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Bachelor thesis

Quality of life and functional outcome after different types of Total Mesorectal Excision in Dutch patients with rectal carcinoma

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Abstract

Introduction The interest in robot-assisted surgery as an alternative TME approach in rectal cancer has grown over the years. Although this technique is more expensive than the open or laparoscopic approach, advantage is expected in different outcomes. This is due to the magnification possibility and free movements during the procedure. However, the superiority of robotic surgery to laparoscopic surgery in the treatment of rectal cancer is still debated. This research described the quality of life and functional outcomes after robot-assisted TME for rectal cancer and compared them to the outcomes of the laparoscopic and transanal TME.

Method Three patient groups with a total of 101 patients were included in this study: 24 patients who underwent laparoscopic TME, 25 patients who underwent TaTME and 52 patients who underwent robot-assisted TME. All patients were asked to complete five questionnaires related to quality of life and function [EQ-5D-3L, EORTC-QLQ C30, EORTC-QLQ C29, Low Anterior Resection Syndrome score (LARS), and International Prostate Symptom Score IPSS]. In the robot-assisted group the female patients also filled in the FSFI questionnaire.

Results The EORTC-QLQ C30 and EQ-5D-3L questionnaires showed some significant differences in terms of index value and pain when comparing the laparoscopic and transanal group with the robot-assisted group. Outcomes of the LARS, EORTC-QLQ-29 and IPSS showed similar outcomes.

Conclusion There were no overall differences between the groups, although differences were seen in subscores. Therefore, the robot-assisted approach seems to be a reasonable alternative approach in the treatment of rectal cancer. However, the choice of the optimal approach depends on different factors and should be made per individual patient. Further research, which takes the limitations and recommendations of this study into account, is desired to confirm these results.

Contents

Introduction

Colorectal cancer (CRC) is the third most common deadly cancer and the fourth most diagnosed cancer in the world. [1] CRC consists of colon cancer and rectal cancer of which the last type is located in the rectum. The incidence of rectal cancer is relatively high, since it is the eighth most diagnosed cancer in the world. According to data from the global cancer observatory, 0.6 million new cases arose in 2018. In the Netherlands, rectal cancer is one of the most commonly diagnosed cancers. Over a period of almost 30 years, the incidence of rectal cancer almost doubled from 2.600 to over 4.500 cases per year. [2]

In the last decades, survival of patients with a rectal carcinoma in the Netherlands has massively increased. This can be partly attributed to the Dutch national screening programme. It tests for the presence of blood in stool which could be a sign of rectal cancer and therefore could eventually lead to an early diagnosis. [3] Early diagnosis of rectal cancer often results in less invasive treatment and higher survival rates compared to treatment in later diagnosis, due to the fact that the cancer is less developed. [4] Another reason for improved survival is caused by improvements in surgical techniques.

The introduction of the Total Mesorectal Excision (TME) as a surgical technique has shown to be a major improvement compared to the traditional technique during the 1980's. Finally, improvements have been made in the treatment of the carcinoma at a later stadium, as well as the treatment of metastasis. These successes can be attributed to the option to administer (neo-) adjuvant therapy. [5] As a result of these developments and complementary increasing survival rates, the focus on the quality of life and preventing the loss of quality of life has increased.

Developments in the TME led to the laparoscopic TME as standard procedure in rectal resection surgery. However, patients are often left with damaged sympathetic and/or parasympathetic nerves of their pelvic after surgery. Damage to these nerves could result in some sort of dysfunction, such as sexual dysfunction or urinary dysfunction. Due to the fact that the pelvic area is a narrow space, it is difficult for the surgeon to avoid causing damage to the nerves. [5]

Another development, especially used for lower tumors, is the introduction of the Transanal Total Mesorectal Excision (TaTME). [6] In the last few years, the interest in this type of TME has increased rapidly. Due to bending of the rectal canal and the tight space, surgery with the traditional approach is difficult. The transanal approach enhances visualization of the surgical planes, which helps to remove the specimen more precisely and cause less damage.

The introduction of the Da Vinci robot could help to increase the precision of the operating surgeon and improve the outcomes even more. This due to three times magnified images, elimination of human tremor and an increased freedom of movement in the surgical instruments, because of an incorporated wrist joint. This enables the surgeon to perform actions which were impossible with the rigid instruments used during laparoscopic TME. This could contribute to the fact that a surgeon could work with more precision, and thus decrease the risk of damaging the pelvic autonomic nerves. Therefore, the incidence of dysfunction as a result of the TME could be decreased compared to the laparoscopic manner.

Since robot-assisted surgery is a relatively new technique within rectal cancer care, available research focused on its safety and efficiency. Both outcomes were found to be similar to the laparoscopic approach. [7, 8] Limited research has been conducted to evaluate functional outcomes in patients with rectal cancer after the robot-assisted procedure. Robot-assisted surgery has been compared to laparoscopic surgery based on quality of life and functional outcomes in previous researches. [8, 9] Their limitations include a lack of relevant outcome, such as LARS and urinary function. Besides the lack of some outcomes, certain outcomes were only measured for a certain group. Therefore, no comparison could be made. Also, the research groups that were compared differed significantly in, for example, age and tumor height. The possible impact of these factors were not taken into account by executing a multivariate analysis. Furthermore, only patients without recurrence were included. This could lead to overestimation of the quality of life and the functional

outcomes. [9] Combined with recommendations, such as incorporating sexual function, they contribute to the need and importance of new research.

A few researches have been conducted regarding differences in quality of life and functional outcome between patients approached via transanal TME (TaTME) and laparoscopic TME. [10, 11] They did not show any overall differences, but were found to be inconclusive and had limitations in their patient groups, assessment or both. Small sample size, great heterogeneity of the study group and wide confidence intervals were seen as well as a follow-up of only six months. [10] Also, no adequate comparison group could be presented and data was only analyzed through univariate analysis. Further research was advised in order to address the limitations and confirm their results.

Research aim

Further research regarding the quality of life and functional outcomes after robot-assisted TME is desired to compare their performance with other TME techniques. Necessities in this research are larger patient groups and the inclusion of sexual function, among other improvements. Therefore, the purpose of this research is to expand the knowledge regarding the quality of life and functional outcomes of the different types of TME surgery, which involve the laparoscopic TME, TaTME and the traditional robot-assisted TME.

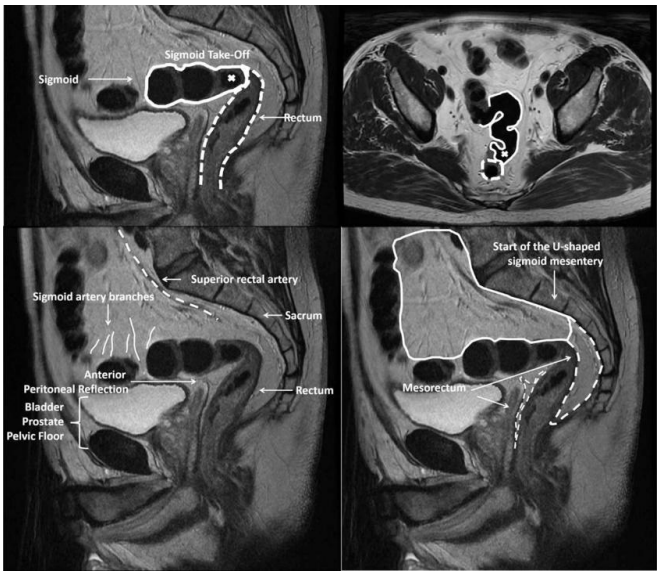
The aim is to answer the following research question: Is there a difference in the quality of life and functional outcome after different types of Total Mesorectal Excision surgery with curative intent in a Dutch population with rectal carcinoma?

Theoretical framework

Definition rectum

Throughout scientific research, many different definitions of the rectum are discussed. This diversity is caused by a broad variation of marks to indicate the transition of the sigmoid colon into the rectum. Due to differences in the anatomy and function of the colon and rectum, optimal treatment differs significantly for these two cancer types. In order to guarantee the best oncological outcome for the patient, it is important to identify the cancer type correctly. [12] Radiotherapy is for example merely administered to rectal cancer patients. Patients with colon cancer would not experience any benefit, when this treatment is administered. However, the burden of the therapy itself would weigh on them. Furthermore, the variance in use of the definition of the rectum leads to contradictions in recruitment of trials, clinical management and outcomes that are significant. [13]

In order to standardize treatment and research outcomes, international multidisciplinary colorectal experts reached a consensus regarding the definition of rectum through the Delphi technique. This technique allows many individuals to come to a consensus effectively by structuring the communication process of the group and is universally applied. They concluded that the sigmoid take-off can be identified with the aid of CT and MRI cross-sectional imaging the horizontal course of the sigmoid as shown in Figure 1. [13]



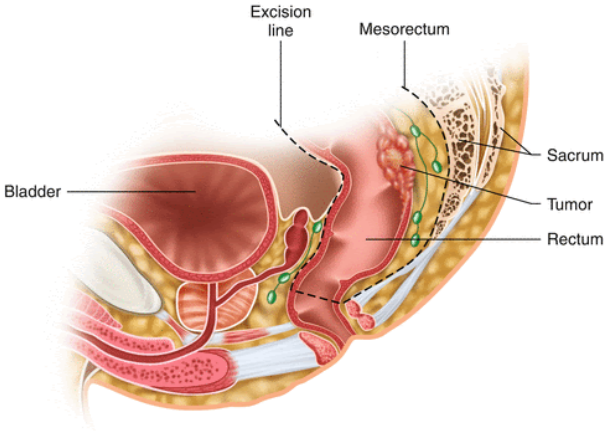


Figure 1 (left): Clockwise from top left. (1) Sagittal view of the sigmoid and rectum (dashed outline): horizontal sweep of sigmoid. (2) Axial views of the sigmoid and rectum (dashed outline): ventral projection of sigmoid, when the upper mesorectum, tethered to the sacrum by the rectosacral/presacral fascia, transitions to the mesocolon. (3) U-shaped sigmoid mesocolon. (4) Spidery sigmoid arteries supply the sigmoid through its fan-shaped mesocolon. Larger caliber superior rectal artery (dashed) bifurcates and supplies the rectum through its cylindrical fatty envelope. [13]
Figure 2 (right): The correct plane in a Total Mesorectal Excision. [14]

Total Mesorectal Excision

Total Mesorectal Excision (TME) is nowadays the golden standard within rectal cancer surgery, due to its decreasing effect on local recurrence and improvement of survival. A section of the rectum as well as the mesorectum are removed during a TME. The mesorectum is the fatty tissue surrounding the rectum, which contains lymph nodes, where the cancer cells could manifest and form metastases if they were not successfully removed. The surgeon cuts along the plane between visceral and parietal fascia in order to reduce injuries as shown in Figure 2. [15, 16]

Depending on the patient specific situation, a certain area of the rectum and mesorectum are removed or the complete rectum with the mesorectum are removed. This resection could

determine that the surgeon will create a definitive stoma or a temporary stoma. If a patient receives a definitive stoma, he or she will have this for the rest of his or her life. Another possibility is the creation of a temporary stoma which enables the anastomosis to heal and which will be reversed, mostly after 6 months. [8]

The TME is a difficult procedure to execute due to the narrowness of the pelvic area and the complicated anatomic dissection planes. The nerves which are responsible for sexual as well as urinary functioning are located in this confined area. Therefore, a decreased quality of life and urinary and sexual dysfunction are possible and widely experienced consequences of the TME. [8, 16, 17]

Surgery types

There are several approaches a surgeon can consider to execute a TME as can be seen in Table 1. The choice is often based on characteristics like the location and the size of the tumor but also experience of the surgeon. The first option is the open procedure where the surgeon creates a big incision in the abdomen through which the surgery is performed. This used to be a frequently used approach, but nowadays minimally invasive surgery is preferred to open surgery. [17] However, complications during the procedure could lead to the fact that a conversion takes place. Excessive bleeding, for example, could cause a transition into open surgery in order to enable the surgeon to stop the bleeding. [17]

