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DISSERTATION

Benefits of the protective loop ileostomy in the oncological rectal
resections – a retrospective center analysis
Benefit der doppelläufigen protektiven Ileostomie bei onkologischen
Rektumresektionen – Eine retrospektive Center-analyse

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Abbreviation

AIDS – Acquired Immune Deficiency Syndrome
AJCC – American Joint Committee on Cancer
ASA – American Society of Anesthesiologists
AUA – American Urological Association
BPH – Benign Prostatic Hypertrophy
CRC – Colorectal Cancer
DM – Diabetes Mellitus
EBM – Evidence-Based Medicine
ED – Erectile Dysfunction
EORTC – European Organization for Research and Treatment of Cancer
EQ-5D-3L – European Quality of Life – 5 Dimensions – 3 Level Version
EQ-VAS – European Quality of Life – Visual Analogue Scale
FS – Functional Scale
GI – Gastrointestinal
HIV – Human Immunodeficiency Virus
HrQoL – Health-related Quality of Life
IIEF-5 – International Index of Erectile Function – 5
IPSS – International Prostate Symptom Score
LAR – Low Anterior Resection
LARS – Low Anterior Resection Syndrome
LUTS – Lower Urinary Tract Symptoms
PONV – Postoperative Nausea and Vomiting
PRO – Patient Reported Outcome
QLQ – Quality of Life Questionnaire
QoL – Quality of Life
RCT – Radio Chemotherapy
SD – Standard Deviation
SS – Symptom Scales
TaTME – Transanal Total Mesorectal Excision
TME – Total Mesorectal Excision
UICC – Union for International Cancer Control
WHO – World Health Organisation

Abstract

Background and objectives:

Colorectal surgery is an inevitable part of the treatment of colorectal cancer. Total mesorectal excision (TME) is usually performed as continence sparing surgery in treating low and mid rectal cancers. Complex surgery newly created colorectal/coloanal anastomosis, and the protective ileostomy, are all prone to complications. Stoma needs special nursing care and also massively affects the quality of life (QoL). The best time for the closure of the stoma is still controversial. With this study, we aim to measure the rate of complications after TME surgery and protective ileostomy and to assess the quality of life of colorectal cancer patients. We extended the research to compare those complications and quality-of-life between the patients with earlier and later closure of a protective ileostomy.

Methods:

We performed a retrospective analysis from data collected from patients with colorectal cancer who underwent TME in any of the three campuses of the Charité Universitätsmedizin Berlin during the period of January 1st, 2010 to May 31st, 2016. We performed statistical analysis through an extensive database we created using all the intra- and postoperative documentation and the information we gathered through the phone calls to assess the quality of life of colorectal cancer patients. The p values were calculated with the Student t-test and the Chi-Square test. If not applicable, the Fisherman-Freeman-Halton test was used.

Results:

The complication rate in the patients was 61.3%, 32.5%, and 22.5% for general postoperative complications, complications related to colorectal/coloanal anastomosis, and those related to the protective ileostomy, respectively. Pain (23.3% of all responders), diarrhea (mean score – 23), and impotence (mean score – 57) in male patients, and stool frequency (mean score – 43) in female patients, affected quality of life the most. 74% of the male patients had mild urinary symptoms, while almost 89% of them reported some sort of erectile dysfunction. 4.9% of patients with ileostomy and 19% of TME needed revision surgery. Patients with a smoking history needed significantly more revision surgeries due to TME ($p = 0.033$). Parastomal hernia ($p = 0.03$) and dry mouth ($p = 0.03$), trouble of taste ($p = 0.01$) and inability to defer defecation for 15 minutes ($p = 0.03$) were significantly lower in patients undergoing earlier closure of stoma.

Zusammenfassung (Deutsch)

Hintergrund und Ziele:

Die kolorektale Chirurgie ist ein fester Bestandteil der Behandlung von Darmkrebs. Die totale mesorektale Exzision (TME) wird normalerweise als kontinenz-erhaltende Operation für die Behandlung von unterem und mittlerem Rektumkarzinom durchgeführt. Nicht nur der komplexe chirurgische Eingriff selbst, sondern auch die neu geschaffene kolorektale / koloanale Anastomose und die protektive Ileostomie können mehrere Komplikationen verursachen. Stoma benötigt eine spezielle Pflege und wirkt sich massiv auf die Lebensqualität aus. Die beste Zeit für die Rückverlegung des Stomas ist noch umstritten. Mit dieser Studie wollen wir die Häufigkeit von Komplikationen nach TME-Operationen und protektiver Ileostomie bestimmen und die Lebensqualität von Darmkrebspatienten bewerten. Wir haben die Forschung erweitert, um diese Komplikationen und die Lebensqualität zwischen den Patienten mit früherem und späterem Verschluss einer schützenden Ileostomie zu vergleichen.

Methodik:

Wir führten eine retrospektive Analyse der Daten aller Patienten mit kolorektalem Karzinom, die in der Zeit von 01.01.2010 bis 31.05.2016 einer TME in einem der drei Standorte der Charité Universitätsmedizin Berlin unterzogen wurden. Die statistische Analyse wurde durchgeführt mittels einer großen Datenbank, die wir mit der intra- und postoperativen Dokumentation und aus der Information erstellten, die wir über die Telefonate mit den Patienten über die Lebensqualität führten. Die p-Werte wurden mit dem Student-t-Test und dem Chi-Quadrat-Test berechnet. Falls nichtzutreffend, wurde der Fisherman-Freeman-Halton-Test verwendet.

Ergebnisse:

Die Komplikationsrate bei den Patienten betrug 61,3%, 32,5% und 22,5% für allgemeine postoperative Komplikationen, Komplikationen im Zusammenhang mit der neuen kolorektaler / koloanaler Anastomose und solche im Zusammenhang mit der protektiven Ileostomie. Schmerzen (23,3% aller Antwortenden), Durchfall (Mittelwert - 23) und Impotenz (Mittelwert - 57) bei den männlichen Patienten und Stuhlfrequenz (Mittelwert - 43) bei den weiblichen Patienten waren die Symptome, die die Lebensqualität am meisten beeinflussten. 74% der männlichen Patienten hatten leichte Harnbeschwerden, während fast 89% von ihnen über eine erektile Dysfunktion berichteten. 4,9% der Ileostomie und 19% der TME musste einer Revision-Eingriff unterzogen werden. Bei den Rauchern war signifikant mehr Revisionsoperationen aufgrund von TME erforderlich ($p = 0,033$). Parastomale Hernie ($p = 0,03$) und Mundtrockenheit ($p = 0,03$), Geschmacksprobleme ($p = 0,01$) und die Unfähigkeit, die Defäkation um 15 Minuten zu verschieben ($p = 0,03$), waren bei Patienten mit früherem Stomarückverlegung signifikant geringer.

1 Introduction

1.1 Ostomy

An ostomy or stoma is an artificial anastomosis created between a part of a hollow organ (usually the gastrointestinal tract or urinary tract) and the abdominal wall [1]. Ostomies are commonly performed to allow fecal diversion to protect the newly created bowel anastomoses or repairs and are widely used for emergency decompression to prevent bowel perforation [2, 3]. This method of fecal diversion is needed to manage many medical conditions, such as congenital intestinal anomalies, gastrointestinal (GI) malignancy, inflammatory bowel disease, bowel obstruction, or traumatic disruption of the intestinal tract [4].

1.1.1 History of Ostomy

Although the history of ostomies dates back to the era of Praxagoras of Kos and Hippocrates, the sound research on ostomy and usages of ostomy began in the late nineteenth century [5, 6]. A story from the late eighteenth century of an innovative surgeon describes a successful colostomy surgery on a 3-day-old neonate with an imperforate anus, yet very little is known about how it was done [5, 6]. In the late nineteenth century, surgeons started using diverting colostomy to manage obstructive bowel and rectal cancer [5, 6].

The first ileostomy was performed in the late 1800s as a temporary fecal diversion in a patient with obstruction of the ascending colon. It has been successfully improved throughout the twentieth century, with three significant advances in using a metal clamp to prevent retraction of a protruding ileostomy, development of rubber appliances with the possibility of fixation of protruding ileostomy, and surgical maturation of ileostomy in the 1910s, 1920s and 1950s respectively.

1.1.2 Types of Ostomy

There are different ways to classify ostomy. However, according to the location of the fecal diversion, there are usually two types: ileostomy and colostomy. While a colostomy is performed to bypass the anus, rectum, or distal colon, an ileostomy is performed to bypass the entire colon and rectum. The latter is also done to protect an anastomosis in the colon, rectum, or anus. Depending on the part of the colon where it is placed, the colostomy can be ascending, transverse, descending, or sigmoid. It is either temporary or permanent.

1.2 Colorectal cancer

Colorectal cancer (CRC) is one of the most common cancers in Europe. It is the second most common cancer in Europe, with 447,000 new cases in 2012, and the second most common cause of death from cancer in Europe, with 215,000 deaths in 2012 [7]. About half of the colorectal cancers are rectal cancers. Rectal cancer can be differentiated into three groups according to the height of the tumor, i.e., the distance between the anocutaneous line and the tumor. The treatment depends on the stage of cancer. Surgical resection is the only possible way to cure colorectal cancer. The choice of resection procedure depends upon the location of the tumor. Low anterior resection (LAR) with total mesorectal excision (TME), usually accompanied by the creation of a proximal fecal diversion, is the standard curative surgery for CRCs of the mid and lower rectum. Fecal diversion is most commonly made with the help of a loop ileostomy or a transverse loop colostomy. Although treatment of the tumor itself is a life-changing situation, stoma care following surgery requires a significant investment of time and effort. Stoma care increases the morbidity and mortality of the patient because it does not only affect the physical activity of the patient, for example, during travel or sexual intercourse but also causes a lot of common issues such as problems with odor and gas leaks [8]. The stoma's most commonly described surgical complications are stomal necrosis, stomal bleeding, stomal retraction, parastomal hernia, stomal prolapse, and stomal stenosis [9, 10].

1.2.1 TNM Classification

The American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) replaced the previous Dukes' classification with TNM classification for the tumor staging system of colorectal cancer in 2009/10 [11]. The TNM classification is a classification system used to describe the stage of cancer that involves the size of the primary tumor (T), degree of spread to lymph nodes (N) and other organs (M), and other parameters like the grade of cancer cells (G), invasion of the lymphatic vessels (L), etc. Depending on the characteristics related to T, N, and M, the cancer is classified into a prognostic stage group from stage 0 (Tis (*Carcinoma in situ*), N0, M0) to stage IVC (any T, any N and M1c (metastasis to the peritoneal surface is identified alone or with other site or organ metastases) [12].

2 Methods

2.1 Objectives

Several pieces of research are done about the general complications of stoma care and even about the general complications of continence sparing surgery. However, the research considering both complications in a patient cohort is scarce. Additionally, research addressing the optimal time of reversal of a protective loop-ileostomy is another rarity. This study aims to combine all of the three research questions in a patient cohort. The specific questions are:

- a. How often are complications after TME surgery and protective ileostomy?
- b. How do colorectal cancer patients rate their quality of life?
- c. How do complications and quality of life of colorectal cancer patients with TME surgery differ between patients with earlier and later closure of protective ileostomy? Is earlier closure of stoma safe?

2.2 Study Design and inclusion/exclusion criteria

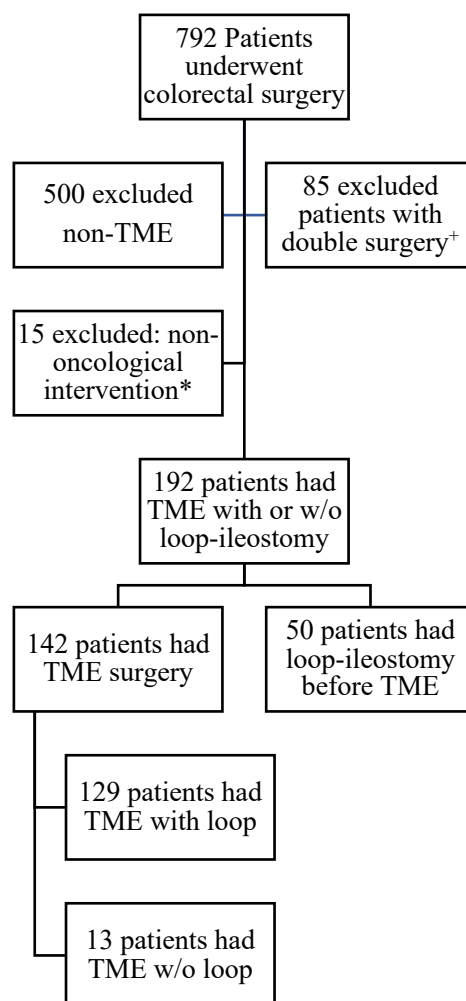
The study includes patients with colorectal cancer who underwent TME in any of the three campuses of the Charité Universitätsmedizin Berlin during the period of 01.01.2010 to 31.05.2016. Out of 192 patients who underwent TME in the observational period, the patients who received their stoma before TME surgery due to any other reasons like bowel obstruction were excluded from the study. We created an extensive database with complete epidemiological, pre-, intra-, and postoperative information.

This information was extracted from the internal patient documentation system, SAP-based, and was checked several times before the statistical analysis. Preoperative information included the medical history, such as diabetes mellitus, inflammatory bowel disease, immunosuppression, HIV/AIDS (human immune-deficiency virus / acquired immune deficiency syndrome), smoking, neoadjuvant therapy (radiotherapy and/or chemotherapy), as well as categorization of the ASA-score (American Society of Anesthesiology). Intraoperative information included relevant events that occurred during the surgery. Postoperative information included any post-operative complications. These complications checked into complications directly related to TME, complications directly associated with ileostomy, complications related to the anastomosis, and general postoperative complications.

Furthermore, the database included information about whether further surgeries were needed to manage those complications. Important pathological information regarding the height of rectal

cancer and TNM classification was also part of the database. We also documented the total hospital stay during TME surgery to analyze the overall health status after surgery.

Secondly, a sheet to measure the quality of life (QoL) was created. The patients were contacted and asked questions to collect the relevant information. The validated German version of the questionnaires was used to assess QoL. The QoL questionnaire included EuroQol 5-Dimensions 3-levels (EQ-5D-3L), European Organization of Research and Treatment – Quality of Life Questionnaire C30 (EORTC QLQ-C30) and EORTC QLQ-CR29, as well as the Low anterior resection syndrome (LARS) score questionnaire, Vaizey incontinence score, International prostate symptom score (IPSS) and International index of erectile dysfunction (IIEF-5).



* Diagnosis of colorectal cancer excluded after the pathological examination.

+ 85 Patients were counted twice because of the revision surgery they had to undergo during the study time, and hence the double count was excluded.

Figure 1. Study Schema with exclusions

2.3 Assessment and time course

We performed phone-interview with our patients between 10 and 87 months after TME, with a mean time since TME of 40.33 months. We used standard QoL questionnaires and questionnaires for major known colorectal surgery-related complication-scoring systems.

2.4 ASA-Score

The American Society of Anesthesiologists introduced the ASA physical status classification system in 1963 to standardize and categorize the surgical risk [13], based on the grading of patients for operative risk in 1941 [14]. ASA score defines the patient's physical state and is usually taken during the pre-surgical consultation with an Anesthesiologist.

Table 1. ASA Physical Status Classification System

ASA Score	Definition
I	A normal healthy patient
II	A patient with mild systemic disease
III	A patient with severe systemic disease
IV	A patient with severe systemic disease that is a constant threat to life
V	A moribund patient who is not expected to survive without surgery
VI	A declared brain-dead patient whose organs are being removed for donor purposes

*The addition of “E” refers to emergency surgery.

2.5 Complications

Complications were differentiated according to the stage of the treatment. We considered three different stages for assessing the major known complications: postoperative complications related to the ileostomy, complications related to the anastomosis, and general complications related to the surgery.

2.5.1 Postoperative complications directly related to ileostomy

One of the most common complications related to TME surgery is a complication related to the ileostomy itself. The ileostomy complications were classified into 11 different categories. The category “others” included high output stoma (with or without acute kidney failure), parastomal varices, and ulcerations.

Table 2. Classification of ileostomy-related postoperative complications

Class	Complication
0	None
1	Stenosis
2	Retraction
3	Prolapse
4	Bleeding
5	Parastomal Infection including Abscess, Phlegmon, Fistula, and Eczema
6	Dehiscence
7	Parastomal Hernia
8	Ischemia of the bowel
9	Others
10	Combined (at least any two from above)

2.5.2 Complications directly related to the anastomosis

The other group of complications is directly related to the newly created vulnerable anastomosis. We classified these complications into six different classes.

