fistula, administration of postoperative chemotherapy following the primary surgery, cancer recurrence, progressive malignancy and postponement of the procedure as ileostomy closure is not deemed an operation of high priority (10) (20).

In our setting 3 months is the usual time frame within which ileostomies are closed. Closure may be considered earlier in patients who are struggling to manage their ileostomies due to high output with resultant dehydration and repeated admissions to correct the same. Even in these cases two months is usually seen as our early closure time.

It is standard practice to perform a contrast radiographic examination (loopogram) to exclude an efferent limb obstruction or leak from a previous pelvic or other anastomosis, prior to closure of the ileostomy.

(2)TECHNIQUE OF ILEOSTOMY CLOSURE

Ileostomy closure techniques are quite standard and include a simple hand sewn anastomosis or a stapled anastomosis. The main steps involved in closure of a loop ileostomy include: (**See Figure 2)**

1. A peristomal incision is made around the stoma.

2. The incision is deepened and dissection carried down to the subcutaneous tissue.
3. A dissection plane is developed between the bowel wall and the subcutaneous tissue and carried on in a circumferential manner until the rectus sheath is reached.
4. The small bowel is then dissected free from the rectus sheath taking care not to injure the bowel wall during this process.
5. Eventually the peritoneal cavity is entered and the remainder of the adhesions are divided using a finger sweep manoeuvre.
6. The loop of ileum is then taken out of the abdominal cavity and the mucocutaneous junction and skin rim are excised and the proximal everted end of the stoma is unfolded using sharp dissection.
7. The freshened edges of the enterotomy are closed using absorbable sutures such as vicryl 2/0 in a continuous or interrupted manner. If the edges of the stoma appear to be in a poor condition, then debridement of the edges and an end to end anastomosis is performed using vicryl 2/0.
   A functional end to end with stapled anastomosis may also be done as an alternative to a hand sewn procedure.
8. The sheath is then closed.
9. The skin is closed using skin staples or interrupted nylon suture. The skin may also be closed using a circular purse string suture or left open so that healing by secondary intention occurs. The rationale for this type of closure is to minimise postoperative wound infection especially in those patients who have had their stomas for a long period of time.

(a)Hand sewn Versus Stapled anastomosis

There have been numerous studies comparing the outcomes after a hand sewn versus a stapled anastomosis. A previous RCT, with about 70 patients in each study arm, concluded that the rate of bowel obstruction was higher in the stapled group (14%) compared to the hand sewn (3%) group, while the mean hospital stay, readmission and reoperation rates did not differ significantly between the two groups (31). The only advantage perceived using a stapled anastomosis according to this study was a shorter length of stay in hospital and a faster surgical time. Several small retrospective studies have also confirmed that the stapled anastomosis results in shorter length of hospital stay, lower rates of anastomotic leakage and reduced overall morbidity compared to a hand sewn procedure (32), (33). In addition, to faster surgical time some studies claim an overall reduction in hospital costs as well (34). Several studies, on the other hand, have shown no difference in the duration of surgery, length of hospital stay, rate of anastomotic leak or time to achieve a bowel action whether the anastomosis was stapled or hand sewn (35), (36). The HASTA trial comparing hand sewn anastomosis and stapled anastomosis with a target of 334 patients recruited, is yet to reveal its results and shed more light on whether a hand sewn or stapled anastomosis is better (37).

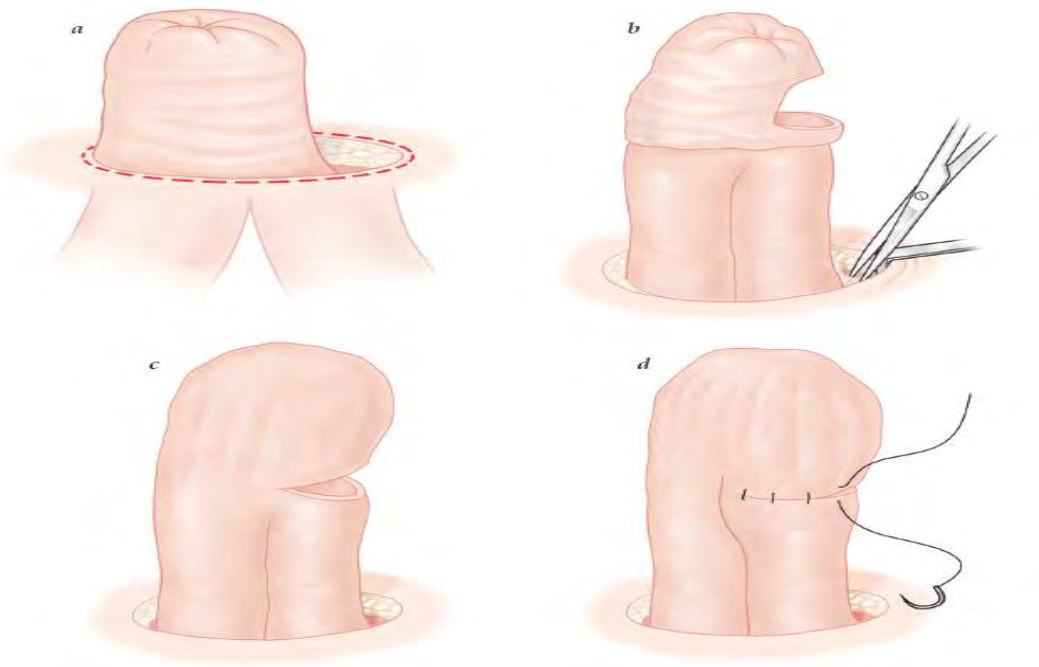

Figure 2: Closure of Ileostomy (23)

COMPLICATIONS OF ILEOSTOMY CLOSURE

Complications after ileostomy closure are varied and are associated with significant morbidity and mortality rates. Ileostomy closure should not be considered a routine procedure as it necessitates another hospital admission and carries its own risks (38). The morbidity rate varies between 3 to 30 % and the mortality rate between 0 to 4%. Most of these rates have been derived from very small retrospective studies done in USA, Spain, Turkey and Europe (27), (39), (40), (41), (42), (43). A recent large retrospective study undertaken by Sharma et al looked at 5,401 patients and demonstrated a major complication rate of 9.3% and a mortality rate of 0.6% (38).