Secondly, the TME could be performed through laparoscopic surgery. This approach is also known as keyhole surgery and is executed with rigid instruments through small holes in the abdominal wall. Air is pumped in through one of these small holes in order to expand the cavity where the surgery takes place to create more space for the other instruments. Besides the camera, which visualizes the internal situation, these other instruments are, for example, scissors, hooks, pouches or needles. [17, 18]

Robot-assisted TME gained popularity over the last years due to the increased freedom of movements, since the presence of a 'wrist joint'. Other reasons for the increase in robotic assisted TME are physical tremor elimination and image quality. With the traditional robot-assisted TME, three times magnified images can be spectated during the procedure. With the Nerve Sparing TME the surgeon even has a ten times magnification possibility at his or her disposal. Furthermore, 3D images are incorporated in the new version, which improves visualization of the surgery even further. [5, 8]

Transanal Total Mesorectal Excision (TaTME) is a relatively new surgical technique where the surgeon operates from an entree to the abdominal wall as well as a transanal one as can be seen in Figure 3. During this procedure, rectal resection is executed through the anus. This leads to better visualization of the hardest aspect of the dissection, which could lead to the prevention of nerve injury. [10, 19]

Table 1: surgery types for rectal cancer [20, 21, 22, 23]

Surgery	Introduction	Cost	Approach	Wound(s)	Recovery	Instruments	Features
Open	Since 1980	+	Abdominal	Large	Slow		Full view
Laparoscopic	± 1999	+	Abdominal	Small	Fast	Rigid movements	
Traditional robot-assisted	Da Vinci Si 2010	++	Abdominal	Small	Fast	Free movements	3x magnification
Nerve Sparing robot-assisted	Da Vinci Xi 2014	+++	Abdominal	Small	Fast	Free movements	10x magnification 3D images Firefly method
Transanal	±2008	+	Abdominal and transanal	Small	Fast	Free movements	Bilateral access

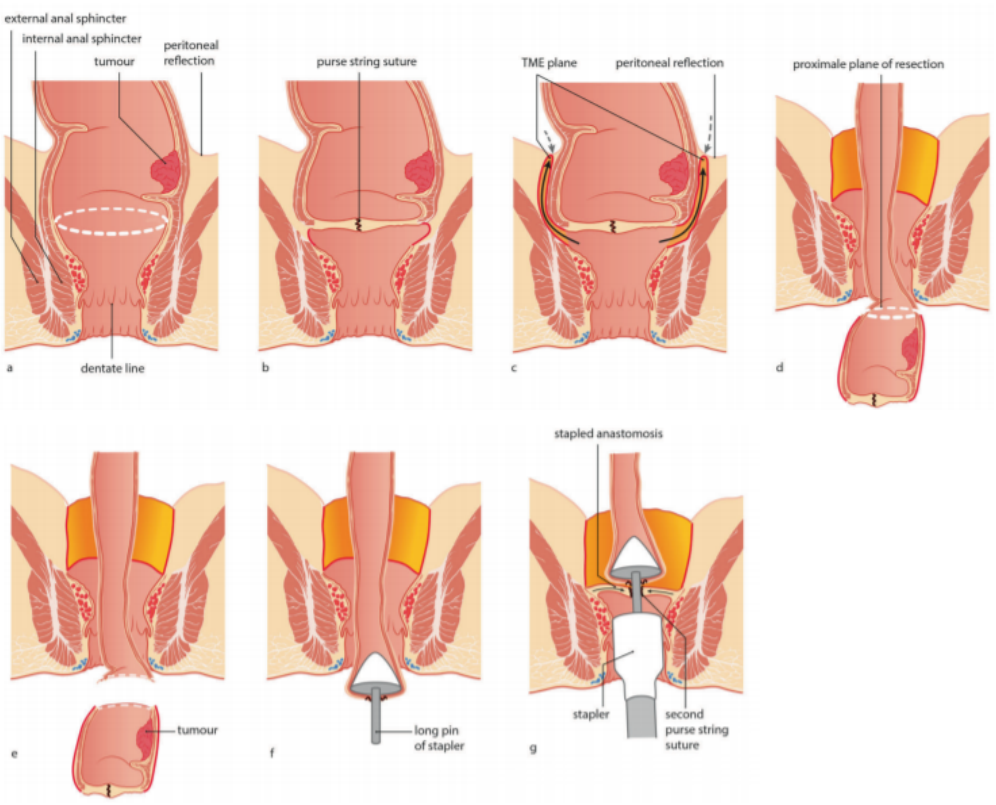


Figure 3: Steps of TaTME: distal resection margin (a), closure with a purse-¬-string suture and transection of the mucosa (b), mobilization according to TME criteria (c), transanal specimen removal (d-¬-e), suturing of stapler head (f), second purse-¬-string and stapled anastomosis (g). [19]

Outcomes

Health related quality of life

Patients as well as health professionals strive for preservation of the maximum quality of life. They are interested in the effect a certain intervention has on the quality of the patient's life. This effect can be measured through the Health Related Quality of Life (HRQoL). This is an important multidimensional measure for the impact of a chronic disease on the patient. It consists of multiple aspects being physical, psychological, functional and social domains. [24]

The HRQoL incorporates the view of the patient regarding the effect of an intervention. [25] Therefore, the HRQoL is not only clinically valuable, but it could also contribute in the decision process when a therapy needs to be selected. In situations where patients may not gain benefits in terms of traditional end points, such as survival or disease-free survival it is often possible to see significant changes in HRQoL. [26]

Furthermore, patients who suffer from the same disease could have a different perception of how the disease has impacted their life. For example, some patients may experience depression while others do not. Therefore, the HRQoL is an important measure to take into account. The higher the quality of life is rated, the less impact the disease has on the patient's life. In this case the objective measure of the severity of the disease says little about the subjective experience of the patient's positive and negative effects. There are different validated questionnaires available to measure the quality of life in rectal cancer patients of which some can be found further in this chapter. [27]

Functional outcome

In terms of outcome after a surgery of rectal cancer, functional outcome is the type of outcome that is used to measure the different functions of the body after surgery. There are several

functional outcomes taken into account. These functional outcomes are: Lower Anterior Resection Syndrome (LARS), bowel function, anorectal function after stoma closure, bladder function, sexual function, interest in sexual intercourse, erection problems, morbidity, anastomotic leakage, metastases. [10] These functional outcomes could impact the perceived (overall) quality of life of the patient. [28, 29]

Patient reported functional outcome

Lower Anterior Resection Syndrome

Although the survival of rectal cancer patients has improved over the years, problems in functional outcome are experienced due to nerve damage. Since the TME became the golden standard, the presence of Lower Anterior Resection Syndrome (LARS) has increased. LARS includes feces and flatus incontinence, urgency, diarrhea and clustering of bowel movements. There are different possible expressions of LARS. The patient experiences obstruction in defecation, urgency and incontinence or a combination of those patterns. [30, 31]

Although LARS is a possible consequence of a lower anterior resection and therefore of a TME, symptoms of major LARS were also found to be present in 15 percent of a Dutch reference population. [32]

There are multiple validated questionnaires available to measure the functional outcome through LARS, urinary and sexual functions in rectal cancer patients.

Clinical outcome

Clavien-Dindo Classification

The Clavien-Dindo Classification (CDC) is a standardized clinical outcome system that brought a worldwide consensus to the grading, definition and registration of post-operative complications. The CDC is a clinical outcome that has been validated and is widely used in scientific research. This classification consists of seven different grades of complications, where the score is linked to severity of the complication through the therapy which is required to correct a certain adverse event. The higher the severity of the complication, the higher the grade following the CDC. [33]

A patient may experience more than one complication, of which only the most severe one is assessed through the CDC. This approach leads to clarity in both registration and investigation of the complications. [34]

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

**brain hemorrhage, ischemic stroke, subarrachnoidalbleeding,but excluding transient ischemic attacks (TIA);IC: Intermediate care; ICU: Intensive care unit.*

Figure 4: The Clavien-Dindo Classification grades with the definitions [35]

Questionnaires

EQ-5D-3L

This questionnaire evaluates the health related quality of life based on five different dimensions, namely mobility, self-care, activity, pain and anxiety. Each of these aspects can be scored by selecting one of the five answer boxes. These answers are based on the Likert scale. All together, these answers generate an overall score.

Furthermore, the EQ-VAS is included, which lets patients visualize their health status with an analogue scale. The minimal value on this scale is 0 which represents the worst health status and the maximal score is 100 which embodies the best possible health status. [27]

EORTC-QLQ C30

The EORTC-QLQ-C30 is a questionnaire designed by the European Organization for the Research and Treatment of Cancer (EORTC). The questionnaire is specifically designed for cancer patients and former cancer patients and uses three different scales. First of all, a functional scale for 5 items. The functional scale measures for example the function of the physique and the function of the cognitive and social aspect. This is then followed by a symptom scale to score 9 aspects which, on the other hand, contains questions regarding fatigue and financial troubles among other symptoms. At last, there is a global indication of health status or the quality of life incorporated. [28]

EORTC-QLQ-CR29

The EORTC-QLQ-CR29 is a questionnaire specifically constructed for and validated through patients with cancer situated in the intestines. The questionnaire is designed to complement the EORTC-QLQ-C30 and uses, similar to the EORT-QLQ-C30, a functional scale as well as a symptom scale. The functional scale measures for example the anxiety and sexual interest of the patient. The symptom scale on the other hand contains questions regarding the loss of hair and abdominal pain. This questionnaire consists of 29 items in scales regarding urinary frequency, blood/mucus in stool, stool frequency and body image. Furthermore, single items were scored based on the patient's sex and on whether the patient has a stoma. [29]

Lower Anterior Resection Syndrome score

The Lower Anterior Resection Syndrome (LARS) score is a short questionnaire to quickly assess the presence of LARS. The questionnaire consists of five questions covering flatus incontinence, liquid stool incontinence, bowel frequency, clustering of stools and urgency as tools for measuring the rectal and bowel function after surgery for rectal cancer. To each of the answer possibilities a score is assigned. Eventually, the combination of these scores indicate the extent in which LARS is present. [36]

There are three different outcome possibilities: no LARS, which is identified with a score between 0 and 20, minor LARS with a score from 21 to 29 scores and major LARS when a number between 30 and 42 is scored.

International Prostate Syndrome Score

The International Prostate Syndrome Score (IPSS) evaluates the presence of any urinary symptoms in men through seven different items. For every item, the frequency of the symptom is discussed. The answers are scored on a six point Likert scale, which are then equally summed up to a total score. There are three different categories for the total score. When 0-7 points are scored, the male experiences none or minor issues. A score from 8 to 19 indicates that the male experiences moderate problems and a score between 20 and 35 shows a severe dysfunction of the urinary function. Additionally, a question regarding the experienced quality of life is incorporated. This

question refers to the feelings of the male, if his urinary function remains the same for the rest of his life. [37]

Female Sexual Function Index

The Female Sexual Function Index (FSFI) is a questionnaire of 19 items that assesses different aspects being sexual desire, arousal and penetration. The desire share contains two questions, the arousal segment contains 14 questions and the penetration aspect contains three questions. All of the questions had multiple choice answers based on the Likert scale. [38]

Method

Study design

This research compares the quality of life and functional outcome after different types of TME techniques for curative treatment of rectal carcinoma. These techniques include the laparoscopic TME, TaTME, traditional robotic TME and Nerve Sparing TME. This research is executed through a combination of self-assessment by patients and data collection from the electronic patient file

Due to limited time for the execution of this study, few patients were included for the prospective section and data for the Nerve Sparing TME group is very limited. Therefore, the focus of the interpretation of the results lie on the retrospective cohorts and the prospective part is not included in the method section. However, it can be found as appendix H in the back of this paper. From this point, the report will cover the retrospective part of the study and the term robot is used to describe the traditional robot-assisted technique.