Table 3. Classification of anastomosis-related postoperative complications

Class	Complication
0	None
1	Anastomotic leakage without Abscess and/or Sepsis
2	Bleeding
3	Abscess and/or Sepsis
4	Anastomotic leakage with Abscess and/or Sepsis
5	Stenosis

2.5.3 General complications following surgery

During surgery, the most common complications are not procedure-related but are generally associated with general anesthesia or other surgery-related restrictions such as reduced mobility. The category “others” included surgical site dehiscence, urinary problems without an infection, constipation and other stool-related problems, acute kidney injury, postoperative hydronephrosis,

compartment syndrome, postoperative neuromuscular blockade, postoperative nausea and vomiting (PONV), and postoperative delirium.

Table 4. Classification of general postoperative complications

Class	Complication
0	None
1	Pneumonia
2	Urinary Tract Infections
3	Cardiac Complications
4	Pulmonary Embolism
5	Thrombosis of the lower extremity
6	Mechanical Ileus
7	Paralytic Ileus
8	Surgical Site Infection
9	Others

2.6 Scores related to the quality of life

For the complete assessment of the QoL, we used three standard QoL questionnaires: EQ-5D-3L, EORTC QLQ-C30, and EORTC QLQ-CR29. Complications related to colorectal surgery were also recorded using LARS, Vaizey, IPSS, and IIEF-5.

2.6.1 EQ-5D-3L

EQ-5D-3L is a standardized and non-disease-specific patient-reported outcome (PRO) - instrument developed by the EuroQoL group to describe the overall health [15]. It consists of two different systems: the EQ visual analog scale (EQ-VAS) and the EQ-5D descriptive system. The EQ-5D descriptive system describes five different items: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each item has three levels: no problems (1), some problems (2), and extreme problems (3).

Table 5. EQ-5D-3L descriptive system and EQ-VAS

EQ-5D-3L descriptive system:

Dimension	Levels	Score
Mobility	No problems	1

	Some problems	2
	Extreme Problems	3
Self-care	No problems	1
	Some problems	2
	Extreme problems	3
Usual activities	No problems	1
	Some problems	2
	Extreme problems	3
Pain/Discomfort	No problems	1
	Some problems	2
	Extreme problems	3
Anxiety/Depression	No problems	1
	Some problems	2
	Extreme problems	3

EQ-VAS:

0 = Worst imaginable health state to 100= Best imaginable health state

2.6.2 EORTC QLQ-C30 (Version 3)

EORTC QLQ-C30 is a gender-neutral, validated scoring system to evaluate the quality of life of cancer patients, assessing all physical, psychological, and social functions. [16, 17]. It was developed by the European Organization of Research and Treatment (EORTC) in 1988 and has been continuously improved since its introduction. Version 3 consists of 30 questions to assess global health status, function, and symptoms. The functional scales consist of 5 items (physical, role, emotional, cognitive, and social functioning) assessed with 15 different questions. In comparison, symptom scales consist of 9 items (fatigue, nausea and vomiting, pain, dyspnea, insomnia, loss of appetite, constipation, diarrhea, and financial difficulties) supported by 13 different questions. Global health status is captured in 2 questions.

Table 6. EORTC QLQ-C30 Functional and Symptom Scales

	Number of items	Item range	Item numbers
Global health status /QoL			
Global health status/QoL (revised)	2	6	29,30
Functional scales (FS)			

Physical functioning	5	3	1 to 5
Role functioning	2	3	6,7
Emotional functioning	4	3	21 to 24
Cognitive functioning	2	3	20,25
Social functioning	2	3	26,27
Symptoms scales (SS)			
Fatigue	3	3	10,12,18
Nausea and vomiting	2	3	14,15
Pain	2	3	9,19
Dyspnea	1	3	8
Insomnia	1	3	11
Loss of appetite	1	3	13
Constipation	1	3	16
Diarrhea	1	3	17
Financial difficulties	1	3	28

Functional scales (FS):

RawScore = Sum of scores of all items of a scale/ Number of items of a scale

Score = $\{1 - ((RS - 1) / \text{range})\} \times 100$

Symptoms scales (SS) and Global health status:

RawScore = Sum of scores of all items of a scale/ Number of items of a scale

Score = $\{(RawScore - 1) / \text{range}\} \times 100$

2.6.3 EORTC QLQ-CR29

This score is a score-system version for use among colorectal cancer patients and was developed by EORTC in 2007. Initially introduced in 1999, the 38-items QLQ-CR38 was designed to assess the QoL of colorectal cancer patients in conjunction with the QLQ-C30, as mentioned earlier. QLQ-CR38 was further refined into QLQ-CR29[18, 19]. This score has 29 questions tailored to assess the quality of life in patients with colorectal cancer. It consists of 4 scales and 18 single items. All of the questions assess the QoL of the past week except for questions related to sexual function that assess the QoL over the preceding four weeks.

Table 7. EORTC QLQ-CR29 Scales and Items

	Number of items	Item range	Item numbers
Scales			

Urinary frequency (SS)	2	3	31,32
Blood and mucus in stool (SS)	2	3	38,39
Body image (FS)	3	3	45,46,47
Single Items			
Urinary incontinence (SS)	1	3	33
Dysuria (SS)	1	3	34
Abdominal pain (SS)	1	3	35
Buttock pain (SS)	1	3	36
Bloated feeling (SS)	1	3	37
Dry mouth (SS)	1	3	40
Hair loss (SS)	1	3	41
Trouble with taste (SS)	1	3	42
Anxiety (future's health) (FS)	1	3	43
Weight (FS)	1	3	44
Patients without stoma			
Flatulence (SS)	1	3	49
Fecal incontinence (SS)	1	3	50
Sore skin around anus (SS)	1	3	51
Stool frequency (SS)	2	3	52,53
Embarrassed by defecation problems (SS)	1	3	54
Defecation problems	1	3	49-54
Patients with stoma			
Flatulence (SS)	1	3	49s
Fecal incontinence/leakage (SS)	1	3	50s
Sore skin around stoma (SS)	1	3	51s
Stool frequency/bag changes (SS)	1	3	52s,53s
Embarrassed by stoma (SS)	1	3	54s
Stoma care problems (SS)	1	3	55s
Stoma problems	1	3	49s-54s
Male			
Sexual functioning (FS)	1	3	26
Impotence (SS)	1	3	27
Female			

Sexual functioning (FS)	1	3	28
Dyspareunia (SS)	1	3	29

Functional scales (FS):

RawScore = Sum of scores of all items of a scale/ Number of items of a scale

Score = $\{1 - ((RS - 1) / \text{range})\} \times 100$

Symptoms scales (SS):

RawScore = Sum of scores of all items of a scale/ Number of items of a scale

Score = $\{(RawScore - 1) / \text{range}\} \times 100$

2.7 Urinary Function and Sexual Function

2.7.1 International Prostate Symptom Score (IPSS)

The IPSS was initially developed in 1992 as the American urological association symptom index (AUA symptom index) to systematically assess the lower urinary tract symptoms (LUTS) in patients with benign prostate hyperplasia (BPH) [20]. It was also called the AUA-7 because of its seven questions. When the International Consensus Committee adopted it as an international questionnaire, the “quality of life” question was added by the World Health Organization (WHO). Therefore, the score consists of seven questions about the urinary symptoms over the previous month and one question about the quality of life due to urinary symptoms. The first seven urinary symptoms have ‘0-5’ as answers, while the last question about the quality of life consists of six choices (0-6, where ‘0’ is delighted ‘while ‘6’ is terrible).

Table 8. Dimensions and Scores of International Prostate Symptom Score

Dimension (In past Month)	Levels	Score
Incomplete Emptying	Not at all	0
	Less than 1 in 5 times	1
	Less than half the time	2
	About half the time	3
	More than half the time	4
	Almost always	5
Frequency	Not at all	0
	Less than 1 in 5 times	1
	Less than half the time	2

	About half the time	3
	More than half the time	4
	Almost always	5
Intermittency	Not at all	0
	Less than 1 in 5 times	1
	Less than half the time	2
	About half the time	3
	More than half the time	4
	Almost always	5
Urgency	Not at all	0
	Less than 1 in 5 times	1
	Less than half the time	2
	About half the time	3
	More than half the time	4
	Almost always	5
Weak Stream	Not at all	0
	Less than 1 in 5 times	1
	Less than half the time	2
	About half the time	3
	More than half the time	4
	Almost always	5
Straining	Not at all	0
	Less than 1 in 5 times	1
	Less than half the time	2
	About half the time	3
	More than half the time	4
	Almost always	5
Nocturia	None	0
	1 time	1
	2 times	2
	3 times	3
	4 times	4
	5 times	5

Total Score:

0-7: Mild

8-19: Moderate

20-35: Severe

2.7.2 International Index of Erectile Function (IIEF-5)

IIEF is a validated questionnaire to assess sexual health in men, including erectile dysfunction (ED), orgasmic function, sexual desire, satisfaction in sexual intercourse, and general sexual satisfaction, with the help of 15 simple questions [21]. IIEF-5 is its successor and abridged version with only five items instead of 15 [22]. The questionnaire, however, takes the last six months into account instead of the last four weeks as in IIEF. The items on the IIEF are ranked from 1 (very low, almost never/ never, or extremely difficult) to 5 (very high, almost always/ always, or not difficult).

Table 9. Items, Score and Grading of International Index of Erectile Function -5

Items (Over the past 6 Months)	Levels	Score
Confidence of an erection	Very low	1
	Low	2
	Moderate	3
	High	4
	Very high	5
Hard enough for penetration	Almost never or ever	1
	A few times (much less than half the time)	2
	Sometimes (about half the time)	3
	Most times (much more than the half time)	4
	Almost always or always	5
Maintaining erection after penetration	Almost never or ever	1
	A few times (much less than half the time)	2
	Sometimes (about half the time)	3
	Most times (much more than the half time)	4
	Almost always or always	5
Maintaining erection for completion	Extremely difficult	1
	Very difficult	2

	Difficult	3
	Slightly difficult	4
	Not difficult	5
Satisfactory	Almost never or ever	1
	A few times (much less than half the time)	2
	Sometimes (about half the time)	3
	Most times (much more than the half time)	4
	Almost always or always	5

Total Score:

22-25: No ED

17-21: Mild ED

12-16: Mild-moderate ED

8-11: Moderate ED

1-7: Severe ED

2.8 Scores related to the anorectal function

2.8.1 Low anterior resection syndrome score (LARS score)

The low anterior resection syndrome (LARS) score is a reliable and validated questionnaire about bowel function after continence-sparing surgery. Items in the questionnaire are weighted according to their impact on quality of life (QoL) [23] [24]. The LARS score can be classified into three categories: no LARS (0-20), minor LARS (21-29 points), and major LARS (30-42 points).

Table 10. Categories of Low anterior resection syndrome score

Bowel function	Points
Incontinence for flatus	0 = never
	4 = less than once per week
	7 = at least once a week
Incontinence for liquid stool	0 = never
	3 = less than once per week
	3 = at least once a week
Fecal frequency	0 = one to three times per day
	2 = four to seven times per day
	4 = more than seven times per day
	5 = less than once per day

Clustering of (less than one hour between) bowel movements	0 = never
	9 = less than once per week
	11 = at least once per week
Urgency	0 = never
	11 = less than once per week
	16 = at least once a week

2.8.2 Vaizey Score

Vaizey Score originally named St. Mark's incontinence score, is a validated and widely used fecal incontinence scoring system [25]. It represents the massive influence of fecal continence on the quality of life. Points of 7 different questions are added to calculate the total score. A total score of 0 means no fecal incontinence, and 24 means complete fecal incontinence. This grading, however, is contradictory in literature.

Table 11. Categories of Vaizey Score

Bowel function	Points				
	never	rarely	sometimes	weekly	daily
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
Alteration in lifestyle	0	1	2	3	4
		No		Yes	
Need to wear a pad or a plug		0		2	
Taking constipating medicines		0		2	
Lack of ability to defer defecation for 15 minutes		0		4	

2.9 Statistical Analysis

A database with all the information was created and analyzed using IBM SPSS for Mac version 21 (SPSS, Chicago, Illinois, USA). Data were presented as scores, means, or categories. The p values were calculated with Students t-test and Chi-Square test. If not applicable, the Fisherman-Freeman-Halton test/Fisher's exact was used.

3 Results

3.1 Patients

Of the 142 patients who underwent the TME procedure, 98 (69%) were male and 44 (31%) were female, and the mean age was 66.75 years (standard deviation (SD): 13.217, Range: 33-89 years). Most patients were in the 61-70 years age group. The mean hospitalization duration during the primary surgery was 18.23 days (SD: 21.25, Range: 3 – 147 days). For the questionnaire related to the quality of life, patients were contacted via telephone. Due to the study's retrospective character, during the questionnaire, respondents were between 10 to 87 months after TME (mean 40.33, SD 23.58). Other demographic and medical features are listed in table 12.

Table 12. Demographics and characteristics of the patients

Demographics or characteristics	Number of patients	Percentage
Age group (at the time of TME)	n=142	%
<=40	10	7
41-50	14	9.9
51-60	32	22.5
61-70	44	31
71-80	33	23.2
>80	9	6.3
Sex		
Male	98	69
Female	44	31
ASA		
I	10	7
II	65	46
III	31	22
IV	1	<1
V	0	0
VI	0	0
n.a.	35	25
History of Diabetes Mellitus	24	17
History of Inflammatory Bowel Disease	2	1
History of Immunosuppression	1	<1

History of HIV	0	0
Smoker	19	13
Neoadjuvant Therapy	76	53.5
RCT	61	43
Radiotherapy	9	6.3
Chemotherapy	6	4.2
TNM		
(pT0)	17	12
pTis	0	0
pT1	13	9.2
pT2	44	31
pT3	63	44.4
pT4a	5	3.5
pT4b	0	0
pN0	88	62
pN1	31	21.8
pN2a	8	5.6
pN2b	15	10.6
pM0	115	81
pM1	27	19
R0	138	97.2
Grade (G)		
(G0)	11	7.7
Gx	20	14.1
G1	2	1.4
G2	89	62.7
G3	20	14.1
G4	0	0
Age group (at the time of QoL Interview)	<i>Number of respondents</i> (n=60/142)	42.25%
<=40	3	5
41-50	4	6.7
51-60	8	13.3

61-70	15	25
71-80	18	18
>80	12	20

The patients had their ileostomy closure procedure within 4 to 1774 days after TME surgery (median 177.43). While 118 patients out of 142 had the procedure within the study period, the exact dates of closure of 18 patients couldn't be traced as the closure was done somewhere else and not at our hospital. Hence, the comparison of the complications and QoL between early and late closure was made using the data of those 100 patients.

The cut-off between early and late closure was different from the conventional cut-off in our study. The details are mentioned below in the discussion section. We divided patients with ileostomy closure into two groups: patients with early closure (ileostomy closure between 0-177 days post TME) and late closure (after 177 days post-TME). The cut-off was calculated from the median (177.43 days).

The interview with the patients was done 10-87 months after TME surgery (mean: 40.33). The acceptance rate was low, and we could only recruit 60 patients for the telephone interview.

3.2 Complications

3.2.1 Postoperative complications directly related to ileostomy

Of the total of 142 patients, 129 (90.8%) had ileostomy during the TME procedure. Of these 129 patients, 100 (77.5%) patients did not develop any complication related to the stoma, and 29 (22.5%) patients suffered from at least one complication. While parastomal hernia was the most common recorded complication (9 patients; 7%), stenosis was the least common (1 patient; 0.8%). Further information about other complications related to ileostomy is available in Figure 2.

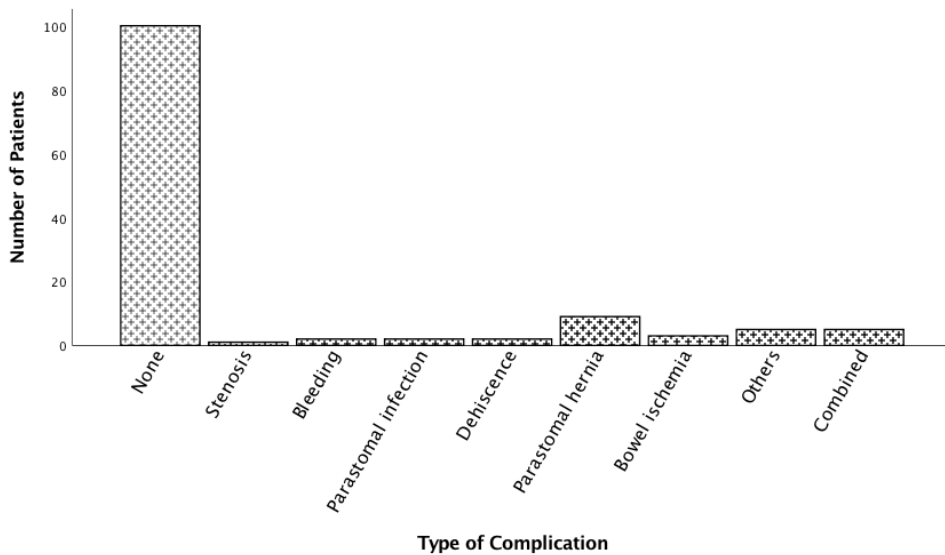


Figure 2. Distribution of ileostomy related postoperative complications

The difference between the sexes regarding the complications are shown in the histogram below. Although most of the male patients and female patients had no complications, the most common complications were parastomal hernia in male patients (8 patients; 8.2 % out of total male patients) and stoma dehiscence in female patients (2 patients; 4.5% out of total females).