The main surgical complications noted after an ileostomy closure include small bowel obstruction (SBO), wound infection, anastomotic leaks, fistulae formation, bleeding from staple lines and incisional hernia formation (40)-(46).

(a)Small Bowel Obstruction

The incidence of SBO ranges from 0 to 15% (10). In most patients the SBO resolves with just conservative management. In those patients who need operative management of bowel obstruction, the aetiology of the obstruction is usually intra-

abdominal adhesions. Other less common causes of bowel obstruction found intraoperatively include strictures, intramural oedema and intramural hematoma. In some cases no cause is found for the obstruction (10). Narrowing of the ileal lumen from oedema after bowel anastomosis compounded by the fact that the distal limb has a narrow lumen due to previous defunctioning is a recognised cause for the SBO post ileostomy closure (10). Some studies have reported a lower incidence of bowel obstruction after stapled anastomosis while others have shown that the type of closure does not make a difference to the incidence of complications (35), (43),(47), (48), (49).

Certain patient groups have been noted to have a higher rate of complications post ileostomy take down. It has been noted that patients with UC who have had IAPA have a higher incidence of SBO than other patients possibly due to the increased number of adhesions secondary to increased bowel manipulation during the primary surgery, therefore making ileostomy closure more difficult and longer (10),(27). It has also been postulated that the short length of the mesentery, extent of inflammatory disease affecting the remainder of the bowel and increased traction placed on the mesentery during ileostomy closure make it technically more difficult (10),(27). It is still unclear as to whether the adhesions from the primary operation or that from the ileostomy closure operation contribute to SBO in this group of patients (10).

The type of incisions utilised during the surgery itself i.e. parastomal, extended parastomal or midline incisions do not influence the development of a SBO post ileostomy closure (10).

(b)Wound Infection

Wound infection is also a common complication after ileostomy closure. It presents as either some erythema or induration around the wound edges to purulent discharge from within the wound (10). This can eventually lead to fistula formation as well as wound sepsis. The rate of wound infection is reported as 18.3% (10). Various wound closure techniques have been advocated in an attempt to minimise the rate of wound infection. These include leaving the wound partially open, completely open, use of subcuticular purse string sutures and standard interrupted primary wound closure. It has been found that subcuticular purse string sutures have a lower wound infection rate and give a better cosmetic outcome too (10).

(c)Anastomotic Leak

Anastomotic leak rates are reported to range from 0 to 8% (10). The anastomotic leak rate is not associated with the type of closure performed. These leaks can be subclinical or overt, and patients may present with overt peritonitis or enteric fistulae

(10). They need to be managed surgically, or may be managed conservatively e.g. in the case of a low output enterocutaneous fistula.

(d)Enterocutaneous Fistula

Enterocutaneous fistula rates range from 0.5 to 7% (10). Several different types of fistulae can form post operatively and they include enterocutaneous, enteroenteric, enterovesical and enterovaginal (10). Some fistulae may heal spontaneously while others require bowel rest and parenteral nutrition. Those fistulae which result from anastomotic breakdown require surgical closure. Patients with Crohn's disease who develop fistulae post operatively are preferentially managed medically as repeated reoperations increases the risk of postoperative complications, and subsequent operations predispose them to development of short bowel syndrome from serial bowel resections.

(e)Incisional Hernias

Incisional hernias develop in 1-12% patients (10). This is usually a late complication seen several months post closure (46). The management is by mesh repair of the hernia.

(f)Risk Factors for developing complications

There have been many studies done to try and determine whether there are certain factors which are associated with or may predict the complication rate after an ileostomy closure. A recent study demonstrated the association between pre-operative hypoalbuminaemia and anaemia and higher complication rate following ileostomy closure (45). Other studies have shown that there are no differences in complication rates whether a trainee or consultant performed the closure (50). Neoadjuvant chemotherapy does not seem to predict the incidence of complications seen after closure (38).

The time interval to ileostomy closure has been reported in some studies as not being a significant contributor to development of postoperative complications while other studies have demonstrated that a longer duration between ileostomy formation and closure causes increased postoperative complications (38), (51). Patients who had benign indications for stoma formation (like diverticulitis) have a higher rate (20%, n=123) of postoperative complications as they were seen to have their stomas for a longer duration than those who had rectal cancer (41). The only complication noted to be significantly lower when stomas were closed earlier was wound infection rate.

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PART C:

COMPLICATIONS OF ILEOSTOMY CLOSURE AND THEIR RISK FACTORS

COMPLICATIONS OF ILEOSTOMY CLOSURE AND THEIR RISK FACTORS

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ABSTRACT

Background: Loop ileostomies are often used to protect a difficult coloanal or ileoanal anastomosis and dampen the clinical effects of an anastomotic leakage (2). Ileostomy closure itself is associated with considerable morbidity and mortality and is not just a routine operation (1).

Objective: The aim of this study was to audit the complications seen after ileostomy closure at Groote Schuur Hospital.

The primary outcome was to determine the complication rate. The secondary outcome was to determine if there was any association between the various perioperative, operative and patient factors and the complications observed.