Participants

This research includes three patient groups. The first patient group consists of patients that experienced a laparoscopic TME. The second patient group consists of patients that have undergone transanal TME and the third group is composed of patients that underwent robot-assisted TME. In all groups patients received standard care following the Dutch protocols for rectal cancer care and surgery took place with curative intention for rectal cancer. Furthermore, patients were only selected if their tumor was situated in the rectum according to the new rectum definition.

Laparoscopic approached patients

This patient group consists of patients who underwent laparoscopic TME between January 2010 and June 2012. The surgeries were performed by three different surgeons. After the placement of a wound protector, all specimens were extracted through an umbilical incision.

Inclusion criteria

- Patients with rectal tumors, according to the new rectum definition.
- Patients who underwent laparoscopic surgery for rectal cancer with curative intention at least twelve months ago.
- If patients received a temporary ileostomy, this has to be reversed at least six months ago.

Exclusion criteria

- The patient was excluded if he or she has been approached in any other way than laparoscopically.
- The patient underwent surgery for benign tumors.
- The patient received other care than standard care.

Transanally approached patients

This patient group consists of patients that underwent a TaTME after its introduction in March 2012 at the Gelderse Vallei hospital in Ede. All patients were operated by a single surgeon. In the first patients, the specimen was transanally extracted, while it was removed through the ileostomy site in the second group of patients.

Inclusion criteria

- Patients with rectal tumors, according to the new rectum definition.
- Patients who underwent transanal surgery for rectal cancer with curative intention at least twelve months ago.
- If patients received a temporary ileostomy, this has to be reversed at least six months ago.

Exclusion criteria

- The patient was excluded if he or she has been approached in any other way than transanally.
- The patient underwent surgery for benign tumors.
- The patient received other care than standard care.

Robot-assisted approached patients

This patient group consists of patients that underwent a robot-assisted TME in the Rijnstate hospital from February 2016 until the tenth of June 2019. Patients who met the inclusion criteria were collected in a research list in the electronic patient file system. Patients were contacted by telephone in order to ask them to consider participation in the study and retrieve their (e-mail) address if they were interested. The information regarding this study, questionnaires as described in the data collection section and informed consent then were sent either digitally or on paper to this address.

Inclusion criteria

- Patients with rectal tumors, according to the new rectum definition.
- Patients who underwent robot-assisted surgery for rectal cancer with curative intention at least twelve months ago.
- If patients received a temporary ileostomy, this has to be reversed at least six months ago.

Exclusion criteria

- The patient was excluded if he or she has been approached in any other way than robot-assisted.
- The patient underwent surgery for benign tumors.
- The patient received other care than standard care.

Data collection

Data for the laparoscopic and transanal group was collected in earlier research and received in a database. [11] Patients were excluded of this database if they did not meet the inclusion criteria.

Data for the robot-assisted group was collected during this study. The robot-assisted patients were reached through telephone and asked if they preferred the questionnaires digitally or physically. If the patient could not be reached, questionnaires were sent on paper to their known home address. An Excel sheet provided an overview through noting the choice of the patient, whether they needed to be sent a reminder and if they did or did not respond. Regardless of the manner the patient preferred, (RM). If patients chose to complete the questionnaires digitally, the data was automatically stored in RM. When patients completed the questionnaires on paper, these were scanned and stored to a folder in the secured system of Rijnstate. Research Manager was also used to export the data regarding the questionnaires into SPSS, where the data was analyzed. The baseline characteristics and experienced complications were collected from the electronic patient file. A database was composed for the questionnaire outcomes, the baseline characteristics of the patients and the possible complications they experienced.

The outcome measures were assessed by validated questionnaires and retrieved from the electronic patient file as shown in Table 2. In all groups, patients received the study information, questionnaires and informed consent at least six months after stoma reversal. The questionnaires were available on paper as well as in a digital manner. All questionnaires were prepared in RM and were available through a link, which was sent via email to patients who desired to complete the questionnaires digitally. Furthermore, the questionnaires were sent to the patient's home addresses if they chose to fill them in on paper. Therefore, all patients we're able to participate from their home.

Since the FSFI was newly included, the laparoscopic and transanal group lack these results and therefore these outcomes cannot be compared. However, it is expected that these outcome measures will help to gain insight in the effects of the traditional robot-assisted TME and will be useful in future studies.

The patient groups will not only be compared through the results of earlier mentioned questionnaires, but also on baseline characteristics and complications collected from the electronic patient file.

All patients were sent the questionnaires at the same point in time. This led to a diversity between 6.6 and 78 months after stoma reversal which is usually executed approximately 3 months post-operative.

Table 2: A visualization of the outcome measures that are collected per technique and in which manner this takes place.

	Laparoscopic	Traditional robot assisted	Transanal	Method	
Outcome measure				Questionnaire	Electronic patient file
Quality of life					
EQ-5D-3L	X	X	X	X	
EORTC-QLQ-C30	X	X	X	X	
EORTC-QLQ-CR29	X	X	X	X	
Functional outcome					
LARS score	X	X	X	X	
IPSS	X	X	X	X	
FSFI		X		X	
Baseline characteristics	X	X	X		X
Complications	X	X	X		X

Analysis

Manuals

The outcomes of the EQ-5D-3L, EORTC-QLQ-C30 and FSFI were constructed through the manuals that come with the questionnaires. [38, 39, 40] However, the index score of the EQ-5D-3L could not be calculated in this manner. This calculation was executed through the Index calculator provided by EuroQoL. Of these outcomes, the mean was obtained for the different TME groups. These scores were multiplied by 100 to present the index score.

Since a manual of the EORTC-QLQ-CR29 lacked, we calculated the domain values with the guidance of a syntax provided be a researcher with focus on this subject.

Statistical analysis

Data is presented as means or categories, with p-values mostly determined by the Student t-test and Chi-Square test. If the Chi-Square was not applicable, the Fisher's Exact test was used. The large amount of tests executed on the EORTC-QLQ-CR29 and the EORTC-QLQ-C30 was corrected with aid of the Bonferroni correction.

The different groups were compared on baseline characteristics, the outcomes of the questionnaires, with exception of the FSFI, and on complications according to the CDC. These were presented in tables.

Results

Baseline characteristics

In the robot-assisted group, 88 patients were eligible. 74 were selected of whom 52 responded (70.3%) (figure 5). The response rate was 70.3%, since 52 out of 74 patients responded. This group consists of 39 males and 13 females, respectively 75% and 25%. In the laparoscopic and transanal group questionnaires of 54 patients in total were collected. [41] The laparoscopic group consists of 24 patients, while the transanal group consists of 25 patients (Table 3). The laparoscopic group consists of 17 male patients and 7 female patients, while the transanal group consists of 16 male patients and 9 female patients. Although no significant differences were seen in the gender between the three groups, a significant difference in mean age is observed in the laparoscopic group compared to the robot-assisted group (62.0 and 67.3 p=0.018). In addition, significant differences were found in mean tumor height in both the laparoscopic and transanal group compared to the robot-assisted group. Of which the means are 7.3, 7.0 and 9.2 centimeter from anal verge respectively (lap-robot; p=0.003 and tat-robot; 0.001).

Also, significant differences were detected in neoadjuvant therapy comparing both the laparoscopic and transanal with the robot-assisted group (p=0.000 and 0.001). The follow-up after surgery and the follow-up after stoma reversal both showed significant differences when comparing the outcomes of the laparoscopic and transanal group with the robot-assisted group. The means of the laparoscopic group were 66.0 months and 54.3 months respectively. These are higher than the means in the robot group, which are 29.9 months and 27.9 months. Follow-up times were significantly shorter in the transanal group with means of 15.8 and 16.1 months.

Furthermore, the anastomosis type differs significantly between the transanal and the robot-assisted group. In the TaTME group, end-to-end anastomosis were used until the change of the extraction site, which resulted in 22 patients with an end-to-end anastomosis and 4 patients with a side-to-end anastomosis. In the robot-assisted group 42 patients had a side-to-end anastomosis and one has an end-to-end.

Complications and pathology

In terms of complications, a significant difference in the CDC was noted in the laparoscopic and robot-assisted group, favoring the robot-assisted group (p=0.001).

Regarding pathology, no differences were seen between the three groups relative to tumor stage or outcomes. For all 27 patients in the TaTME group a complete mesorectum was noted. In the laparoscopic group a nearly complete mesorectum was noted in 2 patients. For the robot-assisted group 39 patients a complete mesorectum was reported, while in 7 patients a nearly complete mesorectum was noted and for 6 patients an incomplete mesorectum was reported. No involvement of the circumferential resection margin (CRM) or recurrence was detected in laparoscopic and transanal patients. In the robot group 2 patients reported a positive CRM and 7 patients experienced recurrence of which 1 local and 6 were distal. These differences proved not to be significant.

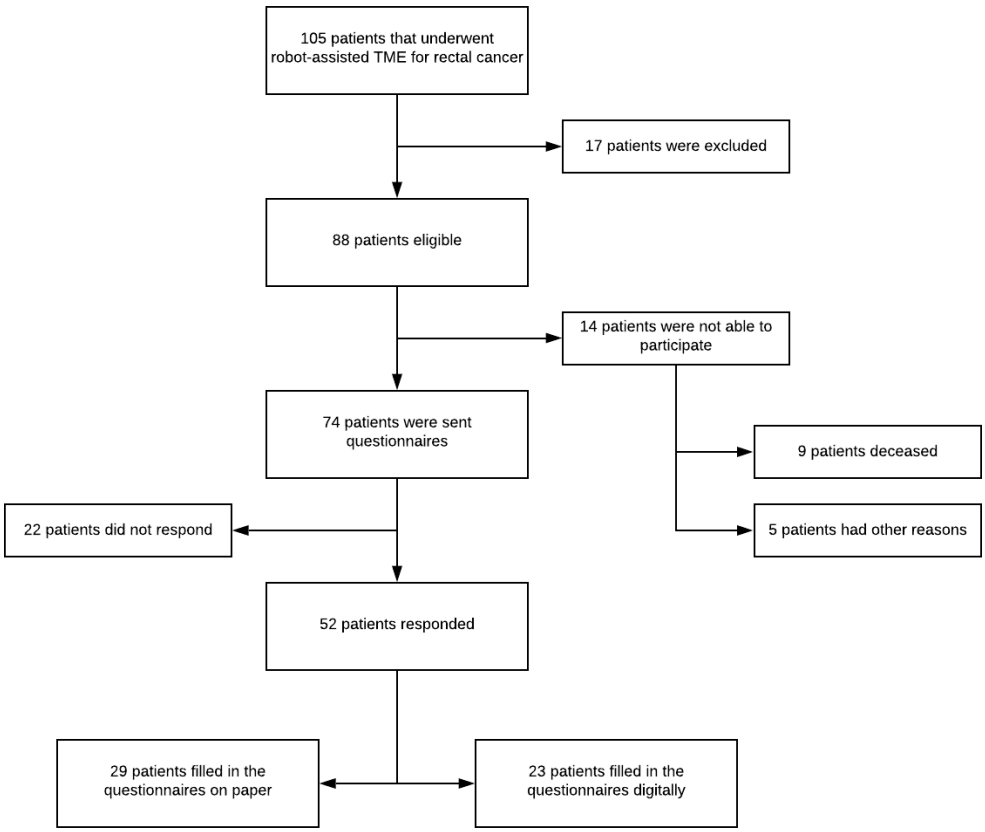


Figure 5: Inclusion process of the robot group

Table 3: Baseline characteristics

	Laparoscopic (n=24)	Transanal (n=25)	Robot-assisted (n=52)	P[1]	P[2]
Age in years μ (SD)	62.0 (7.8)	68.5 (9.2)	67.3 (10.8)	0.018	0.615
Sex n (%)				0.782	0.420
Female	7 (29.2)	9 (36.0)	13 (25.0)		
Male	17 (70.8)	16 (64.0)	39 (75.0)		
BMI μ (SD)	25.8 (2.1)	27.2 (4.6)	26.4 (4.5)	0.422	0.468
ASA Score n (%)				0.000	0.035
1	12 (50.0)	5 (20.0)	3 (5.8)		
2	11 (45.0)	19 (76.0)	36 (69.2)		
3	1 (5.0)	1 (4.0)	12 (23.1)		
4	0 (0.0)	0 (0.0)	1 (1.9)		
TNM stage MRI n (%)					
T				0.546	0.628
- 1	0 (0.0)	1 (4.0)	2 (3.9		
- 2	5 (55.6)	6 (24.0)	15 (29.4)		
- 3	4 (44.4)	16 (64.0)	33 (64.7)		
- 4	0 (0.0)	2 (8.0)	1 (2.0)		
N				0.105	0.837
- 0	5 (55.6)	20 (80.0)	38 (73.1)		
- 1	1 (11.1)	4 (14.0)	10 (19.2)		
- 2	3 (33.3)	1 (4.0)	4 (7.7)		
M				1.000	1.000
- 0	9 (100)	25 (100.0)	50 (96.2)		
1	0 (0.0)	0 (0.0)	2 (3.8)		
Tumor height in cm (anal verge) μ (SD)	7.3 (2.8)	7.0 (2.8)	9.2 (2.4)	0.003	0.001
LOREC n (%)				0.091	0.000
Yes	6 (25.0)	13 (52.0)	5 (9.6)		
No	18 (75.0)	12 (48.0)	47 (90.4)		
Neoadjuvant therapy n (%)				0.000	0.002
None	3 (12.5)	8 (32.0)	33 (63.5)		