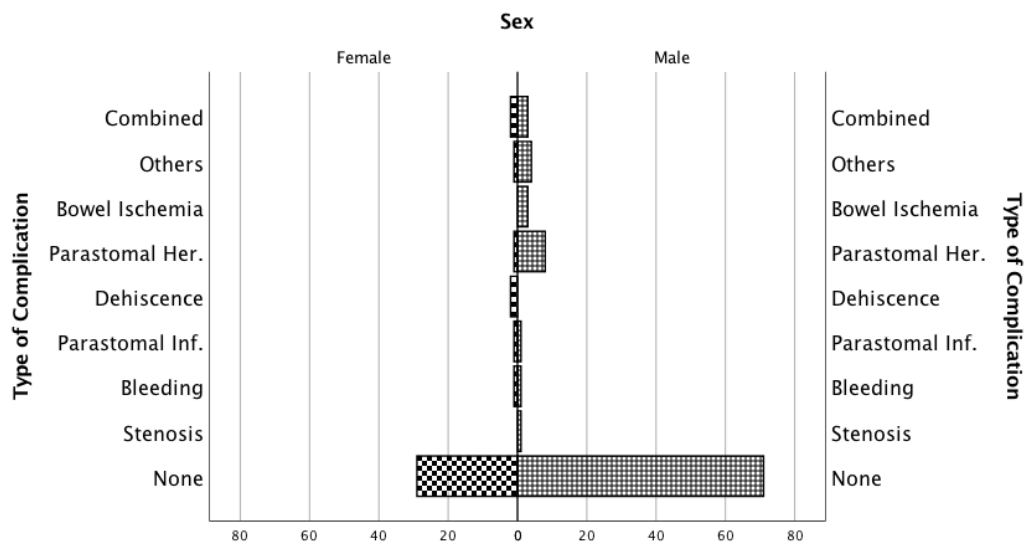


Figure 3. Distribution of ileostomy related postoperative complications, separated by sexes (number)

Further broken down into the age groups, the stacked bar diagram below shows the distribution of the ileostomy-related postoperative complications. The most common complication observed was

parastomal hernia (9 patients; 7%), and the least common was stenosis (1 patient; 0.8%). The distribution was different between age groups. Patients younger than 40 years of age had no ileostomy-related complications, while complications were common in patients of older age. While dehiscence was common in younger patients under 50, complications like parastomal hernia, bowel ischemia, and parastomal infections were more common in older patients. Each of the five patients with more than one complication related to ileostomy was older than 50.

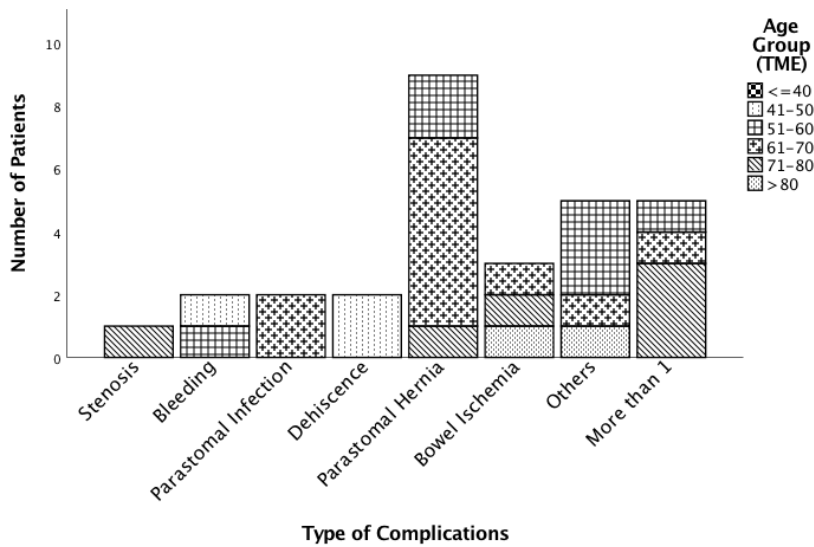


Figure 4. Distribution of ileostomy related postoperative complications adjusted to age

Table 13 compares the risk factors, including ASA score, diabetes mellitus, smoking history, sex, and neoadjuvant treatment with the stoma-related postoperative complication. Although patients with some risk factors had a slightly higher chance of complications, none were statistically significant.

Table 13. Correlation of risk factors with ileostomy related postoperative complications

	no complications	any complications	p-value
ASA Score			0.581 F
I	6	3	
II	47	11	
III	20	8	
IV	1	0	
V	0	0	
VI	0	0	
Diabetes Mellitus			0.313
Yes	16	7	
No	84	22	

Smoker				0.234
Yes	12		6	
No	88		23	
Neoadjuvant treatment				0.937
Yes	56		16	
No	44		13	
Sex				0.882
Male	71		21	
Female	29		8	

3.2.2 Postoperative complications directly related to anastomosis

The next recorded complications were related to the new anastomosis created during the TME surgery. As seen in figure 5, most patients (110 patients; 77.5% of total patients) did not develop any complications. The most common complication related to the anastomosis was anastomotic leakage without abscess (14 patients; 9.9% of total patients). The least common was abscess/sepsis originating from the anastomosis (2 patients; 1.4% of total patients). Other complications included anastomotic leakage with abscess (10 patients; 7% of total patients) and stenosis of the anastomosis (6 patients; 4.2% of total patients).

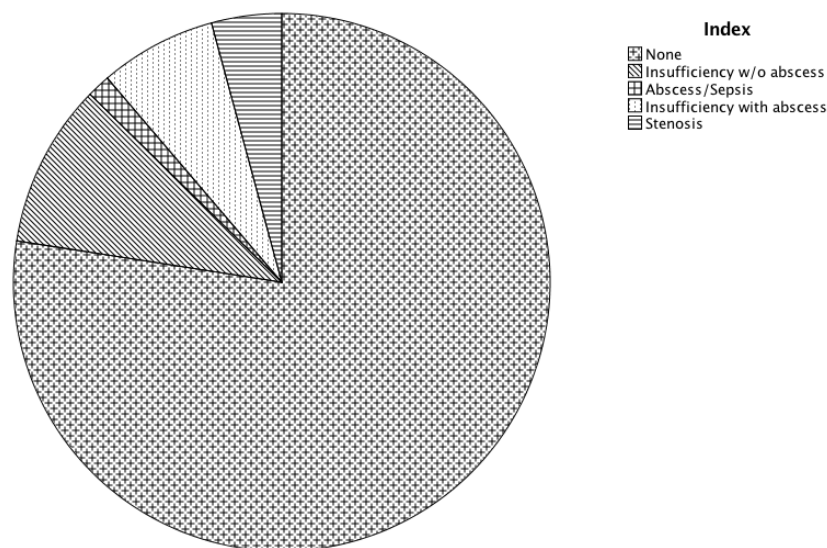


Figure 5. Distribution of anastomosis related postoperative complications

Figure 6 breaks down the frequency of the anastomosis-related complications according to the sex of the patients. 72.5% of male patients and 88.6% of female patients had no complications related to the freshly sutured anastomosis. Anastomotic leakage without abscess was the most common complication in both male patients (10 patients; 10.2% of total male patients) and female patients

(4 patients; 9.1% of total female patients). Stenosis and abscess/sepsis were not seen in female patients.

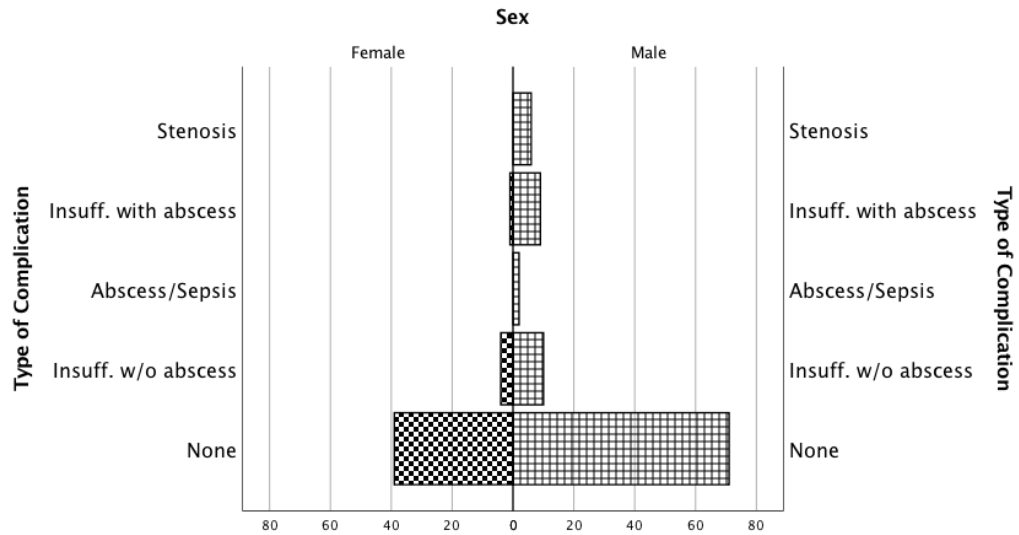


Figure 6. Distribution of anastomosis related postoperative complications related to gender

Figure 7 breaks down the frequency of anastomosis-related complications in various age groups. Patients of age group 61-70 years (13 patients; 9.2% of total patients) had the most complications, while those under 40 years of age (2 patients; 1.4% of total patients) had the least complications. Younger patients (younger than 40) didn't show any stenosis and abscess/sepsis. Anastomotic stenosis was only reported in patients older than 60. Patients older than 80 had only leakage without abscess and stenosis as direct anastomosis-related complications.

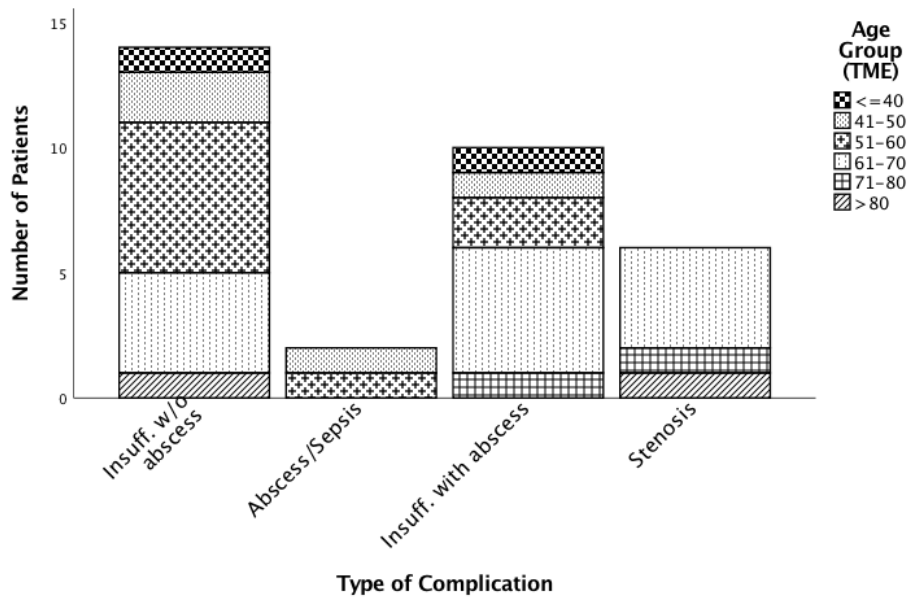


Figure 7. Distribution of anastomosis related postoperative complications in different age groups

Table 14 shows the anastomosis-related complications in patients with different risk factors. While more males had complications than females ($p = 0.032$), no significant differences were seen in patients with or without diabetes, history of smoking, and neoadjuvant treatment of colorectal cancer.

Table 14. Correlation of risk factors with anastomosis related postoperative complications

	no complications (n=110)	any complications (n=32)	p-value
ASA Score			0.265 ^F
I	6	4	
II	49	16	
III	27	4	
IV	1	0	
V	0	0	
VI	0	0	
Diabetes Mellitus			0.751
Yes	18	6	
No	92	26	
Smoker			0.109
Yes	12	7	
No	98	25	
Neoadjuvant treatment			0.350
Yes	55	19	
No	55	13	
Sex			0.032 ^S
Male	71	27	

Female	39	5
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3.2.3 General postoperative complications

The most common yet severe complications were general postoperative complications and are listed in Table 15. Others included a combination of any of these complications or other not explicitly mentioned complications like acute kidney injury, postoperative nausea and vomiting, postoperative neuromuscular blockade, etc., that are not separately noted (defined in 4.5.3). Out of 142 patients, 87 (61.3%) had at least one complication, and the remaining 55 (38.7%) did not develop any of the surgery-related general complications. 52 patients (36.6%) had either a combination of complications or a complication not specifically mentioned. 13 patients (9.2%) had ileus (paralytic – 9 and obstructive 4), 8 (5.6%) had some sort of cardiac complications, and 7 (4.9%) had a surgical site infection (SSI). No deaths were noted. The

Table 15. Distribution of general postoperative complications

Surgical complication	Number of patients (n=142)	Percentage (%)
None	55	38.7
Pneumonia	3	2.1
UTI	2	1.4
Cardiac	8	5.6
PE	1	0.7
DVT LE	1	0.7
Ileus obs.	4	2.8
Ileus para.	9	6.3
SSI	7	4.9
Others	52	36.6

Figure 8 points to the differences in general postoperative complications in different sexes. Individually seen was paralytic ileus (8.2% of total male patients) the most common complication in male patients, while SSI (6.8% of total female patients) was the most common in female patients. Deep vein thrombosis of the lower extremity and pulmonary embolism were observed rarely and didn't occur in the female patients.

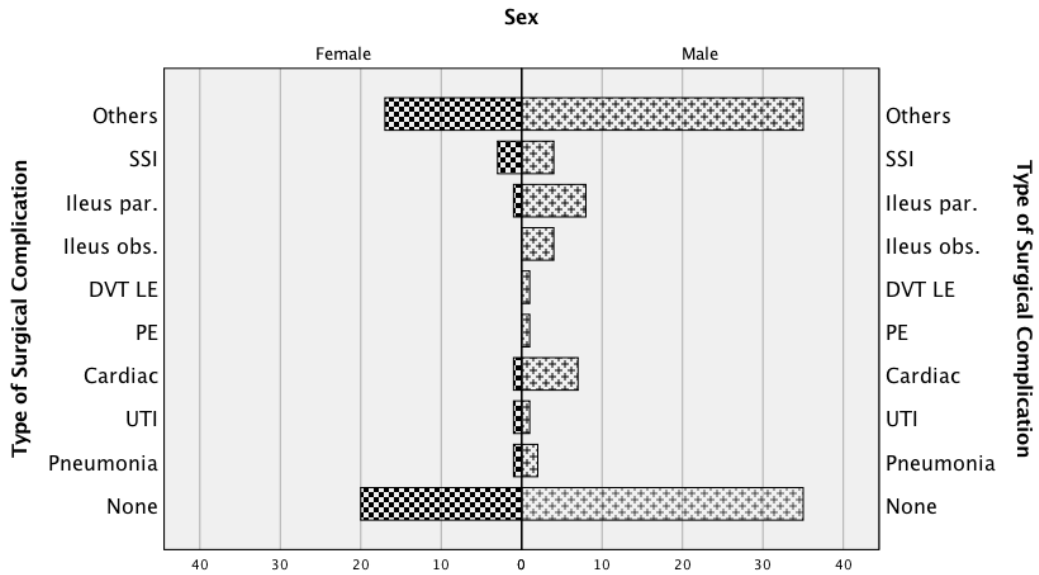


Figure 8. Distribution of general postoperative complications in different sex

Figure 9 shows the difference in complications among the age groups. The postoperative complications were less common in younger patients. In all age groups, complications labeled as ‘others’ (grouped) were the most frequent. Patients younger than 50 mostly had less severe complications and had no pneumonia, cardiac complications, deep vein thrombosis, and pulmonary embolism. Pneumonia and cardiac complications were more common in patients older than 60 years of age.