Method: All patients who underwent closure of ileostomy from January 2008 to December 2012 were included in the study. Individual patient records were used to extract patient demographics, perioperative variables, operative variables and postoperative complications retrospectively. The complications were graded using the Clavien- Dindo classification system

Results: A total of 80 patients were included in the study. There were 45 males and 35 females with a mean age of 50.6 years (18-81yrs). The median time to achieve bowel movement post closure was 3 days (range 2-16 days). The overall complication rate was 47.5%. Major complications were seen in 35% (28/80) of patients and these included bowel obstruction (14% 11/80), enterocutaneous fistula (6% 5/80), incisional hernia (4% 3/80) and stricture (1% 1/80). Minor complications accounted for 25% (18/80) of the total complications of which wound infection accounted for 21% (17/80). Medical complications made up 21% (17/80) of all complications of which the most common complication was pneumonia (6% 5/80). Two patients (2.5%) died after closure from medical complications. After using a stepwise logistic regression model and adjusting for confounders, renal dysfunction was found to be a statistically significant determinant for the development of complications (OR=3.31, p=0.022, 95% CI=1.186 to 9.242). The pathology (p=0.177), type of closure (p=0.285) and the surgeon (p=0.064) did not show any statistically significant association with development of complications.

Conclusion: Ileostomy closure is associated with significant morbidity. Renal dysfunction is associated with a high complication rate.

Keywords: loop ileostomy, complications of closure, morbidity, mortality

Abbreviations: TME=Total mesorectal excision, BMI =Body mass index, SBO= small bowel obstruction, DVT= Deep venous thrombosis, UTI=urinary tract infection, FAP=Familial adenomatous Polyposis, PJS=Peutz Jegher's syndrome, RVF= rectovaginal fistula, ASA=American Society of Anaesthesiologists' classification

INTRODUCTION

A loop ileostomy has been utilised widely in elective colorectal surgery to protect a very low rectal anastomosis such as following a TME or restorative proctocolectomy, which are considered high leak risk anastomoses, as well as for diversion purposes following emergency surgical procedures. Ileostomy construction has been shown to dampen the clinical effects of a leak as well as to reduce the rate of intervention post leakage (2). However the benefits of the covering ileostomy have to be weighed against the problems associated with its closure.

The most commonly reported complications after ileostomy closure include bowel obstruction, surgical site infection, anastomotic leaks, fistulae formation and incisional hernia formation (3)-(9). Although it is considered to be a routine operation, closure of ileostomy is associated with significant morbidity. Furthermore it requires another hospital admission, and also utilises the same if not more resources post operatively than the primary procedure necessitating its formation (1).

The aim of this study was to document the incidence of and identify risk factors for postoperative complications after loop ileostomy closure at Groote Schuur Hospital.

PATIENTS AND METHODS

The study was approved by the Human Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town. All patients who were admitted for closure of ileostomy to the colorectal unit at Groote Schuur Hospital from January 2008 to December 2012 were included in the study.

Individual patient medical, anaesthetic and nursing records were reviewed to extract information retrospectively. Inclusion criteria were all patients with previous loop ileostomy constructed during both elective and emergency surgery during the above time period.

The following information was extracted from the patient records: patient demographics, indication for ileostomy, comorbidity status, BMI, length of hospital stay, duration of stoma, time taken to achieve bowel movement after closure, performance status of the patient, administration of preoperative chemotherapy or radiotherapy or both, experience level of surgeon performing the operation (junior

consultant or registrar), duration of the surgery, type of anastomosis performed (hand sewn or stapled) and whether the patient required re-operation or not.

The complications observed were divided into 3 main groups, major, minor and medical complications. The major complications included the occurrence of SBO, anastomotic leaks, fistulae, hernia and stricture. Minor complications included surgical site infection, bleeding per rectum and occurrence of a stitch granuloma. Medical complications included pneumonia, UTI, line sepsis, cardiac complications, renal failure, anaemia, DVT and allergic reaction to medication. The frequency of these complications was then recorded for each patient.

The 30 day outcomes of the patients was graded from I-IV using the Clavien-Dindo scoring system **(See appendix 1).**

(i)Surgical Technique

All patients had a radiological contrast study (loopogram) done prior to closure to rule out any distal bowel obstruction and leaks. The patients did not receive any bowel preparation prior to closure.

At the operation all patients received a single dose of prophylactic antibiotics (Cefazolin 1g IV) about 30 minutes prior to the skin incision. A peristomal skin incision was used and none of the patients needed a laparotomy for the closure. Standard loop ileostomy closure was performed using either a single layer hand sewn end to end anastomosis with vicryl 2/0 absorbable suture or a functional end to end anastomosis with a 60mm linear GIA stapler.

All operations were performed either by a registrar under the supervision of a junior consultant, or by a junior consultant with a registrar as the first assistant.

(ii)Data Analysis

All the data was entered into an Excel data work sheet directly. The data was then coded and double entered into a statistical software package (Stata version 12.1) for analysis. Descriptive statistics were utilised to analyse the data. The chi squared test and its variants, Student's t- test and logistic regression was used to analyse the variables and their outcomes.

RESULTS

There were 88 patients who underwent closure of ileostomy between January 2008 and December 2012. The data was incomplete in eight patients and they were excluded from the data analysis.

Of the remaining 80 patients 45 patients were male and 35 were female with a mean age of 50.6 ± 15.7 years (range 18-81 years).