RT CRT	17 (70.8) 4 (16.7)	16 (64.0) 1 (4.0)	11 (21.2) 8 (15.4)		
Anastomosis type n (%) End-to-end Side-to-end	 0 (0.0) 24 (100.0)	 22 (85.2) 3 (14.8)	 1 (2.0) 42 (82.4)	0.064	0.000
CDC n (%) Non severe (0-II) Severe (IIIa-V)	 18 (75.0) 6 (25.0)	 22 (88.0) 3 (12.0)	 51 (98.1) 1 (1.9)	0.020	0.316
Stoma n (%) No Temporary Definitive	 2 (8.3) 22 (91.7) 0 (0.0)	 3 (12.0) 22 (88.0) 0 (0.0)	 11 (21.2) 34 (65.4) 7 (13.5)	0.043	0.084
TNM stage PA n (%) T - 0 - 1 - 2 - 3 - 4 N - 0 - 1 - 2 M - No - Yes	 3 (12.5) 3 (12.5) 8 (33.3) 10 (41.7) 0 (0.0) 18 (75.0) 4 (16.7) 2 (8.3) 23 (95.8) 1 (4.2)	 0 (0.0) 4 (16.0) 11 (44.0) 10 (40.0) 0 (0.0) 22 (88.0) 3 (12.0) 0 (0.0) 25 (100.0) 0 (0.0)	 4 (7.7) 7 (13.5) 17 (32.7) 23 (44.2) 1 (1.9) 39 (79.6) 7 (14.3) 3 (6.1) 51 (98.1) 1 (1.9)	 0.950 0.735 0.535 	 0.650 0.676 1.000
CRM Involvement n (%) No Yes	 24 (100.0) 0 (0.0)	 25 (100.0) 0 (0.0)	 49 (96.1) 2 (3.9)	1.000	1.000
Quality mesorectum n (%) Incomplete Nearly complete Complete	 0 (0.0) 2 (8.3) 21 (87.5)	 0 (0.0) 0 (0.0) 25 (100.0)	 6 (11.5) 7 (13.5) 39 (75.0)	0.140	0.017
Recurrence n (%) No Local Distant	 24 (100.0) 0 (0.0) 0 (0.0)	 25 (100.0) 0 (0.0) 0 (0.0)	 45 (86.5) 1 (1.9) 6 (11.5)	0.168	0.169
Follow-up time questionnaire after surgery in months μ (SD)	66.0 (18.4)	15.8 (12.6)	29.9 (12.2)	0.001	0.047
Follow-up time questionnaire after stoma reversal in months μ (SD)	54.3 (10.5)	16.1 (9.9)	27.9 (10.4	0.000	0.000

1 Comparison of the laparoscopic group with the robot-assisted group. 2 Comparison of the transanal group with the robot-assisted group.

Patient reported outcomes

Quality of life

EQ-5D-3L

The index values were both significantly different when comparing the laparoscopic and transanal group with the robot-assisted group (p=0.04 and p=0.019). The question regarding activity was significantly different, favoring the laparoscopic group (p=0.024) (Table 4). Another difference was observed in pain, which showed a significant difference in the transanal group compared to the robot-assisted group (p=0.045). The other outcomes were comparable between the three groups.

EORTC-QLQ-CR29

At first significant differences were observed in hair loss between the laparoscopic group and the robot-assisted group (Table 9). Comparing the robot-assisted group with the transanal group also showed a significant difference regarding embarrassment. However, after applying the Bonferroni correction, no significance could be detected for either of these scales.

EORTC-QLQ-C30

When comparing the laparoscopic group with the robot-assisted group, the functional symptoms fatigue (p=0.042), nausea and vomiting (p=0.025), pain (p=0.005) and diarrhea (p=0.013) seemed to be significant (Table 5). Regarding functional scales, this also applied to role functioning (p=0.033) and social functioning (p=0.004). Comparison of the transanal group and the robot-assisted group led to suspected differences regarding nausea and vomiting (p=0.006) and emotional functioning (p=0.033)

The execution of the Bonferroni correction contradicted some of these findings and showed that appetite loss and financial difficulties were not significantly different between the laparoscopic and robot-assisted group. It also detected no difference in emotional function for the robot group compared to the laparoscopic group as well as the transanal group.

Functional outcome

LARS score

Patients in all three groups reported LARS, but there was no significant difference between the severity of the diagnosis in the laparoscopic and transanal group compared to the robot-assisted group (Table 6). The mean LARS questionnaire scores were also equivalent between the three groups (24.0 vs. 27.7 vs. 27.4, respectively; p=0.615 and p=0.370). However, in some subscales significant differences were detected. The first difference was found in the incontinence for liquid stools between the transanal and robot-assisted group (p=0.028). Secondly, the clustering of stools varied between the laparoscopic and robot-assisted group (p=0.01).

IPSS

No significant differences were seen between the three groups comparing the mean IPSS scores (Table 7). Also, no significant differences were when comparing the IPSS diagnosis of the laparoscopic and transanal group with the robot-assisted group (p=0.775 and p=0.882 respectively). Although, there are some differences in terms of severity in several domains among the three groups, no significant differences were observed.

FSFI

Since the FSFI was newly included, the laparoscopic and transanal group lack these results and therefore these outcomes cannot be compared. However, it is expected that these outcome measures will help to gain insight in the effects of the traditional robot-assisted TME and will be useful in future studies.

10 female patients filled in the FSFI questionnaire, of which 4 completed the questionnaire (Table 10). Since this questionnaire is not used in the laparoscopic and transanal groups, no tests could be performed.

Table 4: EQ-5D-3L

Scale	Laparoscopic (n=24)	Transanal (n=25)	Robot-assisted (n=52)	P[1]	P[2]
EQ-5D VAS µ (SD)	79.2 (15.4)	76.1 (14.0)	75.4 (16.5)	0.365	0.867
EQ-5D index µ (SD)	93.9 (10.1)	91.0 (9.0)	84.8 (12.6)	0.004	0.019
Mobility n (%)				0.150	1.000
Level I	21 (87.5)	18 (72.0)	36 (70.6)		
Level II	3 (12.5)	7 (28.0)	15 (29.4)		
Level III	0 (0.0)	0 (0.0)	0 (0.0)		
Self-care n (%)				0.653	1.000
Level I	22 (91.7)	24 (96.0)	48 (94.1)		
Level II	2 (8.3)	1 (4.0)	3 (5.9)		
Level III	0 (0.0)	0 (0.0)	0 (0.0)		
Activity n (%)				0.024	0.260
Level I	19 (82.6)	17 (68.0)	27 (52.9)		
Level II	4 (17.4)	7 (28.0)	23 (45.1)		
Level III	0 (0.0)	1 (4.0)	1 (2.0)		
Pain/discomfort n (%)				0.055	0.045
Level I	18 (75.0)	19 (76.0)	25 (48.1)		
Level II	6 (25.0)	6 (24.0)	25 (48.1)		
Level III	0 (0.0)	0 (0.0)	2 (3.8)		
Anxiety/depression n (%)				0.179	0.432
Level I	21 (87.5)	21 (84.0)	38 (74.5)		
Level II	3 (12.5)	4 (16.0)	13 (25.5)		
Level III	0 (0.0)	0 (0.0)	0 (0.0)		

Level I indicates no problem, Level II indicates some problems and Level III indicates extreme problems. 1 Comparison of the laparoscopic group with the robot-assisted group. 2 Comparison of the transanal group with the robot-assisted group.

Table 5: EORTC-QLQ-C30

	Laparoscopic (n=24)		Transanal (n=25)		Robot-assisted (n=52)			
Scale	µ (SD)	M	µ (SD)	M	µ (SD)	M	P [1]	P [2]
Symptom[A]								
Fatigue	14.3 (15.5)	0	25.9 (20.4)	1	28.0 (24.8)	6	0.042*	1.000
Nausea and vomiting	2.8 (8.0)	0	3.3 (10.8)	0	13.9 (21.3)	4	0.025*	0.033*
Pain	4.1 (10.1)	0	13.2 (22.5)	1	19.8 (20.8)	4	0.005*	0.520
Dyspnoea	11.1 (23.4)	0	13.9 (21.8)	1	16.0 (19.2)	0	1.000	1.000
Insomnia	15.3 (26.0)	0	16.7 (22.0)	1	21.6 (25.7)	1	0.930	1.000
Appetite loss	2.8 (9.4)	0	8.0 (19.9)	0	12.5 (21.3)	4	0.121	0.997
Constipation	11.1 (18.8)	0	9.3 (18.1)	0	14.3 (20.4)	3	1.000	0.909
Diarrhoea	4.2 (11.3)	0	17.3 (29.1)	0	16.7 (24.2)	3	0.013*	1.000
Financial difficulties	2.8 (9.4)	0	16.0 (27.4)	0	13.9 (21.6)	4	0.114	1.000
Global health status	83.7 (15.6)	0	79.7 (15.2)	1	80.8 (13.9)	3	1.000	1.000
Functional[B]								
Physical functioning	88.9 (14.5)	0	83.5 (15.3)	0	84.0 (18.3)	2	0.725	1.000
Role functioning	89.5 (23.0)	0	81.3 (23.2)	0	74.4 (24.4)	0	0.033*	0.692
Emotional functioning	89.2 (12.9)	0	89.0 (13.5)	1	79.5 (20.1)	6	0.089	0.095
Cognitive functioning	90.3 (13.9)	0	88.7 (19.7)	0	82.0 (18.3)	3	0.187	0.381
Social functioning	91.7 (14.7)	0	86.7 (13.6)	0	74.5 (25.7)	5	0.004*	0.058

*A Symptom scale: A higher score indicates worse symptoms/problems. This scale ranges from 0-100. B Functional scale and global health status: A higher score indicates higher quality. This scale ranges from 0-100. 1 Comparison of the laparoscopic group with the robot-assisted group. 2 Comparison of the transanal group with the robot-assisted group. * Significant after the Bonferroni correction*

Table 6: LARS

Scale	Laparoscopic (n=24)	Transanal (n=25)	Robot-assisted (n=45)	M	P[1]	P[2]
Incontinence for flatus n (%)				1	0.403	0.600
Never	1 (4.2)	2 (8.0)	7 (15.9)			
<Once a week	7 (29.2)	9 (36.0)	12 (27.3)			
Once a week	16 (66.7)	14 (56.0)	25 (56.8)			
Incontinence for liquid stools n (%)				1	0.945	0.028
Never	10 (41.7)	3 (12.0)	16 (36.4)			
<Once a week	9 (37.5)	10 (40.0)	19 (43.2)			
≥Once a week	5 (20.8)	12 (48.0)	9 (20.5)			
Frequency bowel n (%)				1	0.155	0.352
1-3 times a day	11 (45.8)	12 (48.0)	7 (15.9)			
4-7 times a day	11 (45.8)	8 (32.0)	20 (45.5)			
>7 times a day	0 (0.0)	2 (8.0)	15 (34.1)			
<Once a day	2 (8.3)	3 (12.0)	2 (4.5)			
Clustering of stools n (%)				2	0.011	0.610
Never	5 (20.8)	5 (20.0)	8 (18.6)			
<Once a week	10 (41.7)	5 (20.0)	5 (11.6)			
≥Once a week	9 (37.5)	15 (60.0)	30 (69.8)			
Urgency n (%)				3	0.240	0.901
Never	10 (41.7)	5 (20.0)	11 (25.6)			
<Once a week	9 (37.5)	10 (40.0)	15 (34.9)			
≥Once a week	5 (20.8)	10 (40.0)	17 (39.5)			
LARS μ (SD)	24.3 (11.1)	28.8 (13.1)	27.4 (12.6)		0.615	0.370
No LARS n (%)	9 (37.5)	6 (24.0)	12 (30.0)		0.319	0.727
Minor LARS n (%)	7 (29..2)	3 (12.0)	7 (17.5)			
Major LARS n (%)	8 (33.3)	16 (64.0)	21 (52.5)			

No LARS score: 0-20, minor LARS score: 21-29 and major LARS score: 30-42. 1 Comparison of the laparoscopic group with the robot-assisted group. 2 Comparison of the transanal group with the robot-assisted group.