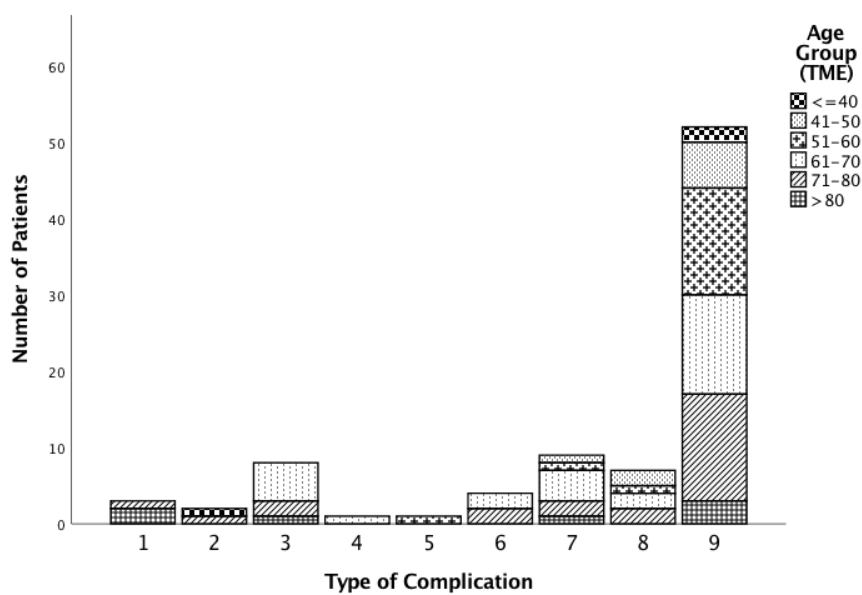


Figure 9. Distribution of general postoperative complications in different age groups

We present the correlation of general postoperative complications with patients' characteristics in Table 16. Patients with diabetes mellitus developed a significantly higher rate of complications ($p = 0.015$). No significant differences were seen in patients with or without a history of smoking, presurgical ASA score, and history of neoadjuvant treatment of colorectal cancer.

Table 16. Correlation of risk factors with general postoperative complications

	no complications (n=55)	any complications (n=87)	p-value
ASA Score (n = 107) *			0.078 ^F
I	7	3	
II	29	36	
III	9	22	
IV	0	1	
V	0	0	
VI	0	0	
Diabetes Mellitus			0.015 ^S
Yes	4	20	
No	51	67	
Smoker			0.065
Yes	11	8	
No	44	79	
Neoadjuvant treatment			0.207
Yes	25	49	
No	30	38	
Sex			0.271
Male	35	63	
Female	20	24	

3.2.4 Surgical reintervention

Out of 129 patients with ileostomy, 7 patients (4.9%) underwent a second surgery because of the complications directly related to the stoma. Of 142 patients, who underwent TME surgery, 27 (19%) patients needed a second surgery.

We calculated the correlation of corrective surgery with patients' demographics, presented in table 17 (corrective surgery due to stoma) and table 18 (corrective surgery due to TME). None of the factors had any significant impact on the earlier one, however, smoking had a significant effect on the latter, i.e., smokers needed more corrective surgery due to TME ($p = 0.033$).

Table 17. Correlation of risk factors with corrective surgery (due to stoma)

	no re-surgery (n=122)	re-surgery (n=7)	p-value
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Diabetes Mellitus			1 ^F
Yes	22	1	
No	100	6	
Smoker			1 ^F
Yes	17	1	
No	105	6	
Neoadjuvant treatment			0.699 ^F
Yes	69	3	
No	53	4	
Sex			1 ^F
Male	87	5	
Female	35	2	

Table 18. Correlation of risk factors with corrective surgery (due to TME)

	no re-surgery (n=115)	re-surgery (n=27)	p-value
Diabetes Mellitus			0.569 ^F
Yes	21	3	
No	94	24	
Smoker			0.033 ^S
Yes	12	7	
No	103	20	
Neoadjuvant treatment			0.093
Yes	56	18	
No	59	9	
Sex			0.274
Male	77	21	
Female	38	6	

3.2.5 Duration of hospital stay

The hospitalization duration was observed only during the primary surgery. The mean hospitalization duration was 18.23 days (SD: 21.25, Range: 3 – 147 days). The hospitalization duration was slightly higher in male patients (19.8 days) than in female patients and patients without neoadjuvant therapy (20.35) than in patients with neoadjuvant treatment (16.28). Patients with diabetes (31.08) and smoking history (28.21) had to stay almost twice longer in hospital than the patients without diabetes (15.62) and smoking history (16.69).

Table 19. Comparison of hospitalization duration with patients' demographics

	Male (n=98)	Female (n=44)	p-value
Hospitalization days (Mean)	19.81	14.73	0.097

	DM (n=24)	no DM (n=118)	p-value
Hospitalization days (Mean)	31.08	15.62	0.064

	Smoker (n=19)	Non-smoker (n=123)	p-value
Hospitalization days (Mean)	28.21	16.69	0.194

	Neoadjuvant therapy (n=98)	No neoadjuvant therapy (n=44)	p-value
Hospitalization days (Mean)	16.28	20.35	0.256

We also compared the mean hospitalization duration in different age groups. The hospitalization duration increased with age, with an exception in the age group 61-70 (table 20); it was the shortest for patients under 40 (14.30 days) and longest for patients over 80 (36.33).

Table 20. Comparison of hospitalization in different age groups.

Age Group	Number of patients (n)	Hospitalization duration (mean days)	SD
<=40	10	14.30	14.88
41 - 50	14	15.93	18.74
51 - 60	32	18.59	21.08
61 - 70	44	14.57	9.93
71 - 80	33	20	25.40
>80	9	36.33	42.71

3.3 Comparison of complication rate between patients with early closure and those with late closure of the protective ileostomy

Plenty of differences between the different demographics of the patients were observed. We questioned the impact of the time point of ileostomy closure and analyzed this in the following. We defined the time of early and late closure as the median calculated from two groups (177 days after TME).

3.3.1 Complications directly related to the ileostomy

The majority of the patients did not develop any complications related to the ileostomy (table 21). The patients who had earlier closure of the stoma reported fewer ileostomy-related complications, however not statistically significant ($p=0.068$). Parastomal sepsis, ischemia of the deviated small bowel, and complications noted as “others” (grouped) (4% of the patients, who had early closure, each) were the three most common complications in patients with earlier stoma closure. Parastomal hernia (16% of patients with later closure of stoma) was the most common in patients with later closure of stoma. Parastomal hernia was reported significantly higher in patients with late closure of stoma ($p=0.03$).

Table 21. Comparison of ileostomy related complications

	Late Closure (=50)	Early Closure (n=50)	p-value
Ileostomy Complications			0.068
Yes	17	9	
No	33	41	
Ileostomy Complication - Type			
None	33	41	
Stenosis	0	0	1 ^F
Retraction	0	0	1 ^F
Prolapse	0	0	1 ^F
Bleeding	1	1	1 ^F
Parastomal sepsis	0	2	0.5 ^F
Dehiscence	1	1	1 ^F
Parastomal Hernia	8	1	0.03 ^{F, S}
Ischemia	0	2	0.5 ^F
Others	3	2	1 ^F
Combined	4	0	0.12 ^F

3.3.2 Complications directly related to the anastomosis

Table 22 compares the complications related to the anastomosis in patients with early and late ileostomy closure. The complications were slightly more common in the group with earlier closure of the stoma ($p=0.812$). If compared individually, all of the types of anastomosis complications were comparable in both groups.

Table 22. Comparison of anastomosis related complications

	Late Closure (n=50)	Early Closure (n=50)	p value
Anastomosis Complications			0.812
Yes	11	12	
No	39	38	
Complication - Type			
None	39	38	
Anastomosis leakage without Abscess and/or Sepsis	3	4	1 ^F
Bleeding	0	0	1 ^F
Abscess and/or Sepsis	1	1	1 ^F
Anastomosis leakage with Abscess and/or Sepsis	4	4	1 ^F
Stenosis	3	3	1 ^F

3.3.3 Re-surgery due to ileostomy or TME

We also wanted to investigate whether re-surgery was associated with the ileostomy and the TME procedure itself. While re-surgery because of stoma complications was still very uncommon (5%), re-surgery related to TME was more common (20%). On the one hand, more re-surgeries related to the stoma were required in the group with earlier closure (8%) than in the group with late closure (2%), although not statistically significant ($p=0.3622$). On the other hand, there was no difference in re-surgery rates related to the TME procedure ($p = 1$).

Table 23. Comparison of re-surgery due to ileostomy and TME procedure

	Late Closure (n=50)	Early Closure (n=50)	p value
Re-surgery (Stoma)			0.3622 ^F
Yes	1	4	
No	49	46	
Re-surgery (TME)			1
Yes	10	10	
No	40	40	

3.3.4 General complications related to surgery

The most common complications noted were the general complications related to the surgery rather than the individual complications pertaining to the diverting stoma or the TME procedure itself (see Figures 2 and 5, and Table 15). Complications were very common (63%). Both of the groups had comparable complications related to the surgery ($p = 0.8415$). While 44% of the patients from the late closure group suffered from the group: others, only 34% of the patients from the early closure group had complications, grouped under others ($p=0.413$). All of the individual complications were statistically comparable in both groups.

Table 24. Comparison of general post-surgical complications

	Late Closure (n=50)	Early Closure (n=50)	p value
General complications			0.8415
Yes	31	32	
No	19	18	
Complication Type			
None	19	18	
Pneumonia	0	0	1 ^F
Urinary Tract Infections	0	0	1 ^F
Cardiac Complications	2	4	0.678 ^F
Pulmonary Embolism	1	0	1 ^F
Thrombosis of the lower extremity	0	1	1 ^F
Mechanical Ileus	2	2	1 ^F
Paralytic Ileus	2	5	0.436 ^F
Surgical Site Infection	2	3	1 ^F
Others	22	17	0.413 ^F

3.3.5 Length of hospital stay after TME

We also compared the length of hospital stay of the patients who underwent earlier stoma closure with those who underwent later closure of stoma. The patients with earlier closure of stoma had to stay on average three days longer in the hospital after primary surgery than the patients with later closure of stoma.

Table 25. Comparison of hospitalization duration

	Late Closure (n=50)	Early Closure (n=50)	p-value
Hospitalization days (Mean)	13.80	16.88	0.370

3.4 Questionnaire Results

The patients were contacted and assessed for the QoL using the standard questionnaires. We could only reach a fraction of all patients (number of patients = 60 (42%); 39 male and 21 female). The results of the statistical analysis are presented and described individually.

3.4.1 Quality of Life

3.4.1.1 EQ-5D-3L

Table 26 shows the distribution of each of the EQ-5D-3L dimensions in our patients. Patients reported pain as the most common complaint (23.3% of all responders; 25.6% of males and 19% of females). The less common complaints were about self-care (1.7% of all responders, 0% male, and 4.8% female patients). Most of the minor (some) problems were pain-related (23.3% of all responders, 25.6% of male and 19% of female patients), while most of the major (serious) problems were mobility and usual activities related (1.7% of all responders, 0% of male and 4.8% of female patients for each). In male patients, problems related to pain were most frequently reported (25.6%), and in female patients, mobility and pain were most reported (19% each). Except for the mobility, which significantly affected more females than males ($p=0.017$), other characters of EQ-5D-3L had no significant differences in different sexes.

Table 26. Distribution of EQ-5D-3L characters and EQ-VAS

Character	Male (n=39)	Female (n=21)	Total (n=60)/ p-Value
Mobility			0.017 ^{F, S}
No problems	38 (97.4%)	16 (76.2%)	54 (90%)
Some problems	1 (2.6%)	4 (19%)	5 (8.3%)
Extreme problems	0 (0%)	1 (4.8%)	1 (1.7%)
Selfcare			0.35 ^F
No problems	39 (100%)	20 (95.2%)	59 (98.3%)

Some problems	0 (0%)	1 (4.8%)	1 (1.7%)
Extreme problems	0 (0%)	0 (0%)	0 (0%)
Usual Activities			0.4734 ^F
No problems	32 (82.1%)	19 (90.5%)	51 (85%)
Some problems	7 (17.9%)	1 (4.8%)	8 (13.3%)
Extreme problems	0 (0%)	1 (4.8%)	1 (1.7%)
Pain			0.7514 ^F
No problems	29 (74.4%)	17 (81%)	46 (76.7%)
Some problems	10 (25.6%)	4 (19%)	14 (23.3%)
Extreme problems	0 (0%)	0 (0%)	0 (0%)
Anxiety			0.4122 ^F
No problems	34 (87.2%)	20 (95.2%)	54 (90%)
Some problems	5 (12.8%)	1 (4.8%)	6 (10%)
Extreme problems	0 (0%)	0 (0%)	0 (0%)

EQ-VAS showed differences between male and female patients (Figure 10). The average of VAS in females (74.05; range: 50-95) was slightly higher than the average in male patients (72.44; range: 40-95) ($p=0.659$). None of the responders reported their overall health status to be either best or worst. The majority of the responders rated their health status as good. 43% of female patients and 49% of male patients rated their health 80/100 or better, while almost 5% of female patients and 13% of male patients rated their health 50/100 or worse.



Figure 10. Differences of EQ-VAS distributed over male and female patients

Figure 11 plots the difference of EQ-VAS in different age groups. Most of the patients rated their overall health score as 80/100, and the least rated it either 65/100 or 40/100. Younger responders rated their health worse than older responders. The average VAS in patients younger than 40, 41-50, 51-60, 61-70, 71-80 and, older than 80 were 50.67, 71.67, 71.88, 78, 74.17, and 69.58, respectively. It means the youngest and oldest patients were unsatisfied with their health status.

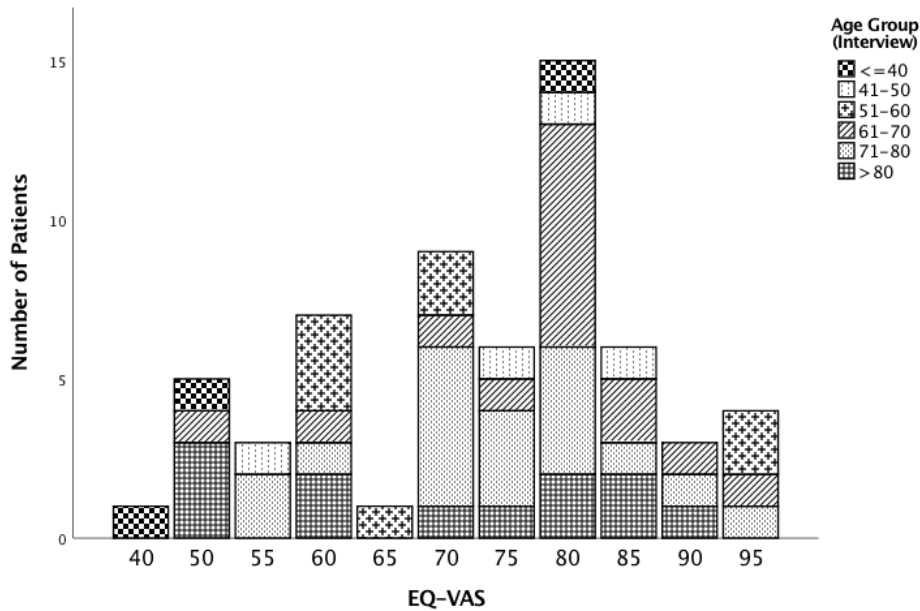


Figure 11. Differences of EQ-VAS in different age groups

3.4.1.2 EORTC-QLQ-C30

The total number of responders for EORTC-QLQ-C30 was 57 (table 27). Regarding the functional scales, patients had the least problems related to the cognitive functioning (mean = 93.3; range: 50-100) and most problems related to the role functioning (mean = 71.3; range: 33.3-100). Similarly, for the symptom scales, diarrhea (mean = 22.8; range: 0-66.7) was the most concerning complaint, whereas financial difficulties (mean = 0.6; range: 0-33.3) were the least concerning one. The mean global health status was 69.6 (range: 25-100). None of the individual functional scales and symptom scales items were significantly different in different sexes (table 28).

Table 27. Distribution of functional scales and symptom scales of EORTC-QLQ-C30

Character	Number of respondents (n)	Mean	SD	Range
Functional Scales				
Physical Functioning ^A	57	89.8	14.9	6.7 - 100
Role Functioning ^A	57	71.3	24.1	33.3 - 100

Emotional Functioning ^A	57	88.9	11.5	58.3 - 100
Cognitive Functioning ^A	57	93.3	12.1	50 - 100
Social Functioning ^A	57	78.1	18.1	33.3 - 100
Symptom Scales/Items				
Dyspnea ^B	57	4.1	14.2	0 - 66.7
Insomnia ^B	57	19.9	33.8	0 - 100
Loss of appetite ^B	57	2.9	14.5	0 - 100
Nausea/vomiting ^B	57	1.2	5.3	0 - 33.3
Constipation ^B	57	5.8	16.8	0 - 66.7
Diarrhea ^B	57	22.8	24.5	0 - 66.7
Fatigue ^B	57	11.7	17	0 - 55.6
Pain ^B	57	12.3	18.2	0 - 83.3
Financial difficulties ^B	57	0.6	4.4	0 - 33.3
Global Health Status				
Health Status ^A	57	69.6	17.2	25 - 100

^A – Higher score indicates a better level of functioning

^B – Higher score indicates a worse level of problems

Table 28. EORTC-QL Q-C30 among male patients and female patients

Character	Mean Males (n=39)	Mean Females (n=18)	p-value
Functional Scales			
Physical Functioning ^A	91.97	85.19	0.111
Role Functioning ^A	71.80	70.37	0.838
Emotional Functioning ^A	88.89	88.89	1
Cognitive Functioning ^A	94.01	91.67	0.502
Social Functioning ^A	77.78	78.70	0.860
Symptom Scales/Items			
Dyspnea ^B	3.42	5.56	0.602
Insomnia ^B	23.93	11.11	0.134
Loss of appetite ^B	3.42	1.85	0.708
Nausea/vomiting ^B	1.71	0	0.103
Constipation ^B	3.42	12.78	0.196

Diarrhea ^B	19.66	29.63	0.155
Fatigue ^B	9.40	16.67	0.135
Pain ^B	12.39	12.04	0.946
Financial difficulties ^B	0.85	0	0.502
Global Health Status			
Health Status ^A	69.02	70.83	0.715

^A – Higher score indicates a better level of functioning

^B – Higher score indicates a worse level of problems

3.4.1.3 EORTC-QLQ-CR29

The response to the EORTC-QLQ-CR29 was similar to that of EORTC-QLQ-C30 (with one female patient refusing to disclose her sexual functioning). For the functional scales, the mean score was highest for body image (92.4; range: 55.6-100) and lowest for sexual functioning (male = 46.2; range: 0-100 and female = 51.0; range: 33.3-66.7). For the symptom scales on the EORTC-QLQ-CR29, the highest and the lowest mean score were for impotence (57.3) and blood/mucus in the stool (2.6), respectively.