Majority of the patients were of mixed race origin (n= 51). Sixteen patients were white, 11 were black and 2 were of Indian origin. Only 43 of the 80 patients had BMI recorded. The mean BMI was 26 with a median of 25.64 (range 7-40.64). The patient characteristics are summarised in **Table 1.**

Total number of patients N = 80	Males= 45	Females = 35	
Age (mean ± SD) years	50.6 ± 15.7		Range 18 - 81
Race	Mixed race	51 (63.75%)	
	White	16 (20%)	
	Black	11 (13.75%)	
	Indian	2 (2.5%)	
BMI (mean ± SD) (kg/m^2)	26.0 ± 6.73		Range 7.00 – 40.64
Co-morbidities	Diabetes	8(10%)	
	Hypertension	25 (31.25%)	
	Renal dysfunction	28 (35%)	
Risk factors	Smoking	42 (53.1%)	
	Immunosuppressive therapy	2 (2.5%)	
Annual income ($ pa)	Unemployed	22 (27.5%)	
	< 4000	49 (61.25%)	
	4000 - 8000	3 (3.75%)	
	>8000	3 (3.75%)	
	Private	3 (3.75%)	

Table 1: Patient characteristics

Eight (10%) patients had diabetes, 25 (31.25%) had hypertension, and 28 (35%) had renal dysfunction (creatinine raised to 1.5 times of baseline levels).There were 42 patients who smoked and 2 were on immunosuppressive therapy.

Fifteen were ASA I, 45 patients were ASA class II and 20 patients were ASA class III.

The most common indication for loop ileostomy formation was following a TME for rectal cancer (51%) as shown in **Figure 1**. Other primary indications for ileostomy formation included ulcerative colitis (18%), Crohn's disease (9%), diverticular disease (6%), intra-abdominal sepsis (5%), FAP (5%), RVF (3%), tuberculosis (1%) and following a traditional enema (1%).