Table 7: IPSS

Scale	Laparoscopic (n=15)	Transanal (n=14)	Robot-assisted (n=38)	M	P[1]	P[2]
Incomplete emptying n (%)				1	0.617	0.621
Not at all	8 (53.3)	6 (50.0)	14 (37.8)			
Less than 1 time in 5	6 (40.0)	2 (16.7)	6 (16.2)			
Less than half the time	1 (6.7)	4 (33.3)	9 (24.3)			
About half the time	0 (0.0)	0 (0.0)	6 (16.2)			
More than half the time	0 (0.0)	0 (0.0)	2 (5.4)			
Almost always	0 (0.0)	0 (0.0)	0 (0.0)			
Frequency n (%)				2	0.933	0.970
Not at all	5 (33.3)	5 (41.7)	13 (36.1)			
Less than 1 time in 5	5 (33.3)	3 (25.0)	6 (16.7)			
Less than half the time	3 (20.0)	2 (16.7)	9 (25.0)			
About half the time	1 (6.7)	2 (16.7)	5 (13.9)			
More than half the time	0 (0.0)	0 (0.0)	2 (5.6)			
Almost always	1 (6.7)	0 (0.0)	1 (2.8)			
Intermittency n (%)				0	0.168	0.249
Not at all	6 (40.0)	6 (50.0)	16 (42.1)			
Less than 1 time in 5	5 (33.3)	0 (0.0)	9 (23.7)			
Less than half the time	1 (6.7)	4 (33.3)	5 (13.2)			
About half the time	2 (13.3)	1 (8.3)	2 (5.3)			
More than half the time	1 (6.7)	1 (8.3)	3 (7.9)			
Almost always	0 (0.0)	0 (0.0)	3 (7.9)			
Urgency n (%)				0	0.667	0.616
Not at all	10 (66.7)	3 (25.0)	16 (42.1)			
Less than 1 time in 5	2 (13.3)	4 (33.3)	9 (23.7)			
Less than half the time	1 (6.7)	3 (25.0)	8 (21.1)			
About half the time	0 (0.0)	2 (16.7)	2 (5.3)			

More than half the time	2 (13.3)	0 (0.0)	2 (5.3)			
Almost always	0 (0.0)	0 (0.0)	1 (2.6)			
Weak stream n (%)				0	0.860	0.924
Not at all	6 (40.0)	6 (50.0)	14 (36.8)			
Less than 1 time in 5	5 (33.3)	2 (16.7)	8 (21.1)			
Less than half the time	3 (20.0)	0 (0.0)	5 (13.2)			
About half the time	0 (0.0)	1 (8.3)	2 (5.3)			
More than half the time	0 (0.0)	1 (8.3)	4 (10.5)			
Almost always	1 (6.7)	2 (16.7)	5 (13.2)			
Straining n (%)				0	0.805	0.812
Not at all	12 (70.6)	8 (66.7)	16 (42.1)			
Less than 1 time in 5	2 (11.8)	2 (16.7)	8 (21.1)			
Less than half the time	0 (0.0)	2 (16.7)	8 (21.1)			
About half the time	1 (5.9)	0 (0.0)	2 (5.3)			
More than half the time	0 (0.0)	0 (0.0)	4 (10.5)			
Almost always	0 (0.0)	0 (0.0)	0 (0.0)			
Nocturia n (%)				1	0.095	0.164
Not at all	4 (26.7)	1 (8.3)	5 (13.5)			
Less than 1 time in 5	6 (40.0)	3 (25.0)	15 (40.5)			
Less than half the time	4 (26.7)	6 (50.0)	5 (13.5)			
About half the time	0 (0.0)	1 (8.3)	6 (16.2)			
More than half the time	1 (6.7)	0 (0.0)	4 (10.8)			
Almost always	0 (0.0)	1 (8.3)	2 (5.4)			
Satisfaction n (%)				3	0.196	0.101
Delighted	4 (26.7)	2 (16.7)	3 (7.9)			
Pleased	5 (33.3)	6 (50.0)	8 (21.1)			
Mostly Satisfied	2 (13.3)	3 (25.0)	13 (34.2)			
Mixed	3 (20.0)	0 (0.0)	11 (28.9)			
Mostly Dissatisfied	0 (0.0)	1 (8.3)	3 (7.9)			
Unhappy	0 (0.0)	0 (0.0)	0 (0.0)			
Terrible	1 (6.7)	0 (0.0)	0 (0.0)			
Mild n (%)	10 (66.7)	6 (50.0)	15 (41.7)		0.775	0.882
Moderate n (%)	5 (33.3)	6 (50.0)	18 (50.0)			
Severe n (%)	0 (0.0)	0 (0.0)	3 (8.3)			
IPSS μ (SD)	6.3 (5.4)	8.5 (6.9)	9.9 (7.2)		0.095	0.572

Mild score: 0-7, moderate score: 8-19, severe score: 20-35. 1 Comparison of the laparoscopic group with the robot-assisted group. 2 Comparison of the transanal group with the robot-assisted group

Discussion

This research described the quality of life and functional outcomes after robot-assisted TME for rectal cancer and compared them to the outcomes of the laparoscopic and transanal TME.

This study did not reveal major differences among the different TME groups with respect to quality of life. However, there were significant differences in subscores in both the laparoscopic and transanal group compared to the robot-assisted group on index value and nausea and vomiting, favoring the laparoscopic and transanal approach. Also, significant differences were observed only between the laparoscopic and robot-assisted group regarding subscores, consisting of activity, role and social functioning, fatigue, pain, diarrhea and clustering of stools, where the robot-assisted group scored worse. Significant differences observed between the transanal group and the robot-assisted group were pain/discomfort and incontinence for liquid stools, favoring the transanal group. Based on these results, the robot-assisted TME does not seem to perform significantly better in terms of functional outcome and quality of life.

Comparing the outcomes of this study to literature, proved to be quite challenging, partly caused by major differences in patient groups. [42] Another factor that complicates comparing the outcomes of different studies is the use of different outcome measures. The International Consortium for Health Outcomes Measurement (ICHOM) developed a standardized outcome set for colorectal cancer. [43, 44] Questionnaires are linked to each of these aspects, but this set is barely utilized. This could be caused by the limited coverage of the set regarding functional outcomes.

In literature, a subanalysis of the COLOR II trial also showed no significant differences between the laparoscopic and robot-assisted group regarding urogenital outcome. [45] Conflicting results were seen in some studies including a prospective study with matched cases. The robot-assisted group scored significantly better compared to the laparoscopic group regarding IPSS on short term. [8, 46, 47] In the long term, these differences were no longer found. These findings match the comparison of laparoscopic and robot-assisted TME in this research. The results of the transanal group of this study were also similar to those in literature. [48, 49, 50]

Our study differed in outcomes with literature that compared the robot-assisted TME to the laparoscopic TME in terms of role and social functioning, favoring the robot-assisted group. [7] Furthermore, research showed a significant difference in reported pain, favoring the robot-assisted TME. [51] This is not in line with the findings of our study, where the robot-assisted group experienced greater pain than the laparoscopic group. A possible explanation for these discrepancies might be the many lower tumors in our group. A lower tumor indicates a lower resection which usually results in more problems.

Regarding interpretation of the outcomes of this study there are a few things to consider. First of all, the different TME techniques used in this study are executed in different hospitals. Because differences among hospitals could result in different outcomes, it is important to take this into account. However, as all patients were treated according to the Dutch guidelines, differences between outcomes in hospitals are considered low.

In contradiction to earlier research, this study used the sigmoidal take-off definition to determine whether a patient suffers from rectal cancer. Using this new definition, which is now located at the sigmoidal take-off, only real rectal cancers are included and not distal sigmoidal cancers. Previously, studies often included rectal cancer when a tumor was maximally 15 centimeters proximal from the anal verge. Due to variations in rectum length, this definition did not provide a reliable indication of where the rectum turns into the sigmoid colon. Therefore, patients that did actually suffer from colon cancer instead of rectal cancer could be included in earlier

studies. When comparing this research to other studies, this particular fact should be taken into account, since this is a different patient group. Their tumors are often located lower in the rectum which, as mentioned before, could contribute to a greater expression of problems.

Furthermore, the follow-up time after surgery and the follow-up time after stoma reversal showed major differences in terms of months. The mean follow-up times of the laparoscopic group were double as long as the robot-assisted group. However, the follow-up time of the transanal group was almost half the time period compared to the robot-assisted. The minimal period between the surgery and the data collection is twelve months in all cases for the robot-assisted group. While functional outcomes can alter in the first year after surgery, they hardly change after this period. Therefore, we believe that the difference between the collection within the groups has negligible or no effect on the results in this study.

The collection period between groups differs fairly considering the fact that the first collection took place in December 2015 and the last in June 2020. The surgeries that led to the collected data were performed between January 2010 and December 2019. Due to the fact that there were no significant changes in the Dutch standard care for rectal cancer, such as indication for neo-adjuvant therapy and standards in post-operative care, this variance is less likely to affect the findings of this research.

The first limitation of this study is the lack of pre-operative data. Literature has shown that LARS is present in a considerable part of the reference population, with major LARS observed in 15% of the population. [32] Since there is no knowledge about their pre-operative situation, a part of the findings could be influenced by baseline differences.

Secondly, five relatively novice surgeons started to perform the robot-assisted TME. However, the effect of the learning curve has not been taken into account in this study. The lack of this consideration could negatively influence the outcomes of the robot group and affect the results of the comparison with the laparoscopic and transanal group.

The rectal dissection is a difficult procedure of which literature emphasized the disadvantages of this approach that sometimes affect the quality of the specimen. Therefore, the expertise of the surgeon has a major impact on the oncological outcomes. This also applies for the transanal and robot-assisted TME approach. The learning curve effect showed an improvement in postoperative outcomes and a decrease in complications after the first 40 transanal patients. [50] Since the effect of the learning curve is not taken into account in this study, patients that were operated during the learning curve might negatively influence the outcomes. The results of the robot-assisted group could therefore be slightly underestimated.

In conclusion, this study showed only significant differences between the laparoscopic, transanal and robot-assisted group in an index score for quality of life. No significant differences were seen in terms of functional outcomes, although differences were seen in subscores. Therefore, the robot-assisted approach seems to be a reasonable alternative approach in the treatment of rectal cancer.