Table 29. Distribution of functional scales and symptom scales of EORTC-QLQ-CR29

Character	Number of responders (n)	Mean	SD	Range
Functional Scales				
Anxiety ^A	57	69.6	24.6	33.3 - 100
Weight ^A	57	91.2	16.1	33.3 - 100
Body Image ^A	57	92.4	13.1	55.6 - 100
Sexual Functioning (m) ^A	39	46.2	23.7	0 - 100
Sexual Functioning (f) ^A	17	51.0	17.2	33.3 - 66.7
Symptom Scales/Items				
Impotence (m) ^B	39	57.3	36.6	0 - 100
Dyspareunia (f) ^B	17	39.2	27.0	0 - 100
Urinary frequency ^B	57	14.6	22.5	0 - 66.7
Urinary incontinence ^B	57	5.3	12.3	0 - 33.3
Dysuria ^B	57	4.1	11.0	0 - 33.3
Abdominal pain ^B	57	7.0	13.7	0 - 33.3
Buttock pain ^B	57	22.2	21.2	0 - 66.7

Bloated feeling ^B	57	9.9	15.4	0 – 33.3
Blood/mucus in stool ^B	57	2.6	10.3	0 – 66.7
Dry mouth ^B	57	5.3	15.2	0 – 66.7
Hair loss ^B	57	8.2	19.2	0 - 100
Trouble with taste ^B	57	4.7	15.7	0 – 66.7
Flatulence ^{B, *}	56	29.8	28.2	0 – 100
Fecal incontinence ^{B, *}	56	38.7	24.4	0 – 100
Sore skin ^{B, *}	56	34.5	25.4	0 – 66.7
Stool frequency ^{B, *}	56	42.9	16.1	0 – 66.7
Embarrassment ^{B, *}	56	35.1	21.5	0 – 66.7

^A – Higher score indicates a better level of functioning

^B – Higher score indicates a worse level of problems

* - Without stoma

3.4.1.4 Comparison of Quality of Life

Further research questions about the comparison of QoL between patients with earlier closure and later closure of protective stoma are answered individually for different scores below.

3.4.1.4.1 EQ-5D-3L

The mean score of EQ-VAS was slightly higher in the group with earlier closure ($p = 0.178$). Each of the individual characters of the EQ-5D-3L was comparable between the groups and showed no significant differences.

Table 30. Comparison of EQ-5D-3L descriptive and EQ-VAS

	Late Closure (n=28)	Early Closure (n=24)	p value
EQ-5D VAS			0.178
Mean	71.25	76.35	
Mobility			1 ^F
No problems	24	22	
Some problems	3	2	
Major problems	1	0	
Selfcare			1 ^F
No problems	27	24	

Some problems	1	0
Major problems	0	0
Usual Activities		1 ^F
No problems	24	22
Some problems	3	2
Major problems	1	0
Pain		0.958
No problems	22	19
Some problems	6	5
Major problems	0	0
Anxiety		1 ^F
No problems	26	22
Some problems	2	2
Major problems	0	0

^F – Fisher Freeman Halton Test instead of Chi-Square Test

3.4.1.4.2 EORTC-QLQ-C30

Table 31 compares the EORTC-QLQ-C30 functional scales and symptom scales between the two groups (earlier vs. later closure of the diverting ileostomy). While there were some differences in the means of each functional and symptom scale, none were statistically significant. The overall health status score of the earlier closure group was slightly higher than that of later closure (p=0.503).

Table 31. Comparison of functional, symptom scales and global health status of EORTC-QLQ-C30

Symptoms	Late Closure (n=26) Mean	Early Closure (n=24) Mean	p-value
Functional Scales			
Physical Functioning	88.21	92.22	0.370
Role Functioning	69.87	76.39	0.323
Emotional Functioning	89.10	91.32	0.482
Cognitive Functioning	92.95	95.14	0.509
Social Functioning	77.56	79.86	0.659
Symptom Scales/Items			

Dyspnea	6.41	1.39	0.214
Insomnia	15.38	20.83	0.550
Loss of appetite	6.4	0	0.134
Nausea/vomiting	1.92	0	0.185
Constipation	6.41	6.94	0.917
Diarrhea	25.64	20.83	0.494
Fatigue	14.10	9.72	0.374
Pain	12.82	9.72	0.561
Financial difficulties	1.28	0	0.342
Global Health Status			
Health Status	69.55	72.57	0.503

3.4.1.4.3 EORTC-QLQ-CR29

Similar to the EORTC-QLQ-C30, each of the functional scales and symptom scales of the EORTC-QLQ-CR29 was compared between the two groups. None of the mean scores of the functional scales showed any significant differences. However, dry mouth ($p=0.018$) and trouble with taste ($p=0.032$) were more significantly concerning in the group with later closure of an ileostomy. Only minor differences were observed in other symptom scales.

Table 32. Comparison of functional and symptom scales of EORTC-QLQ-CR29

Symptoms	Late Closure Mean (n)	Early Closure Mean (n)	p-value
Functional Scales			
Anxiety	71.80 (26)	73.61 (24)	0.792
Weight	88.46 (26)	94.45 (24)	0.190
Body Image	91.89 (26)	91.37 (24)	0.307
Sexual Functioning (m)	50.88 (19)	41.67 (16)	0.275
Sexual Functioning (f)	47.62 (7)	54.17 (8)	0.483
Symptom Scales/Items			
Impotence (m)	45.62 (19)	64.58 (16)	0.134
Dyspareunia (f)	42.86 (7)	37.50 (8)	0.733
Urinary frequency	13.46 (26)	13.89 (24)	0.944
Urinary incontinence	3.85 (26)	4.17 (24)	0.919
Dysuria	5.13 (26)	2.78 (24)	0.454

Abdominal pain	6.41 (26)	6.94 (24)	0.890
Buttock pain	21.79 (26)	19.44 (24)	0.699
Bloated feeling	10.26 (26)	8.33 (24)	0.658
Blood/mucus in stool	2.56 (26)	3.47 (24)	0.774
Dry mouth	10.26 (26)	0 (24)	0.018 ^s
Hair loss	17.82 (26)	4.17 (24)	0.120
Trouble with taste	8.97 (26)	0 (24)	0.032 ^s
Flatulence	26.92 (26)	31.94 (24)	0.536
Fecal incontinence	43.59 (26)	34.72 (24)	0.216
Sore skin	35.90 (26)	34.72 (24)	0.873
Stool frequency	39.74 (26)	45.83 (24)	0.187
Embarrassment	34.61 (26)	34.72 (24)	0.986

^s – statistically significant

3.4.2 Urinary Function and Sexual Function in Patients

We calculated the urinary and sexual functions of the patients and presented the findings for each sex. However, both the IPSS and IIEF-5 are validated only for males, hence only assessed for males.

3.4.2.1 IPSS (Male)

Most of the male patients reported mild urinary symptoms (74.4%). Severe IPSS was reported only in one individual (2.56%). The quality of life due to urinary symptoms was answered most commonly as either “unhappy” (41%) or “terrible” (41%). None of the respondents answered it as delighted, pleased, mostly satisfied, or mixed. Milder IPSS was the most common grading in all the age groups. More male patients older than 70 had moderate or severe IPSS. Figure 12 shows the distribution of the score and the QoL question distribution among the patients. 100% of patients older than 80 answered the IPSS-QoL question as either unhappy (50%) or terrible (50%). We noted a very high dissatisfaction in the younger population; almost 77% of patients younger than 40 and 50% of patients younger than 50 described their quality of life due to urinary symptoms as “terrible”. Not a clear correlation between the severity of the symptom and quality of life could be seen as many patients with milder symptoms also answered the QoL question as terrible.

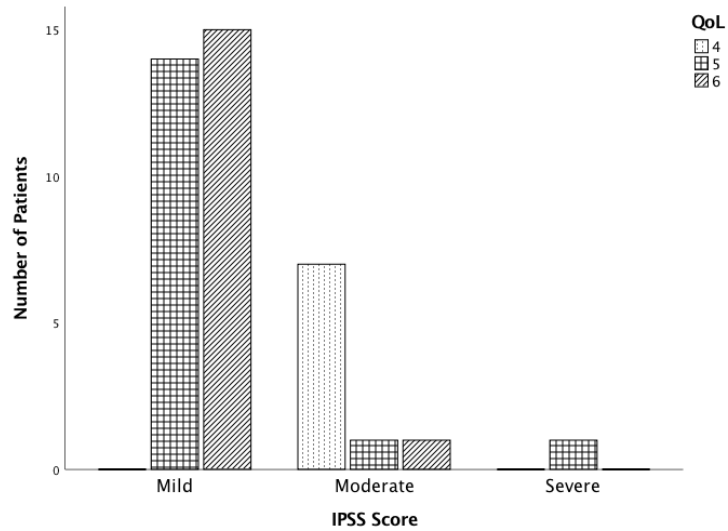


Figure 12. Distribution of IPSS grading and IPSS QoL response

3.4.2.2 IIEF-5 (Male)

Like IPSS, IIEF-5 was also only assessed for male patients (figure 13). Most of the patients (88.89%) reported some grade of erectile dysfunction (ED). Severe ED (55.56%) was reported most commonly, while mild ED (7.41%) was the least common reported dysfunction. No significant differences in ED severity were seen in different age groups.

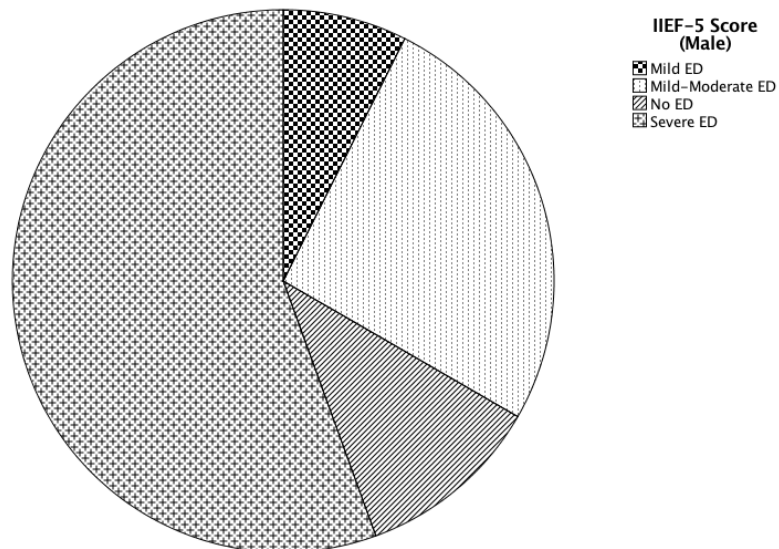


Figure 13. Distribution of ED grading with IIEF-5

3.4.2.3 Comparison of Urinary Function and Sexual Function between patients with early and late closure of ileostomy

These scores calculated to assess men's urinary and sexual function were further compared in two different groups. The results are reported separately.

3.4.2.3.1 Urinary Function (Male)

Table 33 compares the IPSS grades and mean scores between male patients with earlier and later closure of the protective ileostomy. Slightly more mild and moderate symptoms were observed in the group with the later closure (19 patients, 100%) than earlier closure (15 patients, 93.8%) ($p = 0.827$). None of the patients with later stoma closure reported severe urinary symptoms. The mean IPSS score was slightly higher in the earlier closure group ($p = 0.456$). However, the QoL-related score was rated somewhat worse in patients with earlier stoma closure ($p = 0.597$).

Table 33. Comparison of urinary function in males (IPSS)

	Late Closure (n=19)	Early Closure (n=16)	p value
IPSS Grade			0.827 ^F
Mild	15 (78.9%)	12 (75%)	
Moderate	4 (21.1%)	3 (18.8%)	
Severe	0 (0%)	1 (6.2%)	
IPSS Score			
Mean	4.16	5.69	0.456
IPSS QoL			
Mean	5.32	5.19	0.597
0	0 (0%)	0 (0%)	
1	0 (0%)	0 (0%)	
2	0 (0%)	0 (0%)	
3	0 (0%)	0 (0%)	
4	2(10.5%)	3 (18.8%)	
5	9 (47.4%)	7 (43.7%)	
6	8 (42.1%)	6 (37.5%)	

^F – Fisher Freeman Halton Test instead of Chi-Square Test

3.4.2.3.2 Sexual Function (Male)

Even fewer patients could be assessed for their sexual function. Almost no differences were noted between the two groups related to the IIEF-5 score. However, the mean score of IIEF-5 was relatively high in the group with earlier closure of stoma ($p = 0.523$).

Table 34. Comparison of sexual function in males (IIEF-5)

	Late Closure (n=11)	Early Closure (n=13)	p value
IIEF-5			0.999 ^F
No ED	1 (9.1%)	2 (15.4%)	
Mild ED	1 (9.1%)	1 (7.7%)	
Mild-Moderate ED	2 (18.2%)	4 (30.8%)	
Severe ED	7 (63.6%)	6 (46.1%)	
IIEF-5 Total			
Mean	8.55	10.77	0.523

^F – Fisher Freeman Halton Test instead of Chi-Square Test

3.4.3 Anorectal Function

The anorectal function was assessed using the LARS and Vaizey score. The major results and comparison of the scores are presented in the following.

3.4.3.1 LARS

Almost 67% of all the responders (Figure 14) reported having some problems related to LARS. Major LARS (51.85%) was more common than minor LARS (14.81%). Figure 15 compares the LARS score between male and female patients. LARS was common in both male and female patients. For both males (52.78%) and females (50%), if they had reported LARS, it mainly was major LARS.

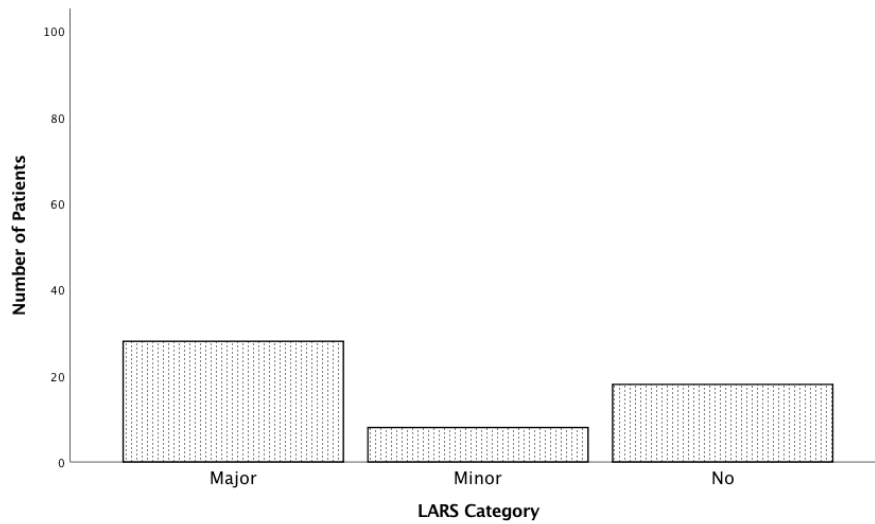


Figure 14. Distribution of LARS categories

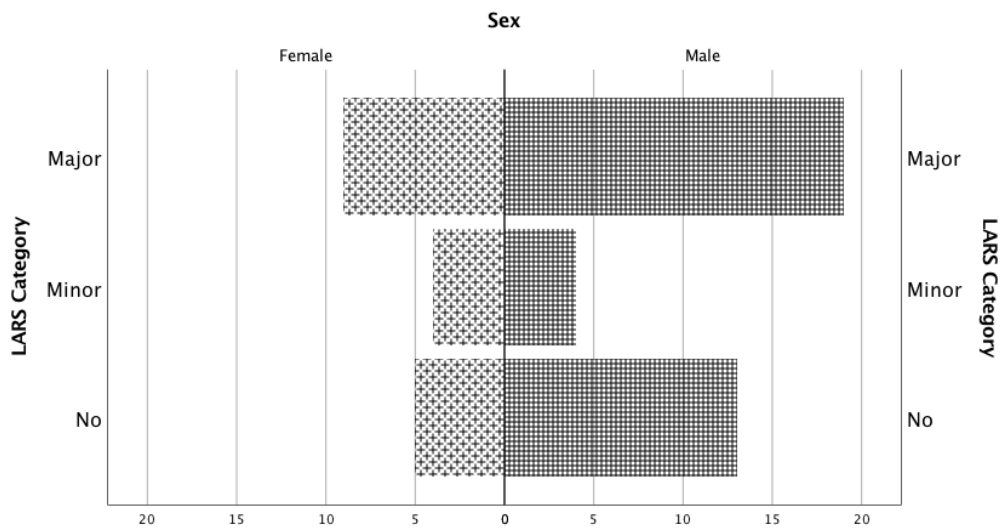


Figure 15. Distribution of LARS categories adjusted to gender

The distribution of LARS grades among the different age groups was not consistent (Figure 16). Patients younger than 40 had no LARS. One-half of patients aged 41-50 had some problems (50%), while the other half didn't have any problems. Patients aged 51-60 only reported either no LARS (33.33) or major LARS (66.67%) but no minor LARS. In patients older than 60, more major LARS were observed.