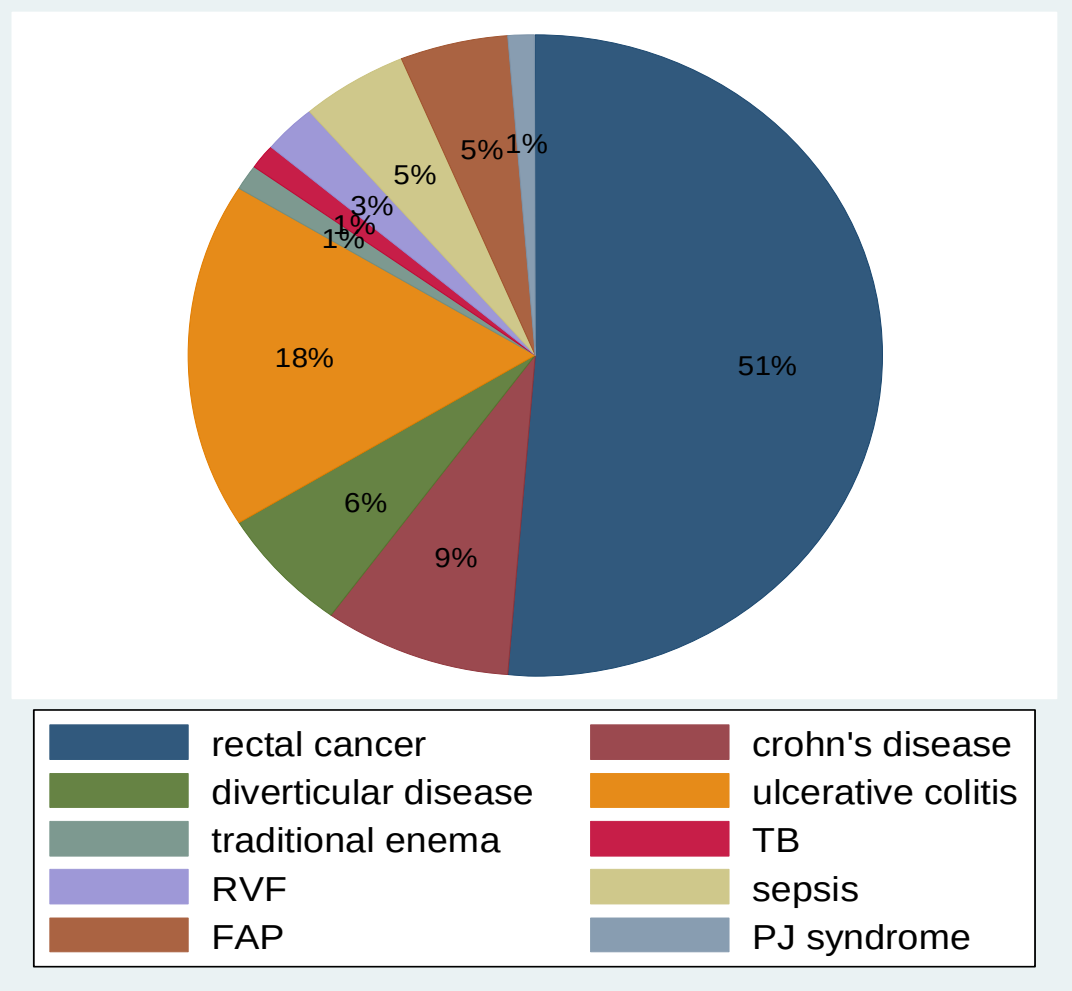

Figure 1: Indications for loop ileostomy

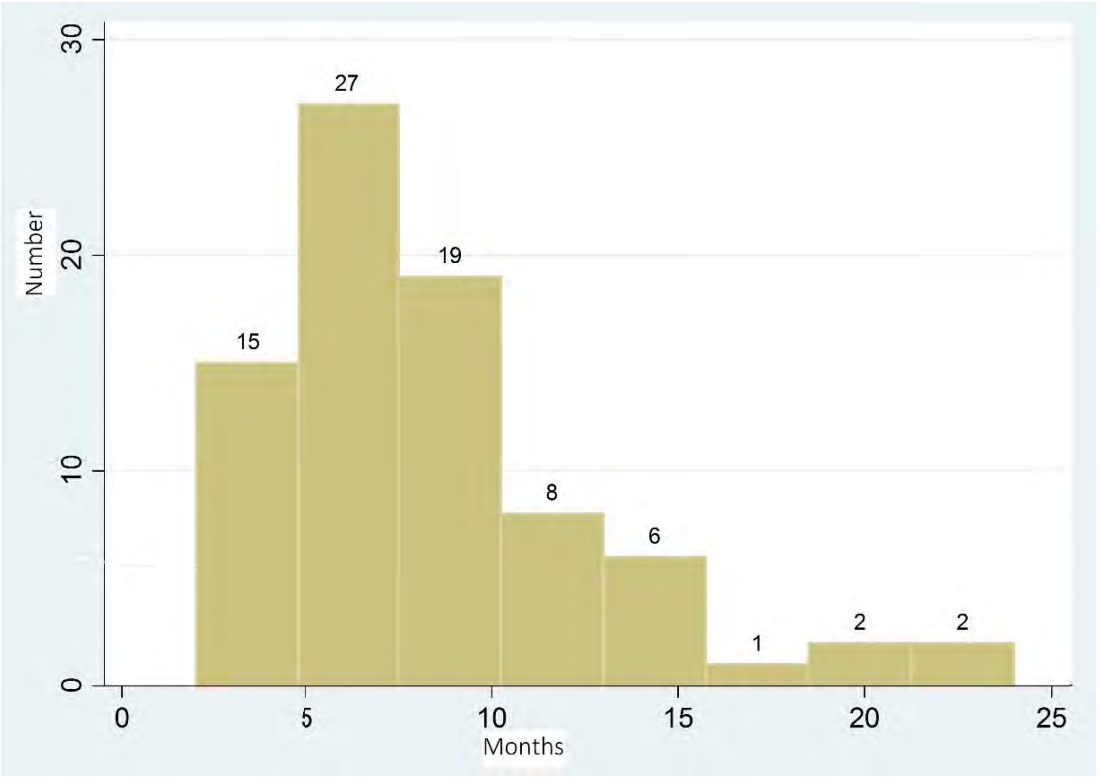

Figure 2: Duration of Ileostomy prior to closure

The duration of the ileostomy prior to closure is shown in **Figure 2**. The mean duration of ileostomy prior to closure was 8.23 ±4.42 months, with a median of 7 months (range 2-24months). This long duration is due to the prolonged waiting time in a resource stretched hospital.

Forty two (52%) of the operations were performed by registrars while 38(48%) were performed by junior consultants.

The majority of the anastomoses performed were hand sewn (n=71, 89%), and only 9 (11%) were stapled anastomoses.

The duration of the surgery is shown in **Figure 3**. The duration of surgery varied from 30 to 183 minutes with a mean of 86 ± 32.76 minutes. The duration of the surgery did not correlate with the development of complications (p= 0.58, OR=1.0, CI= 0.99 to 1.02).

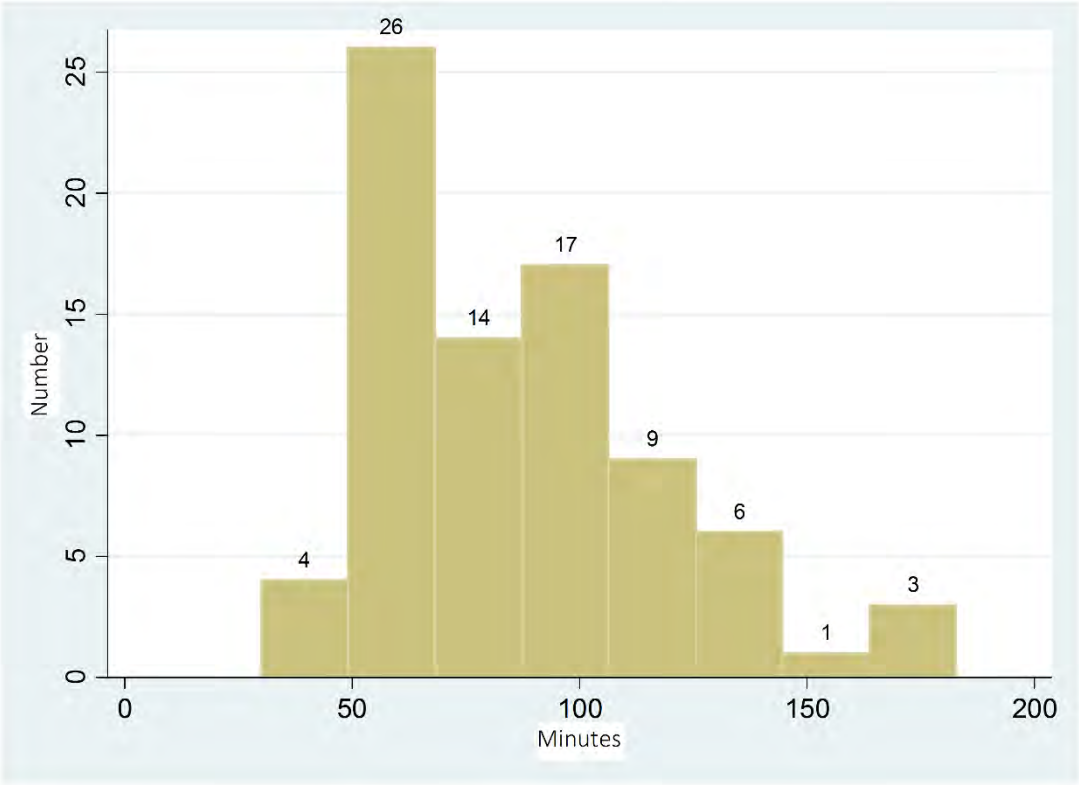

Figure 3: Duration of the surgery

The mean length of hospital stay was 7.04 ± 6.57 days with a maximum duration of stay of 37 days in one patient who had recurrent episodes of bowel obstruction postoperatively.