To confirm these findings, further research is recommended to acquire insight in the effect of the learning curve of the robotic procedures on the outcomes. Secondly, pre-operative and several post-operative measurements need to be included in order to correctly assess the impact of surgery by looking at the alteration over time and prevent contribution of coincidence. Besides, expansion of the ICHOM set for colorectal cancer is advised in order to enable appropriate comparison between different studies, especially regarding their functional outcome measures.

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Appendices

Appendix A: Planning

Onderdeel Week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Voorbereidende fase															
Artikelen lezen		X													
Plan van aanpak maken		X													
OK's en MDO bijwonen			X												
Literatuuronderzoek			X	X	X										
Afspraak met verpleegkundigen				X	X										
Afspraak met Bianca over systeem vragenlijsten					X										
Afspraak met begeleider universiteit				X			X		X		X		X		X
Afspraak met Harald over lopende studies GIO-poli					X										
Concept onderzoeksvoorstel inleveren						X									
Onderzoeksvoorstel presenteren							X								
Feedback onderzoeksvoorstel verwerken							X								
Uitvoerende fase / onderzoeksfase															
Database maken							X								
Database testen en verbeteren								X	X	X	X	X	X	X	X
Dataverzameling								X	X	X	X	X	X	X	X
Data verwerken								X	X	X	X	X	X	X	X
Data analyse / statistische analyse											X	X	X	X	X
Schrijffase															
Bronnen bijhouden		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Introductie			X	X											
Theoretisch kader				X	X										
Methode					X	X									
Resultaten															
Conclusie				X											X
Discussie				X	X										X
Abstract					X	X									
Scriptie evalueren met begeleider						X	X								
Groen licht gesprek															
Feedback verwerken en presentatie voorbereiden															
Conceptverslag inleveren															
Presentatie															
Feedback verwerken en definitief verslag inleveren															

Oranje: deadlines vanuit de UT

Appendix B: Information leaflet GIO nurses

Functionele uitkomsten na endeldarmchirurgie (FUNE)

Inleiding

Wij zijn Jan-Willem Bauhuis en Iris Hulshof, derdejaars bachelorstudenten Gezondheidswetenschappen aan de Universiteit Twente (UT) in Enschede. Voor de afronding van onze bachelor doen wij onderzoek naar de kwaliteit van leven en functionele klachten na chirurgische behandeling van rectumtumoren met behulp van de Da Vinci Xi robot. Ons onderzoek zal een periode van 20 weken omvatten.

Doel van het onderzoek

In de afgelopen jaren zijn de operatietechnieken voor de behandeling van rectumcarcinomen aanzienlijk verbeterd. Een gevolg hiervan is dat de focus op overleving verschuift naar het beperken van post-operatieve klachten en het verhogen van de kwaliteit van leven. Daarbij wordt beoogd dat de patiënt zoveel mogelijk functies behoudt na de operatie. De inzet van de Da Vinci robot zou hierbij kunnen helpen. Deze robot maakt gebruik van een 10x vergroting en 3D beelden. Hiermee kan in theorie zenuwsparend worden geopereerd, doordat de marges rondom de tumor beter ingeschat zouden kunnen worden en meer gezond weefsel behouden kan worden. Zenuwen in het nauwe bekken kunnen hiermee beter gespaard worden. Dit zou mogelijk kunnen leiden tot minder klachten op het gebied van ontlasting, seksualiteit en urineren na een operatie. Echter, is er nog onvoldoende bewijs dat dit daadwerkelijk zo is.

Achtergrondinformatie

Rectumcarcinoom heeft een incidentie van zo'n 50-60 per 100.000 personen/jaar. Samen met coloncarcinoom staat dit op de derde plaats van meeste voorkomende maligne tumoren. Patiënten die niet worden behandeld met lokale verwijdering van de tumor, worden chirurgisch behandeld door middel van
laparoscopische totaal mesorectale excisie (TME), al dan niet voorafgegaan door (chemo) radiotherapie.

Probleem

Langs het rectum lopen veel zenuwbanen die betrokken zijn bij de functie van de bekkenbodem en in het bekken gelegen organen. De operatieve behandeling van rectumcarcinoom is enkel zinvol als al het tumorweefsel wordt verwijderd (radicale chirurgie). Op dit moment heeft een groot aantal patiënten functionele klachten (mictie- en defecatiestoornissen en/of seksuele disfunctie) na de operatie door zenuwschade.

Door inzet van de operatierobot wordt de laparoscopische operatie verrijkt met 3D beelden en een 10x vergroting en kan mogelijk zenuwsparend worden geopereerd. Op deze manier is er, naast radicale tumorchirurgie, een betere identificatie en behoud van zenuwstructuren mogelijk, waardoor er vermoedelijk minder functionele klachten na de operatie zijn.

Opzet onderzoek

Tijdens het onderzoek zal gebruik worden gemaakt van vragenlijsten met betrekking tot de kwaliteit van leven en de functionele klachten. Patiënten zal worden gevraagd deze in te vullen 1 week voor de operatie en 1, 3, 6 en 12 maanden na de operatie. Dit doen wij door patiënten tijdens bezoek aan de polikliniek te benaderen en de vragenlijsten digitaal in te laten vullen.
Deze data zullen wij vervolgens verzamelen en gaan analyseren, om dit vervolgens te vergelijken met data van operaties die uitgevoerd zijn zonder de Da Vinci robot.

Andere onderzoeken

Op dit moment lopen er ook andere studies op uw afdeling. Dit zijn de COLON en PLCRP studie. HIer zijn wij ons zeker van bewust. In overleg met de coördinator van de oncologische onderzoeken is ervoor gekozen dat de FUNE studie bij nieuwe patiënten voorrang krijgt op de COLON en PLCRP studie. De patiënten die aan deze studie deelnemen, worden dan ook niet gevraagd voor de twee eerder genoemde studies. Hier is voor gekozen omdat meedoen aan beide studies een te grote belasting kan vormen voor de patiënten, waardoor de respons negatief beïnvloed wordt. Daarnaast zijn patiënten met een rectumcarcinoom verantwoordelijk voor slechts een klein deel van de data bij de COLON en PLCRP studie.

Indien u behoefte heeft aan meer informatie over de lopende studies kunt u op onderstaande websites kijken:

- Colon studie: www.voedingenkankerstudies.nl/nl/voedingenkankerstudies/COLON-Studie
- PLCRC studie: www.plcrc.nl

Uw rol in dit onderzoek

Zonder u zijn wij natuurlijk nergens. U ziet de patiënt en bent op de hoogte van wat er met hem of haar gaat gebeuren. Zodoende willen wij u enkele dingen vragen om dit onderzoek tot een succes te brengen.

- Wij zouden u willen vragen om de patiënt te informeren over de FUNE studie op het moment dat de behandeling vaststaat. Hierbij zijn er 4 zaken van belang:
    1. Dat u de patiënt de patiënt informatiefolder (PIF) meegeeft.
    2. Dat u de informed consent meegeeft.
    3. Dat u de patiënt vraagt of zij het goed vinden of zij gebeld worden door een van ons.
    4. Dat u in Hix noteert of bovenstaande zaken zijn gebeurd en of de patiënt akkoord gaf.
- Verder willen wij u vragen om de patiënt duidelijk te maken dat hij of zij minimaal 5 dagen bedenktijd heeft en wij daarna, indien akkoord, contact met hem of haar opnemen.
- Daarnaast is het voor de patiënt belangrijk om te weten dat zij, indien zij kiezen voor deelname, 30 minuten voorafgaand aan hun afspraak met de anesthesist worden verwacht. Dit zodat zij dan de informed consent in kunnen leveren en de vragenlijsten rustig in kunnen vullen.

Deze stappen kosten slechts een paar minuten van uw tijd, maar betekenen veel voor ons en voor een gestructureerd verloop van het onderzoek. Wij hopen dan ook op uw medewerking en zien u graag binnenkort op de poli.

Vragen of opmerkingen

Bij vragen of opmerkingen kunt u contact met ons opnemen:

- J.G.J Bauhuis, student gezondheidswetenschappen, University of Twente,
- I.M. Hulshof, student gezondheidswetenschappen, University of Twente,

Appendix C: EQ-5D-3L questionnaire

Zet bij iedere groep in de lijst hieronder een kruisje in het hokje dat het best past bij uw gezondheid VANDAAG.

MOBILITEIT

Ik heb geen problemen met lopen ❑
Ik heb een beetje problemen met lopen ❑
Ik heb matige problemen met lopen ❑
Ik heb ernstige problemen met lopen ❑
Ik ben niet in staat om te lopen ❑

ZELFZORG

Ik heb geen problemen met mijzelf wassen of aankleden ❑
Ik heb een beetje problemen met mijzelf wassen of aankleden ❑
Ik heb matige problemen met mijzelf wassen of aankleden ❑
Ik heb ernstige problemen met mijzelf wassen of aankleden ❑
Ik ben niet in staat mijzelf te wassen of aan te kleden ❑

DAGELIJKSE ACTIVITEITEN *(bijv. werk, studie, huishouden, gezins- en vrijetijdsactiviteiten)*

Ik heb geen problemen met mijn dagelijkse activiteiten ❑
Ik heb een beetje problemen met mijn dagelijkse activiteiten ❑
Ik heb matige problemen met mijn dagelijkse activiteiten ❑
Ik heb ernstige problemen met mijn dagelijkse activiteiten ❑
Ik ben niet in staat mijn dagelijkse activiteiten uit te voeren ❑

PIJN / ONGEMAK

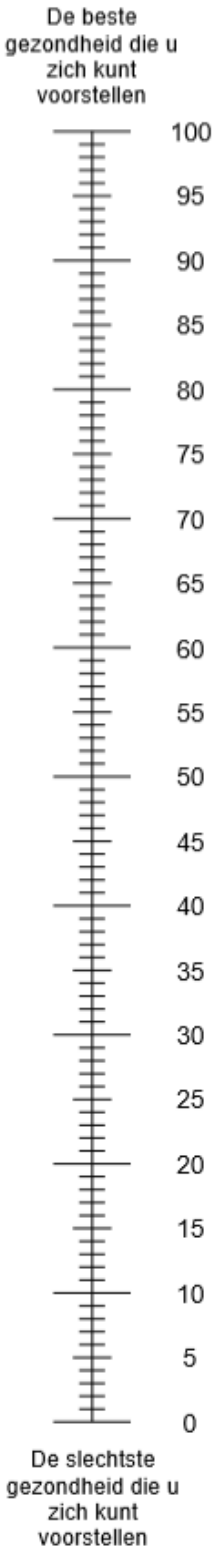
Ik heb geen pijn of ongemak ❑
Ik heb een beetje pijn of ongemak ❑
Ik heb matige pijn of ongemak ❑
Ik heb ernstige pijn of ongemak ❑
Ik heb extreme pijn of ongemak ❑

ANGST / SOMBERHEID

Ik ben niet angstig of somber ❑
Ik ben een beetje angstig of somber ❑
Ik ben matig angstig of somber ❑
Ik ben erg angstig of somber ❑
Ik ben extreem angstig of somber ❑

- We willen weten hoe goed of slecht uw gezondheid VANDAAG is.
- Deze meetschaal loopt van 0 tot 100.
- 100 staat voor de beste gezondheid die u zich kunt voorstellen.
  0 staat voor de slechtste gezondheid die u zich kunt voorstellen.
- Markeer een X op de meetschaal om aan te geven hoe uw gezondheid VANDAAG is.
- Noteer het getal waarbij u de X heeft geplaatst in onderstaand vakje.

UW GEZONDHEID VANDAAG = ☐



Appendix D: EORTC-QLQ C30 questionnaire

EORTC QLQ-C30 (version 3)

Wij zijn geïnteresseerd in bepaalde dingen over u en uw gezondheid. Wilt u alle vragen zelf beantwoorden door het getal te omcirkelen dat het meest op u van toepassing is. Er zijn geen "juiste" of "onjuiste" antwoorden. De informatie die u geeft zal strikt vertrouwelijk worden behandeld.