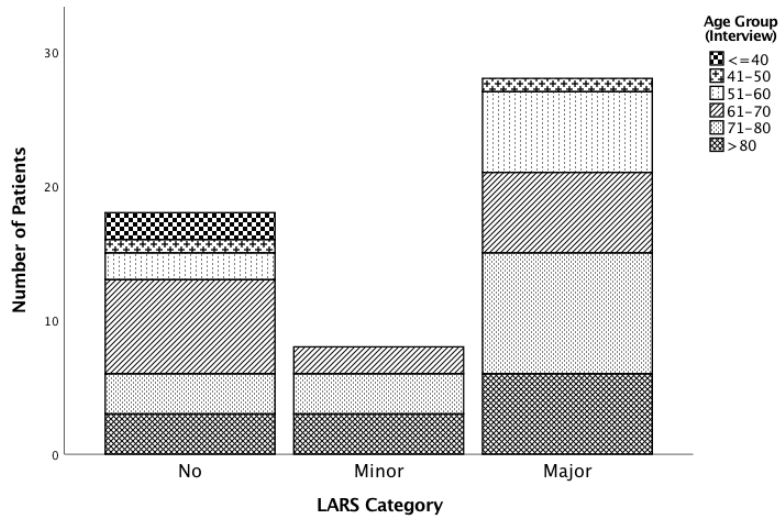


Figure 16. Distribution of LARS categories in different age groups

3.4.3.2 Vaizey Score

Very high (3 patients, 5.5%) and very low (3 patients, 5.5%) Vaizey scores were uncommon. Most of the patients had scores somewhere between 5-12 (47 patients, 85.45%). Worst incontinence (score of 24) was not reported.

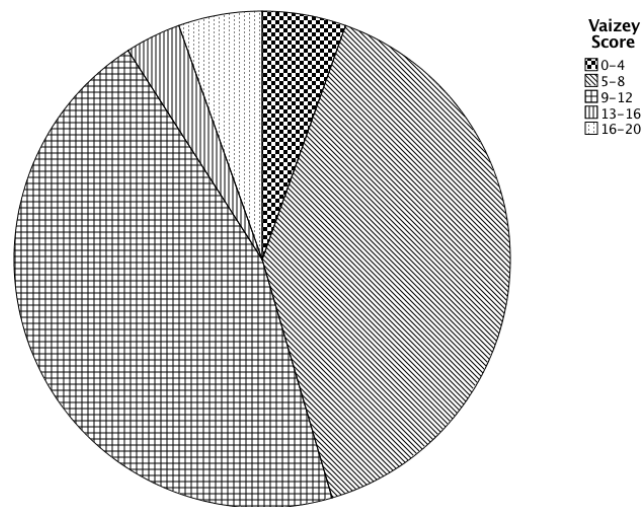


Figure 17. Distribution of Vaizey categories (individual clustering)

Vaizey scores in male and female patients had a slightly different distribution (figure 18). The majority of both the male (32 patients, 86.49%) and female patients (15 patients, 83.33%) were in the range of 5-12. The more severe incontinence (Score: 17-20) was more common in male patients (3 patients, 8.1%). Vaizey scores in the range of 13-16 were not observed in male patients.

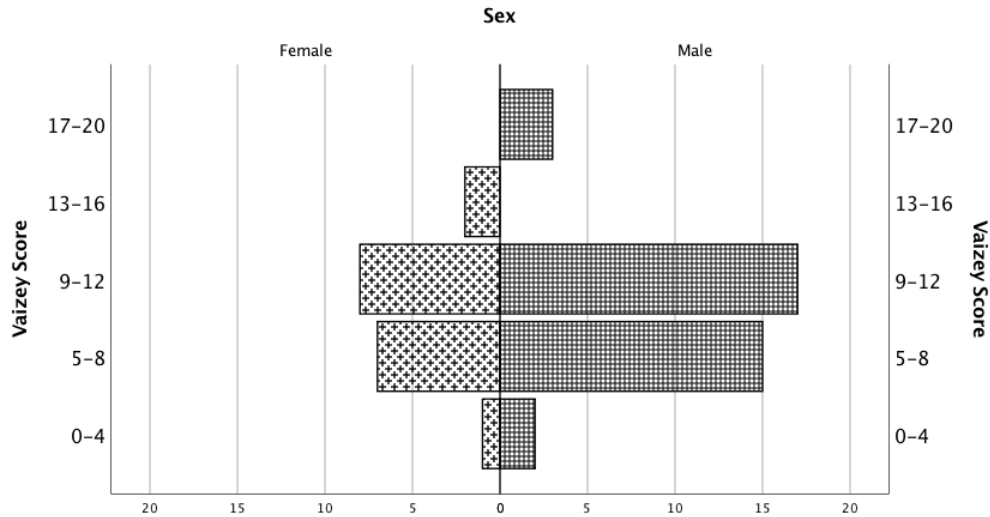


Figure 18. Distribution of Vaizey categories (non-universal) in different sexes

Figure 19 breaks down the grade of fecal incontinence among the age groups. Younger people (< 40) had no severe incontinence problems, while severe incontinence was more common in older patients. The majority had some issues related to fecal incontinence. Almost all severe incontinence (score over 13) cases were seen in people over 60.

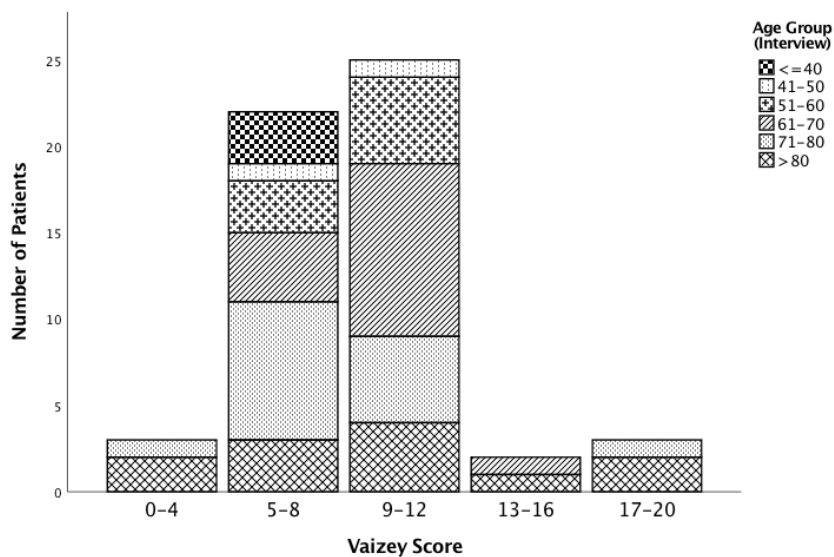


Figure 19. Distribution of Vaizey categories (non-universal) in different age groups

3.4.3.3 Comparison of Anorectal Function

The results of the anorectal function were also compared among the two groups. Only a small number of patients could be recruited for the comparison of anorectal function.

3.4.3.3.1 LARS

There was almost no difference in both groups regarding the presence of LARS ($p = 0.92$). However, minor LARS was somehow more common in the group with later closure (20.8%) compared to the group with earlier closure (9.1%). But in both of the groups, most of the patients had major LARS. The mean LARS score was slightly higher in the group with earlier closure ($p = 0.450$). Table 27 also compares the individual aspects of the LARS score to demonstrate the slight differences in each of the categories; none of them were, however, significantly different.

Table 35. Comparison of mean scores and individual characters of LARS

	Late Closure (n=24)	Early Closure (n=22)	p value
LARS Grade			0.92
No LARS	8 (33.3%)	7 (31.8%)	
Minor LARS	5 (20.8%)	2 (9.1%)	
Major LARS	11 (45.9%)	13 (59.1%)	
LARS Total			
Mean	25.58	27.95	0.450
LARS Categories			
Incontinence for flatus			0.058
never	10 (41.7%)	4 (18.2%)	
< once per week	11 (45.8%)	9 (40.9%)	
>= once per week	3 (12.5%)	9 (40.9%)	
Incontinence for liquid stools			0.609
never	5 (20.8%)	6 (27.3%)	
< or >= once per week	19 (79.2%)	16 (72.7%)	
Bowel Frequency			0.1 ^F
1-3 times a day	0 (0%)	0 (0%)	
4-7 times a day	11 (45.8%)	16 (72.7%)	
>7 times a day	12 (50%)	6 (27.3%)	
< once a day	1 (4.2%)	0 (0%)	
Clustering of stools			0.174 ^F
never	1 (4.2%)	1 (4.5%)	
< once a week	7 (29.2%)	12 (54.6%)	
>= once a week	16 (66.6%)	9 (40.9%)	

Urgency			0.623
never	11 (45.8%)	7 (31.8%)	
< once a week	6 (25%)	7 (31.8%)	
>= once a week	7 (29.2%)	8 (36.4%)	

^F – Fisher Freeman Halton Test instead of Chi-Square Test

3.4.3.3.2 Comparison of Vaizey-Score

The mean Vaizey score was slightly higher in the later closure group ($p = 0.700$). Little to no differences were noted in different subsets of problems defined in the Vaizey score. The ability to defer the defecation for 15 minutes was significantly higher in the patients with the earlier closure of the protective ileostomy ($p = 0.030$).

Table 36. Comparison of mean scores and individual characters of Vaizey

	Late Closure (n=25)	Early Closure (n=22)	p value
Vaizey			0.700
Mean	9.44	8.95	
Incontinence for solid stool			0.710 ^F
never	15 (60%)	14 (63.6%)	
rarely	7 (28%)	3 (13.6%)	
sometimes	2 (8%)	3 (13.6%)	
weekly	1 (4%)	1 (4.6%)	
daily	0 (0%)	1 (4.6%)	
Incontinence for liquid stool			0.976 ^F
never	6 (24%)	5 (22.7%)	
rarely	5 (20%)	3 (13.6%)	
sometimes	8 (32%)	8 (36.4%)	
weekly	5 (20%)	5 (22.7%)	
daily	1 (4%)	1 (4.6%)	
Incontinence for gas			0.197 ^F
never	12 (48%)	5 (22.7%)	
rarely	7 (28%)	8 (36.4%)	
sometimes	5 (20%)	5 (22.7%)	
weekly	0 (0%)	3 (13.6%)	

daily	1 (4%)	1 (4.6%)	
Alteration in Lifestyle			0.477 ^F
never	6 (24%)	6 (27.4%)	
rarely	8 (32%)	5 (22.7%)	
sometimes	9 (36%)	5 (22.7%)	
weekly	1 (4%)	3 (13.6%)	
daily	1 (4%)	3 (13.6%)	
Need to wear a pad or a plug			0.318
No	17 (68%)	19 (86.4%)	
Yes	8 (32%)	3 (13.6%)	
Taking constipating medicines			0.730
No	9 (36%)	9 (40.9%)	
Yes	16 (64%)	13 (59.1%)	
Lack of ability to defer defecation for 15 minutes			0.030 ^S
No	5 (20%)	11 (50%)	
Yes	20 (80%)	11 (50%)	

^F – Fisher Freeman Halton Test instead of Chi-Square Test

4 Discussion

As the incidence of colorectal cancer is increasing [26], the one inevitable part of the cancer treatment, surgery [27], more minimal-invasive surgeries, and enhanced recovery programs are needed to face the higher demand for surgical treatment of colorectal cancer. Depending on the stage of cancer, the rectal surgery would be either locally or radically removed. While local excision is done trans-anally, radical surgery is performed transabdominally, either via a sphincter-sparing procedure or an abdominal perineal resection. It may require a multi-visceral resection if the cancer is spread to the adjacent organs.

There are specific criteria and indications for one or another surgery. A sphincter-sparing resection is suggested if a negative distal margin can be achieved in a patient with rectal cancer (cT2-4) if an adequate presurgical anorectal sphincter function could be assessed. TME is the gold standard in the oncological resection of cancers in the mid and the low rectum. Sphincter preservation depends on the tumor localization. A standard TME is performed transabdominally; the technique could be open, laparoscopic, or robotic. It involves removal of the mesorectum, blood supply, and lymphatics of the origin of the superior rectal artery with the use of sharp dissection. A new surgical technique TaTME (Transanal TME), could also be used. The transanal approach improves the visualization of the most challenging part of the dissection [28, 29]. This might prevent injury to the inferior hypogastric plexus. Multiple short-term benefits such as a lower conversion rate have been reported following TaTME [30, 31]. We didn't differentiate TME from TaTME in this study.

This study aimed to assess the complications of the TME procedure and diverting ileostomy in patients with colorectal cancer, including the quality of life. The study also aimed to compare the complications and quality of life between the patients who had stoma closure earlier and later.

The latter question could only be partly answered by the study as none of the patients had early (within 14 days after TME) closure of the stoma. The research question was formulated with the considerations that we had a fair number of patients who had their stoma closure earlier than the conventional closure, and these patients would have profited from the earlier closure of stoma in terms of improvement of the quality of life with no stoma and no stoma-related complications such as stenosis, dehiscence, prolapse, infection, etc. However, we compared the complications and quality of life between the patients with earlier and later stoma closure. We used the median of the whole cohort (the time when the stoma was closed) to define early and late closure.

A diverting protective stoma is of great surgical importance for the overall morbidity and mortality after colorectal cancer surgery. However, many patients are restricted in their daily life and experience multiple challenges due to stoma. 22.5% of our patients with an ileostomy had at least one complication. The literature reports 9 to 74% of patients experience stoma-related complications [32-37]. Parastomal hernia, bowel ischemia, and a combination of more than one complication were most common in our study. Literature states that skin problems (15-34%), intestinal obstruction (11-23%), retraction (4-17%) and parastomal herniation (16%) were the most common ones [38-40].

In some of the other former studies, a reduction of hospital stay and medical complications [41-43] and reduction of stoma-related morbidity and complications [44, 45] were reported in the patients with an earlier closure of the protective diverting ileostomy. We observed a similar pattern in our study. Even if not all the complications were significantly less reported in the patients with earlier closure of protective stoma, there was a clear tendency seen. However, the hospital stay was not reduced in our cohort. The exact reasons could not be traced as the closure of stoma in our study was not done during the same hospital stay as it's usually done in the conventional early closure of stoma. None of the characteristics of the patients or treatments such as ASA grade, history of neoadjuvant therapy of cancer, history of DM, and smoking history showed any significant differences in complications. Relatively fewer patients with earlier ileostomy closure had ileostomy-related complications than those with later closure ($p = 0.068$). The complications were more common in male and older patients. A re-surgery was slightly more done in the earlier closure group ($p = 0.3622$). None of the patients' demographics had any significant effect on the need for re-do surgery.

While the complications related to the newly created anastomosis were not commonly seen, anastomotic leakage (16.9%) was the most frequent, with or without an abscess. It is seen as much as 7-12% in patients after TME [46-48]. While the sex of the patients had a significant effect, if a patient developed any complication or not ($p = 0.032$), none of the other factors (ASA grade, treatment with or without neoadjuvant therapy, diabetes mellitus, and smoking history) significantly affected the anastomotic complications. We observed no differences in the anastomosis-related complications between the two groups of patients with earlier and later stoma closure. Sometimes a revision surgery was needed, either because of the anastomosis or the TME procedure itself. The rate was, however, similar in both groups ($p = 1$). Significant more re-surgery surgery needed to be performed in patients with a history of smoking (active or past smokers) than

in non-smoker patients ($p = 0.033$). Other demographics had no significant effect on the need for re-do surgery.