The median time to achieve bowel movement was 3 days (range 2-16 days). One patient took 16 days to open bowels, while one patient had missing data. First bowel movements occurred mostly between days 1 and 5. Fewer bowel movements occurred between days 6 and 10. The time taken to achieve bowel movement is shown in **Figure 4**.

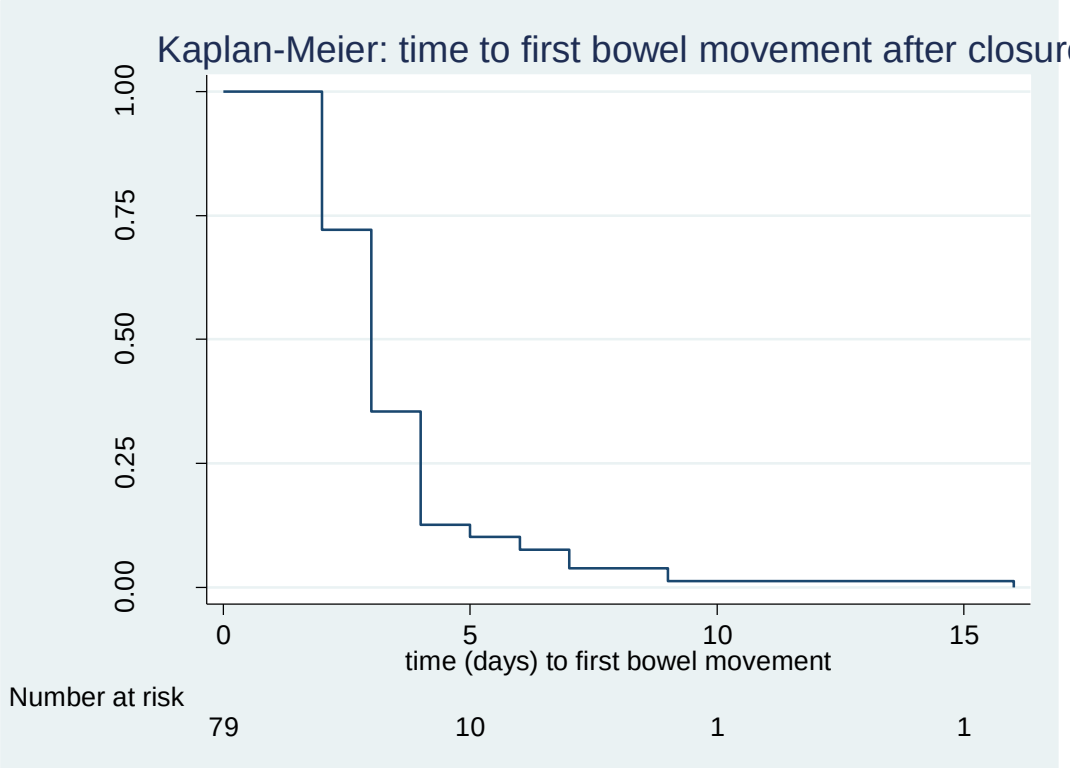

Figure 4: Time to first bowel action

Complications

Two patients died post ileostomy closure **(See Figure 5)**. Overall, 38 (47.5%) patients developed complications post closure of ileostomy **(See Table 2).** Major complications accounted for a large proportion of complications (n=28), while minor (n=18) and medical complications (n=17) were less common. More than half (52.6%) of the complications were seen in patients with rectal cancer while 6 of the 7 patients with Crohn's disease developed complications. Patients with sepsis, RVF, PJS and traditional enemas did not develop any complications **(See Table 2)** but rectal cancer was the most common indication for surgery so the denominator is made up of these patients (41/80).

Pathology	Overall complications N= 38	Major complications N= 28	Minor complications N= 18	Medical complications N= 17	Mortality N= 2
Rectal cancer N = 41	20	13	5	9	1
Crohn's Disease N = 7	6	4	4	2	0
Diverticular disease N = 5	2	2	2	1	0
Ulcerative colitis N = 14	6	5	4	3	0
TB N = 1	1	1	1	1	0
FAP N = 4	3	3	2	1	1
Others: **Traditional Enema** N=1 **RVF** N=2 **Sepsis** N=4 **PJS** N=1	0	0	0	0	0

Table 2: Complications post ileostomy closure

(a)Major complications

Major complications were seen in 28 (35%) patients **(see Table 2)**. The major complications included SBO (n=11, 14%), enterocutaneous fistula (n=5, 6%), incisional hernia (n=3, 4%), stricture (n=1, 1%). Ten percent of the patients had multiple major complications. One patient developed an anastomotic leak, after developing an enterocutaneous fistula and stricture 4 weeks post closure.

(b)Minor complications

Minor complications occurred in 18 (25%) patients. Of the minor complications noted, 21% (n=17) had wound infection, one patient had bleeding per rectum, one

patient had constipation and three patients had stitch granulomas which needed excision. Only one patient had multiple minor complications.

(c)Medical complications

Medical complications were seen in 17 (21%) patients and included pneumonia (n=5, 6%), UTI (n=3, 4%), line sepsis (n=2, 3%), anaemia (n=1, 1%) cardiac complications (n=1, 1%), DVT (n=1, 1%) and allergic reaction (n=1, 1%).Three (4%) patients had multiple medical complications.

(d)Deaths

Two patients died of medical complications. One died on day 17 of ventilator associated pneumonia and the other on day 43 of complications of recurrent DVT. The types of complications are summarized in **Figure 5**.