Naam: Geb.dat.: Datum:

	Helemaal niet	Een beetje	Nogal	Heel erg
1.Heeft u moeite met het doen van inspannende activiteiten zoals het dragen van een zware boodschappentas of een koffer?	1	2	3	4
2. Heeft u moeite met het maken van een lange wandeling?	1	2	3	4
3. Heeft u moeite met het maken van een korte wandeling buitenshuis?	1	2	3	4
4. Moet u overdag in bed of op een stoel blijven?	1	2	3	4
5. Heeft u hulp nodig met eten, aankleden, uzelf wassen of naar het toilet gaan?	1	2	3	4

Gedurende de afgelopen week:	Helemaal niet	Een beetje	Nogal	Heel erg
6. Was u beperkt bij het doen van uw werk of andere dagelijkse bezigheden?	1	2	3	4
7. Was u beperkt in het uitoefenen van uw hobby's of bij andere bezigheden die u in uw vrije tijd doet?	1	2	3	4
8. Was u kortademig?	1	2	3	4
9. Heeft u pijn gehad?	1	2	3	4
10. Had u behoefte om te rusten?	1	2	3	4
11. Heeft u moeite met slapen gehad?	1	2	3	4
12. Heeft u zich slap gevoeld?	1	2	3	4
13. Heeft u gebrek aan eetlust gehad?	1	2	3	4

Gedurende de afgelopen week:	Helemaal niet	Een beetje	Nogal	Heel erg
14. Heeft u zich misselijk gevoeld?	1	2	3	4
15. Heeft u overgegeven?	1	2	3	4
16. Had u last van obstipatie? (was u verstopt?)	1	2	3	4
17. Had u diarree?	1	2	3	4
18. Was u moe?	1	2	3	4
19. Heeft pijn u gehinderd in uw dagelijkse bezigheden?	1	2	3	4
20. Heeft u moeite gehad met het concentreren op dingen, zoals een krant lezen of televisie kijken?	1	2	3	4
21. Voelde u zich gespannen?	1	2	3	4
22. Maakte u zich zorgen?	1	2	3	4
23. Voelde u zich prikkelbaar?	1	2	3	4
24. Voelde u zich neerslachtig?	1	2	3	4
25. Heeft u moeite gehad met het herinneren van dingen?	1	2	3	4
26. Heeft uw lichamelijke toestand of medische behandeling uw familieleven in de weg gestaan?	1	2	3	4
27. Heeft uw lichamelijke toestand of medische behandeling u belemmerd in uw sociale bezigheden?	1	2	3	4
28. Heeft uw lichamelijke toestand of medische behandeling financiële moeilijkheden met zich meegebracht?	1	2	3	4

Wilt u voor de volgende vragen het getal tussen 1 en 7 omcirkelen dat het meest op u van toepassing is

29. Hoe zou u uw algehele gezondheid gedurende de afgelopen week beoordelen?

1	2	3	4	5	6	7
Erg slecht						Uitstekend

30. Hoe zou u uw algehele "kwaliteit van het leven" gedurende de afgelopen week beoordelen?

1	2	3	4	5	6	7
Erg slecht						Uitstekend

Appendix E: EORTC-QLQ-CR29 questionnaire

EORTC QLQ-CR-29

Soms zeggen patiënten dat ze de volgende klachten of problemen hebben. Wilt u aangeven in welke mate u deze klachten of problemen gedurende de afgelopen week heeft ervaren. Wilt u de vragen beantwoorden door het getal te omcirkelen dat het meest op u van toepassing is.

Gedurende de afgelopen week:		**Helemaal niet**	**Een beetje**	**Nogal**	**Heel erg**
31.	Heeft u overdag vaak geplast?	1	2	3	4
32.	Heeft u 's nachts vaak geplast?	1	2	3	4
33.	Heeft u ongewild urine verloren?	1	2	3	4
34.	Heeft u pijn gehad bij het plassen?	1	2	3	4
35.	Heeft u buikpijn gehad?	1	2	3	4
36.	Heeft u pijn gehad in uw zitvlak of bij uw anus?	1	2	3	4
37.	Heeft u een opgeblazen gevoel gehad in uw buik?	1	2	3	4
38.	Heeft u bloed in uw ontlasting gehad?	1	2	3	4
39.	Heeft u slijm in uw ontlasting gehad?	1	2	3	4
40.	Heeft u een droge mond gehad?	1	2	3	4
41	Heeft u haaruitval gehad ten gevolge van uw behandeling?	1	2	3	4
42.	Heeft u problemen met uw smaak gehad?	1	2	3	4

Gedurende de afgelopen week:		**Helemaal niet**	**Een beetje**	**Nogal**	**Heel erg**
43.	Heeft u zich zorgen gemaakt over uw gezondheid in de toekomst?	1	2	3	4
44.	Heeft u zich zorgen gemaakt over uw gewicht?	1	2	3	4
45.	Voelde u zich lichamelijk minder aantrekkelijk ten gevolge van uw ziekte of behandeling?	1	2	3	4
46.	Voelde u zich minder vrouwelijk/mannelijk ten gevolge van uw ziekte of behandeling?	1	2	3	4
47.	Was u ontevreden met uw lichaam?	1	2	3	4
48.	Heeft u een stoma? (dunnedarm-stoma of dikkedarm-stoma) (omcirkel het juiste antwoord)		**Ja**		**Nee**

Wilt u a.u.b. naar de volgende bladzijde gaan

Gedurende de afgelopen week:	Helemaal niet	Een beetje	Nogal	Heel erg
Beantwoord deze vragen ALLEEN ALS U EEN STOMA HEBT, zo niet, ga dan naar het volgende vak:				
49. Heeft u last gehad van het ongewild vrijkomen van gas (winderigheid) uit uw stoma?	1	2	3	4
50. Was er lekkage van ontlasting uit uw stomazakje?	1	2	3	4
51. Heeft u een pijnlijke huid gehad rond uw stoma?	1	2	3	4
52. Heeft u overdag vaak het stomazakje moeten vervangen?	1	2	3	4
53. Heeft u 's nachts vaak het stomazakje moeten vervangen?	1	2	3	4
54. Voelde u zich opgelaten door uw stoma?	1	2	3	4
55. Heeft u problemen gehad met de verzorging van uw stoma?	1	2	3	4
Beantwoord deze vragen ALLEEN ALS U GEEN STOMA HEBT:				
49. Heeft u last gehad van ongewild vrijkomen van gas (winderigheid)?	1	2	3	4
50. Heeft u ongewild ontlasting verloren?	1	2	3	4
51. Heeft u een pijnlijke huid gehad rondom uw anus?	1	2	3	4
52. Heeft u overdag vaak ontlasting gehad?	1	2	3	4
53. Heeft u 's nachts vaak ontlasting gehad?	1	2	3	4
54. Voelde u zich opgelaten door uw ontlastingspatroon?	1	2	3	4

Gedurende de afgelopen 4 weken:	Helemaal niet	Een beetje	Nogal	Heel erg
Alleen voor MANNEN:				
56. In hoeverre had u zin in seks?	1	2	3	4
57. Indien u seksueel actief was (met of zonder geslachtsgemeenschap): Had u moeite met het stijf worden of blijven van uw penis?	1	2	3	4
Alleen voor VROUWEN:				
58. In hoeverre had u zin in seks?	1	2	3	4
59. Indien u geslachtsgemeenschap hebt gehad: Had u pijn of ongemak tijdens de gemeenschap?	1	2	3	4

Appendix F: LARS questionnaire

Deze vragenlijst heeft tot doel de darmfunctie van patiënten met endeldarmkanker te meten. Per vraag mag u één antwoord aankruisen. Het kan moeilijk zijn om maar één antwoord te kiezen, aangezien we weten dat bij sommige patiënten de symptomen van dag tot dag variëren. Echter vragen we u het antwoord te kiezen die het beste uw dagelijks leven beschrijft. Als u recent een darminfectie heeft gehad, vragen we u deze symptomen niet mee te nemen in uw antwoorden, maar u te focussen op uw dagelijks leven.

Vraag 1: Komt het wel eens voor dat u geen controle heeft over uw winderigheid?

☐ Nee, nooit	0
☐ Ja, minder dan 1 keer per week	4
☐ Ja, minstens 1 keer per week	7

Vraag 2: Heeft u wel eens last van ongewenste lekkage van dunne ontlasting?

☐ Nee, nooit	0
☐ Ja, wel eens, dat wil zeggen minder dan eenmaal per week	3
☐ Ja, vaak, dat wil zeggen minstens eenmaal per week	3

Vraag 3: Hoe vaak heeft u ontlasting?

☐ Meer dan 7 keer per dag (24 uur)	4
☐ 4-7 keer per dag (24 uur)	2
☐ 1-3 keer per dag (24 uur)	0
☐ Minder dan 1 keer per dag (24 uur)	5

Vraag 4: Als u ontlasting heeft gehad, moet u dan wel eens binnen het uur nog een keer naar het toilet voor ontlasting?

☐ Nee, nooit	0
☐ Ja, minder dan 1 keer per week	9
☐ Ja, minstens 1 keer per week	11

Vraag 5 :Heeft u wel eens zo een sterke aandrang voor ontlasting, dat u zich naar het toilet moet haasten?

☐ Nee, nooit	0
☐ Ja, minder dan 1 keer per week	11
☐ Ja, minstens 1 keer per week	16

Tel de scores van de bovenstaande vijf antwoorden bij elkaar op, tot één uiteindelijke score.
Interpretatie: 0-20 = Geen LARS 21-29 = Minimale LARS 30-42 = Ernstige LARS

Appendix G: IPSS questionnaire

VRAGENLIJST VOOR PLASKLACHTEN BIJ MANNEN (IPSS*)

Naam: .....

Geboortedatum: ..... Datum: .....

Hoe vaak in de afgelopen maand:	Nooit	Minder dan 1 op de 5 keer	Minder dan de helft van de keren	Ongeveer de helft van de keren	Meer dan de helft van de keren	Bijna altijd	Score
...had u het gevoel dat uw blaas na het plassen nog niet helemaal leeg was?	0	1	2	3	4	5	
...moest u binnen twee uur na het plassen opnieuw plassen?	0	1	2	3	4	5	
... gebeurde het tijdens het plassen dat de straal enige keren stopte en dan weer begon?	0	1	2	3	4	5	
...had u moeite om het plassen uit te stellen?	0	1	2	3	4	5	
...had u een slappe straal bij het plassen?	0	1	2	3	4	5	
...moest u persen voordat de urinestraal op gang kwam?	0	1	2	3	4	5	
...moest u gemiddeld per nacht het bed uit om te plassen?	0x	1x	2x	3x	4x	5x	
						Totaal symptoomscore	

Uitleg score: 0-7 = mild, 8-19 = matig, 20-35 = ernstig

*IPSS: Internationale Prostaat Symptoom Score.

Als het plassen de rest van uw leven zou blijven zoals het nu is, hoe zou u zich daarbij voelen?

Zeer tevreden	Tevreden	Grotendeels tevreden	Neutraal	Grotendeels ontevreden	Ontevreden	Zeer ontevreden
0	1	2	3	4	5	6

Met bovenstaande vragen kan worden ingeschat hoeveel plasklachten u heeft. De vragenlijst helpt niet om de oorzaak van uw plasklachten te bepalen. De P van Prostaat in IPSS is misleidend, omdat de prostaat meestal niet de oorzaak is van plasklachten. U kunt deze vragenlijst bespreken met uw huisarts of specialist.

Meer informatie over plasklachten bij mannen is te vinden op www.thuisarts.nl.

nhg nederlands huisartsen genootschap

Appendix H: FSFI questionnaire

Female Sexual Function Index (FSFI)©

Subject code: _____ Datum: _____

INSTRUCTIE: Deze vragen gaan over uw seksuele gevoelens en seksuele reacties gedurende de afgelopen 4 weken. Beantwoord deze vragen alstublieft zo eerlijk en duidelijk mogelijk. Uw antwoorden zullen strikt vertrouwelijk behandeld worden.