Nearly 63% of the patients had general postoperative complications. Paralytic or obstructive ileus (9%), cardiac complications (6%), and surgical site infections (5%) were commonly seen. These findings are complementary to the results of other complication-related studies in colorectal surgery. Postoperative ileus (1-8%) and surgical site infections (1-30%) are two commonly reported complications related to colorectal surgery in literature [49-57]. Similar to the complications related to the stoma, postoperative complications were also slightly more common in males and older patients. A significantly higher number of complications was recorded in patients with diabetes mellitus ($p = 0.015$). Literature states history of diabetes mellitus, smoking, and age as independent risk factors for postoperative complications. No significant differences were seen in postsurgical complications between early and late closure ($p = 0.8415$). A meta-analysis from 2017, however, also showed no significant differences in any complications between the early and late closure of defunctioning ileostomy [58].

EQ-5D-3L is a generic QoL instrument, often used for economic evaluation and not specific to the QoL of cancer patients [59]. Even if patients were encouraged to answer these questions keeping cancer, stoma, and surgery in mind, the age and mood of the patient might have had a substantial effect on the result of the questionnaire. This instrument revealed significantly higher problems related to immobility in female patients ($p = 0.0169$), while other parameters did not show any significant differences between males and females. The average of VAS in females (74.04; range: 50-95) was slightly higher than the average in males (72.43; range: 40-95), which, however, was not significantly different ($p=0.659$). Most problems reported were concerning pain (23.3%), and least were affecting self-care (1.7%). Severe problems of any kind were extremely rare (0 – 1.7%). These severe problems were only reported from female patients. Both of these categories were activity-related. The possible explanation could be that the female patients enjoyed being more mobile and could not compensate for those deficits, as the male patients did. Each of the EQ-5D-3L symptoms and the mean of EQ-VAS was comparable between both groups of stoma closure. Literature suggests, these problems are usually temporary, and the quality of life increases with time [60].

EORTC-QLQ-C30 and EORTC-QLQ-CR29 are specific quality-of-life instruments developed and widely used in the research of general assessment of cancer and colorectal cancer patients,

respectively. EORTC-QLQ-C30 showed that patients had significantly severe problems with role functioning (mean – 71.3) and complained mostly of diarrhea (mean - 22.8). The average overall health score was 69.6 (range: 25–100). Neither any questions related to the functional scales and symptom scales nor the average overall health score had any significant differences between the earlier and later closure groups.

Both male and female patients answered sexual functioning to be their worst functional scale of EORTC-QLQ-CR29. Fecal incontinence was the most concerning symptom. Only questions regarding dry mouth and trouble with taste were found to be significantly different, favoring the earlier closure group ($p = 0.018$ and $p = 0.032$, respectively). All other functional and symptom scales regarding the EORTC-QLQ-CR29 questionnaire were comparable between the two groups. The literature is not consistent and shows different results regarding the QoL. Some of them show clear and significant favor for the early closure of stoma [61, 62], while in the others, the results in both groups were comparable [41]. These differences must be seen with consideration to the early closure and could simply be favored because of stoma closure, as the morbidity of having a stoma is already reduced pretty early, and the quality of life is massively affected.

Urinary and sexual dysfunctions are common after colorectal surgeries. The prevalence of urinary and sexual dysfunction after colorectal surgery might be as high as 30% [63, 64] and 60% [65-68] respectively. These dysfunctions are probably the combined result of neoadjuvant chemoradiation and neural injury during surgery. Even if there are several reasons for these neural lesions (pelvic hypogastric and splanchnic nerves), such as tumor infiltration, difficulty during dissection of large tumors, and inadequate dissection of the anatomic planes, they might simply occur even if no suspicious event happened during the surgery [69]. Most of the males reported problems related to urinary function (IPSS), which in the majority were mild. And so was the sexual dysfunction in males (IIEF-5), these, however, being more severe. Between the two groups of earlier and later closure of stoma, no significant differences were reported in the severity of urinary dysfunction or the mean IPSS score. The erectile dysfunction in males was comparable in both groups.

One of the limitations remains the improper assessment of the urinary and sexual dysfunction in women. Even if IPSS is used here and there in literature to quantify the urinary function in women, it doesn't fully explore the female lower urinary tract symptoms. This could have a possible negative impact on QoL [70]. Overactive bladder symptom score (OABSS) and King's Health Questionnaire (KHQ) are usually considered better scores to assess the urinary symptoms in

women [71] [72]. Some of these scores do not have any German verified versions. Our study was more focused on the general QoL and we think these scores also assess the urinary function in women and hence we didn't consult urology department to discuss the other scores. We think, the comprehensive research should be performed in another setting. The same goes for the sexual function score. We only considered IIEF-5 to assess the sexual function, which is used to self-assess the erectile dysfunction in males. We didn't modify the scores during the interview process. Hence, a proper assessment of sexual function in female patients could not be done.

Anorectal dysfunction is a significant concern in most colorectal cancer patients after surgery. The postoperative symptoms after LAR surgery are known explicitly as LARS. A systemic review reported the most frequent symptoms recorded after the surgery, which were incontinence (97%), stool frequency (80%), urgency (67%), evacuatory dysfunction (47%), and gas-stool discrimination (34%) [73]. Major LARS was very common in our cohort, and most of the patients with major LARS were males and over 70 years of age. The distribution of higher and lower Vaizey scores, however, was comparable. Similar to LARS, the highest Vaizey scores were more frequent in older males. Grades, mean scores, and individual categories of LARS all showed no statistical differences between the two groups of earlier and later closure of loop-ileostomy. The mean Vaizey score was also comparable in both groups. Except for "lack of ability to defer defecation for 15 minutes", which favored the earlier stoma closure ($p = 0.030$), none of the other Vaizey categories had any significant differences between the groups. Even though our study was not directly deriving the risk factors for anorectal dysfunction in colorectal cancer patients, higher scores/grades of LARS and Vaizey in older males could indirectly point out male sex and old age as risk factors.

While many study findings were comparable to the literature, there were some standouts. However, the comparison with the other studies should be cautiously treated. Our research question was specific only for a setting of colorectal cancer with TME and concomitant protective ileostomy as part of the procedure. Besides that, the number of patients was small in the comparison groups as the response rate was pretty low. The selection bias cannot be unnoticed, as some patients were already deceased before the questionnaire. The characters of non-respondents weren't taken for the comparative analysis, and hence the possible differences couldn't be consequently determined.

The study brings the limitations that a retrospective study has on it. Even if we've tried to reduce some biases with strict inclusion and exclusion criteria, the analysis of pre-existing data is subject to numerous biases. The surgery protocols and other documentation from 2010-11 had multiple minor errors, and some were not adequately documented. The questionnaires couldn't be conducted within a defined period, and hence the temporal differences and relations couldn't be best assessed.

Our definition of early and late closure doesn't match the conventional definition. As the expectation during the research question formulation was unmet, we took the median of all closures of protective stoma and formed two groups. Therefore, the assessment of the quality of life in these groups is not comparable to the literature. Nevertheless, earlier stoma closure seems to be beneficially affecting the quality of life. Finally, even if most of the questionnaires we used are standards in the literature, the answered could be only the snapshot of the captured moment. Without the recurring and timely assessment of the QoL questionnaire, the results should be cautiously interpreted.

More research analyzing the racial/ethnic differences among colorectal cancer patients with a stoma is needed to reduce the bias as culture and ethnicity influence our perception of health, well-being, and illness. This influence might not be massive while assessing the immediate complications; however, it is inevitable during the assessment of the quality of life. We need studies with a larger patient cohort and patients from multiple hospitals and treatment centers to derive suggestions for future practice in the era of evidence-based medicine (EBM). As a retrospective study design is flawed and cannot adapt to the changes seen during the early study periods, prospective randomized trials are needed in the future. The research questions from the findings of the retrospective studies can be used as a draft in those studies.

5 Conclusion

Our study identifies the various postoperative complications of TME surgery, either as a direct effect of protective stoma, newly created colorectal anastomosis, or the surgery itself. Some of these complications were strongly affected by specific characteristics of the patients like their age, sex, medical history (diabetes mellitus, immunocompromised status, smoking, and ASA grade), the course of treatment (neoadjuvant treatment before surgery). The study also compares the quality of life in patients, those who had their protective stoma closed earlier to those who had their stoma closed later. This comparison was made using the standard QoL questionnaires that were already validated in the setting of (colorectal) cancer patients.

Our study demonstrated the frequency of complications in surgical patients with colorectal cancer. The general postoperative complications (61.3%) were most common. 32.5% of patients had any complications related to bowel anastomosis, and 22.5% of the patients with an ileostomy had some complications because of their stoma. Regarding EQ-5D-3L, the most reported problems were concerning pain (23.3%), and the least were concerning self-care (1.7%). While 2.7% to 23.3% of the patients had some problems (mild or moderate), extreme problems were rare (0% to 1,7%). Severe problems were only reported by female patients. Likewise, problems related to mobility were significantly higher in patients of the female sex.

The best and worst rated items of functional scales regarding EORTC-QLQ-C30 were cognitive functioning (mean – 93) and role functioning (mean – 71) for both male and female patients. However, the worst-rated symptom of EORTC-QLQ-C30 was overall diarrhea (mean – 23); it was insomnia (mean – 24) for male patients and diarrhea (mean – 30) for female patients. The least concerning item on the symptom scale was financial difficulties for both male (mean – 1) and female (mean – 0) patients. Similarly, concerning EORTC-QLQ-CR29, patients rated body image (mean- 92) as best and sexual functioning as worst functional scale (mean – 46 (male), 51 (female)). Regarding the symptom scales of EORTC-QLQ-CR30, blood/mucus in stool was the least concerning symptom, while the most concerning symptoms were impotence (mean – 57) in male patients and stool frequency (mean – 43) in female patients. All male patients reported some urinary problems; however, 74% reported it to be mild (IPSS). Erectile dysfunction was prevalent and was seen in 89% of total male patients.

4.9% of patients with an ileostomy had to undergo a re-do surgery, while 19% of patients with TME needed one. Significantly more revision surgery due to TME was required in patients with a

history of smoking ($p = 0.033$). Male patients, patients with a history of diabetes and smoking habits without any neo-adjuvant treatment of colorectal cancer, and older patients had more extended hospital stay after the primary TME surgery than their counterparts.

We could show that early closure of protective ileostomy is favorable in colorectal cancer patients who underwent a TME procedure. On the one hand, complications like parastomal hernia were reported significantly lower in patients undergoing earlier closure of stoma; on the other hand, quality of life was also significantly higher in the same group (fewer problems regarding dry mouth, trouble of taste, and ability to defer defecation for 15 minutes). Other questionnaires related to the quality of life did not favor any of the groups.

However, prospective multicenter studies with larger numbers of patients need to be conducted for higher-quality evidence. Even if the questionnaires are validated and widely used, they mainly cover the organic symptoms and problems; future research should also consider and measure mental issues.

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PATIENTENFRAGEBOGEN

Sehr geehrte(r) Patient(in)!

Wir sind an einigen Angaben interessiert, die Sie und Ihre Gesundheit betreffen.

Bitte beantworten Sie die folgenden Fragen selbst, indem Sie ankreuzen, was am besten auf Sie zutrifft. Es gibt keine "richtigen" oder "falschen" Antworten. Ihre Angaben werden streng vertraulich behandelt.

Bitte tragen Sie Ihre Initialen ein. Nachname: _____ Vorname: _____

Ihr Geburtstag (Tag, Monat, Jahr): _____

Das heutige Datum (Tag, Monat, Jahr): _____

Bitte geben Sie an, welche Aussagen Ihren heutigen Gesundheitszustand am besten beschreiben, indem Sie ein Kreuz in ein Kästchen jeder Gruppe machen. (EQ-5D-3L)

1 Beweglichkeit/Mobilität			
<i>Ich habe keine Probleme herumzugehen</i>	<input type="checkbox"/>		
<i>Ich habe einige Probleme herumzugehen</i>	<input type="checkbox"/>		
<i>Ich bin ans Bett gebunden</i>	<input type="checkbox"/>		
2 Für sich selbst sorgen			
<i>Ich habe keine Probleme, für mich selbst zu sorgen</i>	<input type="checkbox"/>		
<i>Ich habe einige Probleme, mich selbst zu waschen oder mich anzuziehen</i>	<input type="checkbox"/>		
<i>Ich bin nicht in der Lage, mich selbst zu waschen oder anzuziehen</i>	<input type="checkbox"/>		
3 Alltägliche Tätigkeiten (z. B. Arbeit, Studium, Hausarbeit, Familien- oder Freizeitaktivitäten)			
<i>Ich habe keine Probleme, meinen alltäglichen Tätigkeiten nachzugehen</i>	<input type="checkbox"/>		
<i>Ich habe einige Probleme, meinen alltäglichen Tätigkeiten nachzugehen</i>	<input type="checkbox"/>		
<i>Ich bin nicht in der Lage, meinen alltäglichen Tätigkeiten nachzugehen</i>	<input type="checkbox"/>		
4 Schmerzen/Körperliche Beschwerden			
<i>Ich habe keine Schmerzen oder Beschwerden</i>	<input type="checkbox"/>		
<i>Ich habe mäßige Schmerzen oder Beschwerden</i>	<input type="checkbox"/>		
<i>Ich habe extreme Schmerzen oder Beschwerden</i>	<input type="checkbox"/>		
5 Angst/Niedergeschlagenheit			
<i>Ich bin nicht ängstlich oder deprimiert</i>	<input type="checkbox"/>		
<i>Ich bin mäßig ängstlich oder deprimiert</i>	<input type="checkbox"/>		
<i>Ich bin extrem ängstlich oder deprimiert</i>	<input type="checkbox"/>		

Ihr persönlicher Gesundheitszustand

Um Sie bei der Einschätzung, wie gut oder wie schlecht Ihr Gesundheitszustand ist, zu unterstützen, haben wir eine Skala gezeichnet, ähnlich einem Thermometer. Der best denkbare Gesundheitszustand ist mit einer „100“ gekennzeichnet, der schlechteste mit „0“. Wir bitten Sie nun, auf dieser Skala zu kennzeichnen, wie gut oder schlecht Ihrer Ansicht nach Ihr persönlicher Gesundheitszustand heute ist. Bitte markieren Sie dazu die nebenstehende Skala mit einem Punkt, der Ihren heutigen Gesundheitszustand am besten wiedergibt.

Best denkbarer
Gesundheitszustand



Schlechtest denkbarer
Gesundheitszustand

Bitte beantworten Sie die folgenden Fragen selbst, indem Sie die Zahl ankreuzen, die am besten auf Sie zutrifft.
EORTC QLQ-C30 (version 3)

		Überhaupt nicht	Wenig	Mäßig	Sehr
1	Bereitet es Ihnen Schwierigkeiten sich körperlich anzustrengen (z.B. eine schwere Einkaufstasche oder einen Koffer zu tragen?)	1	2	3	4
2	Bereitet es Ihnen Schwierigkeiten, einen längeren Spaziergang zu machen?	1	2	3	4
3	Bereitet es Ihnen Schwierigkeiten, eine kurze Strecke außer Haus zu gehen?	1	2	3	4
4	Müssen Sie tagsüber im Bett liegen oder in einem Sessel sitzen?	1	2	3	4
5	Brauchen Sie Hilfe beim Essen, Anziehen, Waschen oder Benutzen der Toilette?	1	2	3	4
	Während der letzten Woche:	Überhaupt nicht	Wenig	Mäßig	Sehr
6	Waren Sie bei Ihrer Arbeit oder bei anderen tagtäglichen Beschäftigungen eingeschränkt?	1	2	3	4
7	Waren Sie bei Ihren Hobbys oder anderen Freizeitbeschäftigungen eingeschränkt?	1	2	3	4
8	Waren Sie kurzatmig?	1	2	3	4
9	Hatten Sie Schmerzen?	1	2	3	4
10	Mussten Sie sich ausruhen?	1	2	3	4
11	Hatten Sie Schlafstörungen?	1	2	3	4
12	Fühlten Sie sich schwach?	1	2	3	4
13	Hatten Sie Appetitmangel?	1	2	3	4
14	War Ihnen übel?	1	2	3	4
15	Haben Sie erbrochen?	1	2	3	4
16	Hatten Sie Verstopfung?	1	2	3	4
17	Hatten Sie Durchfall?	1	2	3	4
18	Waren Sie müde?	1	2	3	4
		Überhaupt nicht	Wenig	Mäßig	Sehr
19	Fühlten Sie sich durch Schmerzen in Ihrem alltäglichen Leben beeinträchtigt?	1	2	3	4
20	Hatten Sie Schwierigkeiten sich auf etwas zu konzentrieren, z.B. auf das Zeitunglesen oder das Fernsehen?	1	2	3	4
21	Fühlten Sie sich angespannt?	1	2	3	4
22	Haben Sie sich Sorgen gemacht?	1	2	3	4
23	Waren Sie reizbar?	1	2	3	4
24	Fühlten Sie sich niedergeschlagen?	1	2	3	4
25	Hatten Sie Schwierigkeiten, sich an Dinge zu erinnern?	1	2	3	4
26	Hat Ihr körperlicher Zustand oder Ihre medizinische Behandlung Ihr Familienleben beeinträchtigt?	1	2	3	4
27	Hat Ihr körperlicher Zustand oder Ihre medizinische	1	2	3	4