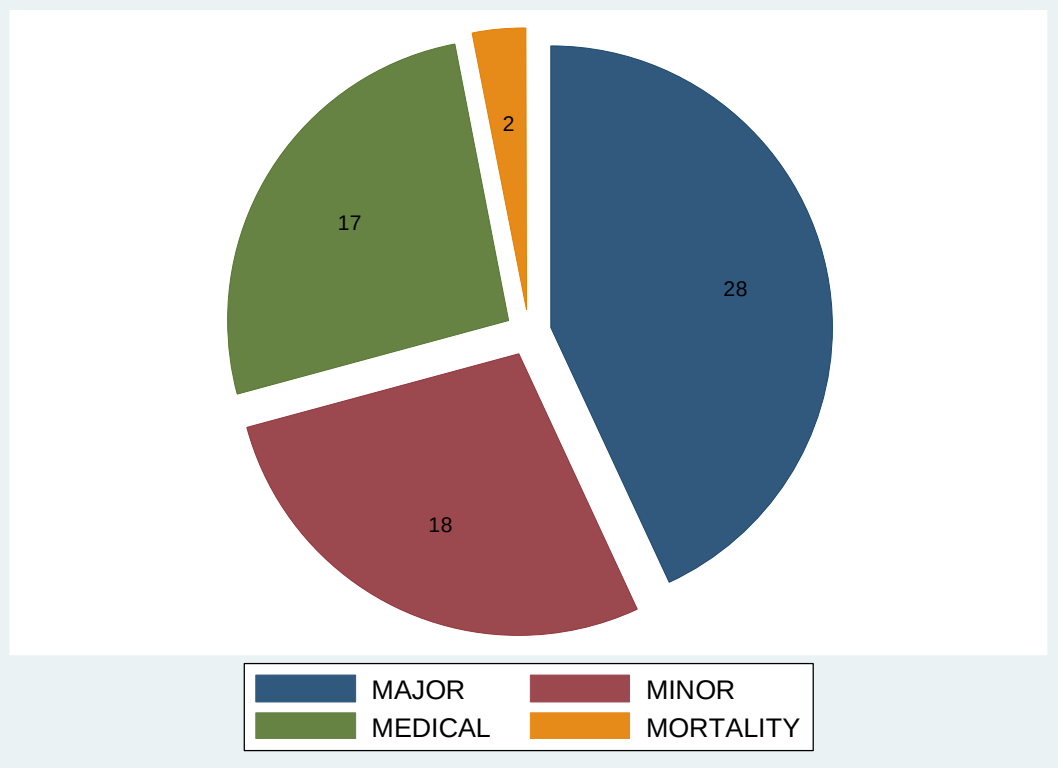

Figure 5: Types of complications post ileostomy closure

The reoperation rate was 11.25% (n=9). The indications for reoperation were stitch granulomas (n=3), incisional hernias (n=2), enterocutaneous fistula (n=1), relook for suspected leaks (n=2) and incision and drainage of an abscess in the wound (n=1).

The 30 day Clavien-Dindo grading system classified fifty seven (71%) patients into Grade I, 15 (19%) into grade III and 6 (7.50%) into grade IV.

Factors associated with development of complications

Twenty percent (n=16) of the patients received adjuvant chemotherapy between their rectal excision and ileostomy closure. Twenty one percent (n=17) had received preoperative radiotherapy prior to the rectal excision for which the ileostomy was created. The use of preoperative chemotherapy and preoperative radiotherapy did not correlate with the development of complications in the rectal cancer group of patients.

Univariate analysis of potential risk factors associated with development of complications showed that renal dysfunction was the only factor which was a statistically significant determinant of the development of complications (OR=3.38 p=0.014, 95% CI 1.280-8.911) **(See Table 3)**.

Risk Factor	**Odds Ratio**	**p-value**	**95%CI**
Smoking	1.23	0.642	0.511 to 2.573
Diabetes	1.86	0.418	0.414 to 8.384
Hypertension	1.94	0.178	0.741 to 5.067
Renal dysfunction	3.38	0.014	1.280 to 8.911
Type of closure	0.26	0.110	0.510 to 1.352
Pathology	0.88	0.177	0.737 to 1.058
Age	1.02	0.304	0.987 to 1.044
Duration of Surgery	1.00	0.580	0.99 to 1.02

Table 3: Univariate analysis

Multivariate analysis of risk factors was performed using a forward stepwise logistic regression model. The analysis was adjusted for confounders which included age, gender, performance status, duration of ileostomy prior to closure, duration of surgery, ethnicity and annual income. Other variables which were entered into the stepwise logistic regression model were smoking, diabetes, hypertension, renal dysfunction, type of closure, surgeon, and pathology.

Renal dysfunction was found to be a statistically significant determinant for the development of complications (OR=3.31, p=0.022, 95%CI=1.186 to 9.242) **(See Table 4)**.

Complications	Odds Ratio	P-value	95%CI
Renal dysfunction	3.31	0.022	1.186 to 9.242
Surgeon	0.39	0.064	0.145 to 1.054
Annual income	0.58	0.094	0.311 to 1.096
Type of closure	0.39	0.285	0.0681 to 2.205

Table 4: Multivariate analysis

Risk Factors for development of Major Complications

Thirteen out of 28 patients with renal dysfunction developed major complications. However, renal dysfunction was not a statistically significant risk factor for the development of major complications on univariate (OR =2.14, P-value= 0.119, 95% CI= 0.823 to 5.55) and multivariate analysis (OR= 3.60, P-value= 0.224, 95% CI= 0.46 to 28.46).

DISCUSSION

Although closure of ileostomy is regarded as a relatively minor surgical procedure, it does require a second hospital admission which is accompanied by considerable costs, and is associated with significant morbidity (1).

In this study almost half the patients (47.5%) developed a complication which is much higher than that quoted in the literature. The mortality rate was 2.5% which is within the reported range. Of the two patients who died of medical complications, one had rectal cancer and the other FAP and both were elderly males, with renal dysfunction and a poor performance status prior to closure. Most of the data regarding complications following ileostomy closure comes from a small number of reviews done in USA, Spain, Turkey and Europe reflecting a morbidity of 3-30% and a mortality rate of 0-4% (3), (4), (5), (10), (11). A recent study on 5,401 patients demonstrated a complication rate of 9.3% and a mortality rate of 0.6% (1).

The indications for the ileostomy closure in this study included a mixture of patients with both rectal cancer and inflammatory bowel disease mainly. Almost all (six out of seven) of the patients with Crohn's disease and almost half (six out of fourteen) of the patients with ulcerative colitis developed complications. This could be one of the reasons for the overall high complication rate observed.

However, on comparison of the individual complication types with that reported in literature, most complications fall within the expected reported range.

In the present study, SBO occurred in 14% of patients, and is reported as 0-15% in the literature (12). The anastomotic leak rate in this study was interestingly low (1 patient, 1%) and occurred as part of multiple major complications. In the literature the anastomotic leak rate alone varies between 0- 8% (12). The enterocutaneous fistula rate of 6% in the present study was also in accordance with that reported (0.5-7%) (12).The rate of incisional hernia development was 4% and falls within the reported range of 1-12% (9), (12). The time taken for the hernia to develop in this study ranged from 3-17 months post ileostomy take down.

The rate of surgical site infection of 21%, was higher than that reported in literature (18.3%) (12). This could possibly be explained by poor wound care related to patients having a higher threshold to come to hospital for follow up postoperatively due to financial constraints or long travelling distances. Most of our patients were of lower socioeconomic status. Another problem is the inadequate wound care provided at local clinics within the patient's home area.

The reoperation rate in this study was 11% which is much higher than that reported in the literature (6-8%) (5), (13).

In an attempt to identify any possible risk factors which may have contributed to this high complication rate, univariate and multivariate analysis were performed. Renal dysfunction was the only identifiable factor found on both univariate and multivariate analysis to be associated with a high complication rate. This is in keeping with the findings of Sharma et al who described a 2.5 times risk of developing major complications in patients with renal dysfunction (1). However renal dysfunction was not a statistically significant determinant for the development of major complications. This could possibly be due to the small sample size or the fact that there were too many variables and few major complications.

Patient factors such as age, gender, performance status, ethnicity, hypertension, diabetes, pathology and annual income did not influence the development of complications. Perioperative factors such as experience level of the surgeon, type of closure and duration of surgery did not contribute to development of complications. This is in keeping with the literature (1), (14), (15), (16).Pre-operative radiotherapy and chemotherapy also did not influence the development of complications in the rectal cancer group, which has been quoted in the literature as a significant contributor for the development of minor complications (17).

The sample size in the present study was not big enough to determine if the possible risk factors were significant or not. However, this does not explain the overall high complication rate observed, implying that there may be other risk factors besides those which were measured in this study, and which may contribute to the development of complications post ileostomy closure. Environmental, genetic and sociocultural health seeking behaviour are possibly some factors which may require further investigation in the future as plausible contributory factors.

Some of the limitations of this study which could be improved upon in the future include a bigger sample population, randomisation of patients to eliminate bias, inclusion of other unmeasured variables in the study design such as patient health seeking behaviour patterns and HIV status of the patient.

This study has several important clinical implications. Patients with renal dysfunction may benefit from early closure of their ilesostomies. In addition to just fast tracking them to surgery, the informed consent process should clearly include a warning about the increased likelihood of development of complications post operatively and a longer hospital stay. These patients are also likely to benefit from being in a high care unit post operatively rather than a general surgical ward. Although this may have cost implications in an already resource stretched environment, it may in the long term save the money that might be utilised to manage the complications in this group of patients.

In conclusion, the complication rate observed post ileostomy closure in this study was high. The magnitude of these complications are attributable to a multifactorial causality in the South African setting. Renal dysfunction was identified as a statistically significant risk factor for the development of a high complication rate.

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PART D:

APPENDICES

Appendix 1: Clavien-Dindo classification of surgical complications

Clavien-Dindo Classification of Surgical Complications

Grade	Definition
Grade I	Any deviation from the normal course without the need for pharmacological treatment or surgical, endoscopic and radiologic interventions Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
III a	Intervention not under general anaesthesia
III b	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
IV a	Single organ dysfunction (including dialysis)
IV b	Multiorgan dysfunction
Grade V	Death of a patient

**Brain haemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks.*
CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

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26 April 2013

HREC REF: 238/2013

Dr D Banerjee
General Surgery

Dear Dr Banerjee

PROJECT TITLE: COMPLICATIONS OF ILEOSTOMY CLOSURE-THE SOUTH AFRICAN EXPERIENCE

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

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

Approval is granted for one year till the 30th April 2014

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/research/humanethics/forms)

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

Please quote the HREC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

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18th February 2013

Dr D Banerjee
Department of Surgery
Division of Surgery
Groote Schuur Hospital
University of Cape Town

Dear Dr Banerjee,

RE: PROJECT 2013/014

PROJECT TITLE: Complications of ileostomy closure-The South African experience

The above proposal was reviewed by the Department of Surgery Research Committee and I am pleased to inform you that the committee approved the study.

Please use the above project number in all future correspondence.

Yours sincerely

PROFESSOR ANWAR S MALL
CHAIRMAN: RESEARCH COMMITTEE