Patienten berichten manchmal die nachfolgend beschriebenen Symptome oder Probleme. Bitte beschreiben Sie, wie stark Sie diese Symptome oder Probleme während der letzten Woche empfunden haben. Kreuzen sie bitte die Zahl an, die am besten auf Sie zutrifft. (EORTC QLQ-C29)

		Überhaupt nicht	Wenig	Mäßig	Sehr
1	Mussten Sie tagsüber häufig Wasser lassen?	1	2	3	4
2	Mussten Sie nachts häufig Wasser lassen?	1	2	3	4
3	Kam es bei Ihnen zu unwillkürlichem Harnabgang?	1	2	3	4
4	Hatten Sie Schmerzen beim Wasser lassen?	1	2	3	4
5	Hatten Sie Bauchschmerzen?	1	2	3	4
6	Hatten Schmerzen im Gesäß/Anaalbereich/Rektum	1	2	3	4
7	Hatten Sie das Gefühl, dass Ihr Bauch gebläht ist?	1	2	3	4
8	Hatten Sie Blut im Stuhl?	1	2	3	4
9	Befand sich Schleim in Ihrem Stuhlgang?	1	2	3	4
10	Hatten Sie einen trockenen Mund?	1	2	3	4
11	Hatten Sie aufgrund Ihrer Behandlung Haarausfall?	1	2	3	4
12	Hatten Sie Probleme mit Ihrem Geschmackssinn?	1	2	3	4
13	Waren Sie wegen Ihres zukünftigen Gesundheitszustandes besorgt?	1	2	3	4
14	Haben Sie sich Sorgen über Ihr Gewicht gemacht?	1	2	3	4
15	Fühlten Sie sich wegen ihrer Erkrankung oder Behandlung körperlich weniger anziehend?	1	2	3	4
16	Fühlten Sie sich wegen ihrer Erkrankung oder Behandlung weniger weiblich/männlich?	1	2	3	4
17	Waren Sie mit Ihrem Körper unzufrieden?	1	2	3	4
18	Haben Sie ein Stoma (künstlicher Darmausgang)? (Zutreffendes bitte ankreuzen)	Ja <input type="checkbox"/>	Nein <input type="checkbox"/>		

Beantworten Sie folgende Fragen NUR, WENN SIE EINEN STOMABEUTEL TRAGEN. Fahren Sie ansonsten weiter unten fort		Überhaupt nicht	Wenig	Mäßig	Sehr
19	Hatten Sie unfreiwillige Darmgasentweichungen/Flatulenzen aus Ihrem Stomabeutel?	1	2	3	4
20	Hatten Sie unfreiwillige Stuhlabgänge aus Ihrem Stomabeutel?	1	2	3	4
21	War die Haut um Ihr Stoma wund?	1	2	3	4
22	Gab es im Tagesverlauf häufige Beutelwechsel?	1	2	3	4
23	Fanden während der Nacht häufige Beutelwechsel statt?	1	2	3	4
24	War es Ihnen peinlich ein Stoma zu haben?	1	2	3	4
25	Hatten Sie Probleme mit Ihrer Stomapflege?	1	2	3	4

Beantworten Sie folgende Fragen NUR, WENN SIE KEINEN STOMABEUTEL TRAGEN. Fahren Sie ansonsten weiter unten fort		Überhaupt nicht	Wenig	Mäßig	Sehr
19	Hatten Sie unfreiwillige Darmgasentweichungen/Flatulenzen aus Ihrem Darmausgang?	1	2	3	4
20	Hatten Sie unfreiwillige Stuhlabgänge aus Ihrem Darmausgang?	1	2	3	4
21	Hatten Sie wunde Haut in Ihrem Analbereich?	1	2	3	4
22	Gab es im Tagesverlauf häufige Stuhlgänge?	1	2	3	4
23	Gab es während der Nacht häufige Stuhlgänge?	1	2	3	4
24	Waren Ihnen die Stuhlgänge peinlich?	1	2	3	4

NUR FÜR MÄNNER <i>Während der letzten 4 Wochen</i>		Überhaupt nicht	Wenig	Mäßig	Sehr
25	Wie sehr waren Sie an Sexualität interessiert?	1	2	3	4
26	Hatten Sie Schwierigkeiten eine Erektion zu bekommen oder zu halten?	1	2	3	4

NUR FÜR FRAUEN <i>Während der letzten 4 Wochen</i>		Überhaupt nicht	Wenig	Mäßig	Sehr
25	Wie sehr waren Sie an Sexualität interessiert?	1	2	3	4
26	Verspürten Sie Schmerzen oder Beschwerden während des Geschlechtsverkehrs?	1	2	3	4

Beantworten Sie bitte folgende Fragen über Stuhlprobleme durch Ankreuzen (Vaizey Score)

<i>Während der letzten 4 Wochen</i>		nie	selten *	manchmal *	wöchentlich *	täglich *
1	Inkontinenz (unfreiwilliger Verlust) für festen Stuhl	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2	Inkontinenz für flüssigen Stuhl	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	Inkontinenz für Winde	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	Beeinträchtigung des täglichen Lebens durch Inkontinenz	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

* selten: einmal in 4 Wochen
 manchmal: mehr als einmal in 4 Wochen aber weniger als 1x pro Woche
 wöchentlich: ein- oder mehrmals pro Woche aber seltener als täglich
 täglich: ein- oder mehrmals pro Tag

		nein	ja		
5	Notwendigkeit eine Vorlage zu tragen	<input type="checkbox"/>	<input type="checkbox"/>		
6	Einnahme von stuhlverstopfenden Medikamenten	<input type="checkbox"/>	<input type="checkbox"/>		
7	Unfähigkeit den Stuhl länger als 15 Minuten zu halten	<input type="checkbox"/>	<input type="checkbox"/>		

Zielsetzung dieses Fragebogens besteht in der Bewertung ihrer Darmfunktion. Bitte kreuzen Sie bei jeder Frage jeweils nur ein Kästchen an. Es ist möglicherweise schwierig, nur eine der Antworten auszuwählen, da, wie wir wissen, die Symptome bei einigen Patienten von Tag zu Tag andere sind. Wir möchten Sie höflich bitten, die eine Antwort zu wählen, die Ihre tägliche Lebenssituation am besten beschreibt. Sollten Sie kürzlich eine Infektion gehabt haben, die Ihre Darmfunktion beeinträchtigte, so ziehen Sie dies bitte nicht in Betracht, sondern konzentrieren sich bitte darauf, die Antworten zu geben, die Ihre alltägliche Darmfunktion widerspiegeln.

(LARS)

1	Kommt es gelegentlich vor, dass Sie Ihre Blähungen nicht kontrollieren können?			
	Nein, niemals	<input type="checkbox"/>	0	
	Ja, weniger als einmal pro Woche	<input type="checkbox"/>	4	
	Ja, mindestens einmal pro Woche	<input type="checkbox"/>	7	
2	Kommt es bei Ihnen jemals zu einer unbeabsichtigten Ausscheidung von flüssigem Stuhl?			
	Nein, niemals	<input type="checkbox"/>	0	
	Ja, weniger als einmal pro Woche	<input type="checkbox"/>	3	
	Ja, mindestens einmal pro Woche	<input type="checkbox"/>	3	
3	Wie oft haben Sie Stuhlgang?			
	Mehr als 7 Mal pro Tag (24 Stunden)	<input type="checkbox"/>	4	
	4-7 Mal pro Tag (24 Stunden)	<input type="checkbox"/>	2	
	1-3 Mal pro Tag (24 Stunden)	<input type="checkbox"/>	0	
	Weniger als einmal pro Tag (24 Stunden)	<input type="checkbox"/>	5	
4	Müssen Sie jemals nach Ihrem letzten Stuhlgang innerhalb von einer Stunde erneut auf die Toilette?			
	Nein, niemals	<input type="checkbox"/>	0	
	Ja, weniger als einmal pro Woche	<input type="checkbox"/>	9	
	Ja, mindestens einmal pro Woche	<input type="checkbox"/>	11	
5	Haben Sie jemals einen solch starken Stuhldrang, dass Sie zur Toilette rennen müssen?			
	Nein, niemals	<input type="checkbox"/>	0	
	Ja, weniger als einmal pro Woche	<input type="checkbox"/>	11	
	Ja, mindestens einmal pro Woche	<input type="checkbox"/>	16	

Während der letzten 4 Wochen		nie	seltener als in 1 von 5 Fällen	seltener als in der Hälfte aller Fälle	ungefähr in der Hälfte aller Fälle	in mehr als der Hälfte aller Fälle	fast immer
1	Wie oft während des letzten Monats hatten Sie das Gefühl, dass Ihre Blase nach dem Wasserlassen nicht ganz geleert war?	<input type="checkbox"/>	1	2	3	4	5
2	Wie oft während des letzten Monats mussten Sie in weniger als zwei Stunden ein zweites Mal Wasser lassen?	<input type="checkbox"/>	1	2	3	4	5
3	Wie oft während des letzten Monats mussten Sie beim Wasserlassen mehrmals aufhören und neu beginnen?	<input type="checkbox"/>	1	2	3	4	5
4	Wie oft während des letzten Monats hatten Sie Schwierigkeiten, das Wasserlassen hinauszuzögern?	<input type="checkbox"/>	1	2	3	4	5
5	Wie oft während des letzten Monats hatten Sie einen schwachen Strahl beim Wasserlassen?	<input type="checkbox"/>	1	2	3	4	5
6	Wie oft während des letzten Monats mussten Sie pressen oder sich anstrengen, um mit dem Wasserlassen zu beginnen?	<input type="checkbox"/>	1	2	3	4	5
7	Wie oft sind Sie während des letzten Monats im Durchschnitt nachts aufgestanden, um Wasser zu lassen? Maßgebend ist der Zeitraum vom Zubettgehen bis zum Aufstehen am Morgen	<input type="checkbox"/>	einmal 1	zweimal 2	dreimal 3	viermal 4	fünfmal 5

Wie würden Sie sich fühlen, wenn sich Ihre jetzigen Symptome beim Wasserlassen künftig nicht mehr ändern würden?

<input type="checkbox"/> ausgezeichnet	<input type="checkbox"/> zufrieden	<input type="checkbox"/> überwiegend zufrieden	<input type="checkbox"/> gemischt, teils zufrieden, teils unzufrieden	<input type="checkbox"/> überwiegend unzufrieden	<input type="checkbox"/> unglücklich	<input type="checkbox"/> sehr schlecht
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NUR FÜR MÄNNER

Dieser Fragebogen behandelt Ihre Sexualfunktion. Die sexuelle Gesundheit ist ein wichtiger Bestandteil des gesamten körperlichen und gefühlsbezogenen Wohlbefindens eines Menschen.

Die Beantwortung dieses Fragebogens ist nicht zwingend.

Wenn Sie bereit sind, diesen Fragebogen ausfüllen, beantworten Sie bitte alle Fragen.

Für jede Frage sind mehrere Antworten vorgegeben, aus denen Sie bitte diejenige auswählen, die auf Sie in den letzten 4 Wochen am ehesten zutrifft. Bitte geben Sie bei jeder Frage jeweils nur eine Antwort. (IIEF-5)

Wie würden Sie Ihre Zuversicht einschätzen, eine Erektion zu bekommen und zu behalten?

<input type="checkbox"/> sehr gering oder nicht vorhanden	<input type="checkbox"/> Niedrig	<input type="checkbox"/> mittelmäßig	<input type="checkbox"/> groß	<input type="checkbox"/> sehr groß
---	----------------------------------	--------------------------------------	-------------------------------	------------------------------------

Wenn Sie bei sexueller Stimulation Erektionen hatten, wie oft waren Ihre Erektionen hart genug für die Penetration?

<input type="checkbox"/> keine sexuelle Stimulation	<input type="checkbox"/> fast nie oder nie	<input type="checkbox"/> selten (viel weniger als die Hälfte der Zeit)	<input type="checkbox"/> manchmal (etwa die Hälfte der Zeit)	<input type="checkbox"/> meistens (viel mehr als die Hälfte der Zeit)	<input type="checkbox"/> fast immer oder immer
---	--	--	--	---	--

Wie oft waren Sie bei Geschlechtsverkehr in der Lage, Ihre Erektion aufrecht zu erhalten, nachdem Sie Ihre Partnerin penetriert hatten (in sie eingedrungen waren)?

<input type="checkbox"/> keinen Geschlechtsverkehr versucht	<input type="checkbox"/> fast nie oder nie	<input type="checkbox"/> selten (viel weniger als die Hälfte der Zeit)	<input type="checkbox"/> manchmal (etwa die Hälfte der Zeit)	<input type="checkbox"/> meistens (viel mehr als die Hälfte der Zeit)	<input type="checkbox"/> fast immer oder immer
---	--	--	--	---	--

Wie schwierig war es, beim Geschlechtsverkehr Ihre Erektion bis zur Vollendung des Geschlechtsverkehrs aufrechtzuerhalten?

<input type="checkbox"/> keinen Geschlechtsverkehr versucht	<input type="checkbox"/> äußerst schwierig	<input type="checkbox"/> sehr Schwierig	<input type="checkbox"/> schwierig	<input type="checkbox"/> ein bisschen schwierig	<input type="checkbox"/> nicht schwierig
---	--	---	------------------------------------	---	--

Wenn Sie versuchten, Geschlechtsverkehr zu haben, wie oft war er befriedigend für Sie?

<input type="checkbox"/> keinen Geschlechtsverkehr versucht	<input type="checkbox"/> fast nie oder nie	<input type="checkbox"/> selten (viel weniger als die Hälfte der Zeit)	<input type="checkbox"/> manchmal (etwa die Hälfte der Zeit)	<input type="checkbox"/> meistens (viel mehr als die Hälfte der Zeit)	<input type="checkbox"/> fast immer oder immer
---	--	--	--	---	--

Eidesstattliche Versicherung

„Ich, [Anish Lamichhane], versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema „Benefit der doppelläufigen protektiven Ileostomie bei onkologischen Rektumresektionen – Eine retrospektive Center-analyse / Benefits of the protective loop ileostomy in the oncological rectal resections – a retrospective center analysis“ selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.org) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Datum

Unterschrift

Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

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Danksagung

In erster Linie möchte ich mich bei meinem Betreuer Herr Prof. Dr. med. Felix Aigner und meinem Doktorvater Prof. Dr. med. Johann Pratschke für die vertrauensvolle Zusammenarbeit und die stetige Förderung meiner Kompetenzen durch Wissensvermittlung, Anregung zu weiteren Forschungsthemen und Fortbildungen bedanken. Diese Arbeit ist meinen Eltern Sharada Devi Chapagain und Anirudra Lamichhane, meiner Frau Suchana Dahal und meiner Tochter Aurelia Lamichhane gewidmet, die mir das Studium der Humanmedizin ermöglicht und mich stets in jeglicher Hinsicht dabei unterstützt haben.

Bescheinigung des akkreditierten Statistikers



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Bescheinigung

Hiermit bescheinige ich, dass Herr Anish Lamichhane innerhalb der Service Unit Biometrie des Instituts für Biometrie und klinische Epidemiologie (iBiKE) bei mir eine statistische Beratung zu einem Promotionsvorhaben wahrgenommen hat. Folgende Beratungstermine wurden wahrgenommen:

- Termin 1: 28.01.2022
- Termin 2: 14.02.2022

Folgende wesentliche Ratschläge hinsichtlich einer sinnvollen Auswertung und Interpretation der Daten wurden während der Beratung erteilt:

- Bei zu kleinen Gruppengrößen ist ein statistischer Test nicht sinnvoll, insbesondere keine Tests von Gruppen mit jeweils einer Fallzahl von $n=0$.
- Um diverse Einflussgrößen zu analysieren, bieten sich multiple Regressionsanalysen an (zum Beispiel hinsichtlich Alter etc.).
- Die verwendeten Tests sind explorativ einzuordnen. Andernfalls wird eine Adjustierung für multiples Testen benötigt.
- Nach Möglichkeit sollte das Alter nicht kategorisch dargestellt werden.

Diese Bescheinigung garantiert nicht die richtige Umsetzung der in der Beratung gemachten Vorschläge, die korrekte Durchführung der empfohlenen statistischen Verfahren und die richtige Darstellung und Interpretation der Ergebnisse. Die Verantwortung hierfür obliegt allein dem Promovierenden. Das Institut für Biometrie und klinische Epidemiologie übernimmt hierfür keine Haftung.

Datum: 14.02.2022

Name des der Beraterin: [REDACTED]

Unterschrift BeraterIn, Institutsstempel