Bij het beantwoorden van de vragen zijn de volgende definities van toepassing:

Seksuele activiteit: dit kan zijn strelen, voorspel, masturbatie en vaginale geslachtsgemeenschap.
Geslachtsgemeenschap: hiermee wordt vaginale penetratie bedoeld (het binnengaan van de penis in de vagina).
Seksuele stimulatie: hieronder worden onder meer situaties verstaan als voorspel met een partner, zelfbevrediging (masturbatie), of fantaseren over seks.

PER VRAAG SLECHTS ÉÉN HOKJE AANKRUISEN S.V.P

Seksuele verlangens: hieronder wordt verstaan zin hebben in seks, in willen gaan op het seksuele initiatief van een partner, en denken aan of fantaseren over het hebben van seks.

1. Hoe **vaak** had u de afgelopen 4 weken seksuele verlangens?

   ❒ Bijna altijd of altijd
   ❒ Meestal (meer dan de helft van de tijd)
   ❒ Af en toe (ongeveer de helft van de tijd)
   ❒ Een paar keer (minder dan de helft van de tijd)
   ❒ Bijna nooit of nooit

2. Hoe **sterk** vond u dat uw seksuele verlangens de afgelopen 4 weken waren?

   ❒ Zeer sterk
   ❒ Sterk
   ❒ Middelmatig
   ❒ Zwak
   ❒ Zeer zwak of niet aanwezig

Seksuele opwinding: hieronder wordt verstaan zowel de lichamelijke als geestelijke gevoelens van seksuele opwinding. Dit kunnen gevoelens zijn van warmte of tintelingen in de geslachtsdelen, vochtig ("nat") zijn, of het samentrekken van spieren.

3. Hoe **vaak** voelde u zich de afgelopen 4 weken seksueel opgewonden ("geil") tijdens seksuele activiteit of geslachtsgemeenschap?

   ❒ Geen seksuele activiteit
   ❒ Bijna altijd of altijd
   ❒ Meestal (meer dan de helft van de tijd)
   ❒ Af en toe (ongeveer de helft van de tijd)
   ❒ Een paar keer (minder dan de helft van de tijd)
   ❒ Bijna nooit of nooit

4. Hoe **sterk** vond u dat uw seksuele opwinding (het "geil" zijn) was de afgelopen 4 weken tijdens seksuele activiteit of geslachtsgemeenschap?

   ❒ Geen seksuele activiteit
   ❒ Zeer sterk
   ❒ Sterk
   ❒ Middelmatig
   ❒ Zwak
   ❒ Zeer zwak of niet aanwezig

5. Hoe **zeker** was u er de afgelopen 4 weken van dat u seksueel opgewonden zou worden tijdens seksuele activiteit of geslachtsgemeenschap?

   ❒ Geen seksuele activiteit
   ❒ Heel zeker
   ❒ Zeker
   ❒ Middelmatig
   ❒ Onzeker
   ❒ Heel onzeker

6. Hoe **vaak** was u de afgelopen 4 weken tevreden over uw seksuele opwinding tijdens seksuele activiteit of geslachtsgemeenschap?

   ❒ Geen seksuele activiteit
   ❒ Bijna altijd of altijd
   ❒ Meestal (meer dan de helft van de tijd)
   ❒ Af en toe (ongeveer de helft van de tijd)
   ❒ Een paar keer (minder dan de helft van de tijd)
   ❒ Bijna nooit of nooit

7. Hoe **vaak** werd u de afgelopen 4 weken vochtig ("nat") tijdens seksuele activiteit of geslachtsgemeenschap?

   - ❒ Geen seksuele activiteit
   - ❒ Bijna altijd of altijd
   - ❒ Meestal (meer dan de helft van de tijd)
   - ❒ Af en toe (ongeveer de helft van de tijd)
   - ❒ Een paar keer (minder dan de helft van de tijd)
   - ❒ Bijna nooit of nooit

8. Hoe **moeilijk** was het de afgelopen 4 weken om vochtig ("nat") te worden tijdens seksuele activiteit of geslachtsgemeenschap?

   - ❒ Geen seksuele activiteit
   - ❒ Heel erg moeilijk of onmogelijk
   - ❒ Erg moeilijk
   - ❒ Moeilijk
   - ❒ Een beetje moeilijk
   - ❒ Niet moeilijk

9. Hoe **vaak** bleef u de afgelopen 4 weken vochtig ("nat") totdat de seksuele activiteit of geslachtsgemeenschap voltooid was?

   - ❒ Geen seksuele activiteit
   - ❒ Bijna altijd of altijd
   - ❒ Meestal (meer dan de helft van de tijd)
   - ❒ Af en toe (ongeveer de helft van de tijd)
   - ❒ Een paar keer (minder dan de helft van de tijd)
   - ❒ Bijna nooit of nooit

10. Hoe **moeilijk** was het de afgelopen 4 weken om vochtig ("nat") te blijven totdat de seksuele activiteit of geslachtsgemeenschap voltooid was?

    - ❒ Geen seksuele activiteit
    - ❒ Heel erg moeilijk of onmogelijk
    - ❒ Erg moeilijk
    - ❒ Moeilijk
    - ❒ Een beetje moeilijk
    - ❒ Niet moeilijk

11. Hoe **vaak** heeft u de afgelopen 4 weken een orgasme (klaarkomen) gehad bij seksuele stimulatie of geslachtsgemeenschap?

- ❒ Geen seksuele activiteit
- ❒ Bijna altijd of altijd
- ❒ Meestal (meer dan de helft van de tijd)
- ❒ Af en toe (ongeveer de helft van de tijd)
- ❒ Een paar keer (minder dan de helft van de tijd)
- ❒ Bijna nooit of nooit

12. Hoe **moeilijk** was het de afgelopen 4 weken voor u om een orgasme (klaarkomen) te krijgen bij seksuele stimulatie of geslachtsgemeenschap?

- ❒ Geen seksuele activiteit
- ❒ Bijzonder moeilijk of onmogelijk
- ❒ Zeer moeilijk
- ❒ Moeilijk
- ❒ Enigszins moeilijk
- ❒ Niet moeilijk

13. Hoe **tevreden** was u de afgelopen 4 weken over uw vermogen een orgasme te krijgen tijdens seksuele activiteit of geslachtsgemeenschap?

- ❒ Geen seksuele activiteit
- ❒ Zeer tevreden
- ❒ Redelijk tevreden
- ❒ Ongeveer even tevreden als ontevreden
- ❒ Tamelijk ontevreden
- ❒ Zeer ontevreden

14. Hoe **tevreden** was u de afgelopen 4 weken over de sterkte van de emotionele band tussen u en uw partner tijdens seksuele activiteit?

- ❒ Geen seksuele activiteit
- ❒ Zeer tevreden
- ❒ Redelijk tevreden
- ❒ Ongeveer even tevreden als ontevreden
- ❒ Tamelijk ontevreden
- ❒ Zeer ontevreden

15. Hoe **tevreden** was u de afgelopen 4 weken over uw seksuele relatie met uw partner?

- ❒ Zeer tevreden
- ❒ Redelijk tevreden
- ❒ Ongeveer even tevreden als ontevreden
- ❒ Tamelijk ontevreden
- ❒ Zeer ontevreden

16. Hoe **tevreden** was u de afgelopen 4 weken met uw seksleven in het algemeen?

- ❒ Zeer tevreden
- ❒ Redelijk tevreden
- ❒ Ongeveer even tevreden als ontevreden
- ❒ Tamelijk ontevreden
- ❒ Zeer ontevreden

Vaginale penetratie: hiermee wordt bedoeld het binnengaan van de penis in de vagina.

17. Hoe **vaak** had u de afgelopen 4 weken een ongemakkelijk gevoel of pijn tijdens vaginale penetratie?

- ❒ Niet geprobeerd om geslachtsgemeenschap te hebben
- ❒ Bijna altijd of altijd
- ❒ Meestal (meer dan de helft van de tijd)
- ❒ Af en toe (ongeveer de helft van de tijd)
- ❒ Een paar keer (minder dan de helft van de tijd)
- ❒ Bijna nooit of nooit

18. Hoe **vaak** had u de afgelopen 4 weken een ongemakkelijk gevoel of pijn nadat de vaginale penetratie voltooid was?

- ❒ Niet geprobeerd om geslachtsgemeenschap te hebben
- ❒ Bijna altijd of altijd
- ❒ Meestal (meer dan de helft van de tijd)
- ❒ Af en toe (ongeveer de helft van de tijd)
- ❒ Een paar keer (minder dan de helft van de tijd)
- ❒ Bijna nooit of nooit

19. Hoe **sterk** zou u het ongemakkelijke gevoel of de mate van pijn noemen die u de afgelopen 4 weken ervoer tijdens of na afloop van de vaginale penetratie?

- ❒ Niet geprobeerd om geslachtsgemeenschap te hebben
- ❒ Zeer sterk
- ❒ Sterk
- ❒ Middelmatig
- ❒ Zwak
- ❒ Zeer zwak of niet aanwezig

Appendix I: Prospective study

The goal of this section of the study is to report short-to-medium term functional outcomes in patients who underwent Nerve Sparing TME surgery for rectal carcinoma. [53] Eventually this report can contribute to the comparison of the Nerve Sparing technique to other TME techniques used in rectal cancer. This research will be executed through a combination of self-assessment by patients and data collection from the electronic patient file. This will lead to data that can be divided into baseline characteristics, results of the questionnaires and complications.

Due to a fixed period of time and an estimation of the possibility to include an average of one patient a week, few patients will be included. Therefore, it will be a pilot study that continues after the period of this bachelor thesis ends.

Participants

This patient group consists of patients that will undergo a Nerve Sparing TME in Rijnstate hospital since April 2020. All patients receive standard care following the Dutch protocols for rectal cancer care and surgery took place with curative intention for rectal cancer. Furthermore, patients are only selected if the tumor is situated in the rectum according to the new definition.

The patients will receive information about this study from a specialized nurse, a GIO-nurse, at their meeting, which takes place one to two weeks before the surgery. The nurse will also ask the patient whether he or she gives permission to be contacted through telephone about the research and notes the answer in the electronic patient file. The patient will be called if he or she gave permission to do so.

If a patient decides to participate in this study, he or she will be sent an informed consent as well as the questionnaires and is asked to send them back when filled in. When arrived at Rijnstate hospital, the informed consent and questionnaires are scanned into a secured map on the Rijnstate system. From here, the data will be transferred into and stored in Research Manager, which makes it easy to export and analyze data in and through SPSS.

Table 8: Questionnaires to measure the health related quality of life and the moments in which these measurements take place.

Questionnaire	Outcome	Moments	
		Pre-operative	Post-operative
EQ-5D-3L	Health related quality of life	1 week	3 months 6 months 9 months 12 months
EORTC-QLQ-C30	Quality of life specific for (former) cancer patients		
EORTC-QLQ-CR29	Quality of life specific for patients with cancer situated in the intestines		
LARS score	Presence of LAR syndrome		
IPSS	Presence of urinary symptoms and quality of life in men		
FSFI	Sexual function in women		

Appendix J: Tables

Table 9: EORTC-QLQ-CR29

	Laparoscopic (n=24)		Transanal (n=25)		Robot-assisted (n=52)			
Scale	**μ (SD)**	**M**	**μ (SD)**	**M**	**μ (SD)**	**M**	**P [1]**	**P [2]**
Symptom								
Urinary frequency	27.8 (21.8)	0	39.3 (20.9)	0	33.0 (23.2)	3	1.000	0.751
Blood and mucus	4.2 (7.4)	0	4.0 (7.3)	0	4.5 (8.9)	4	1.000	1.000
Stool frequency	30.4 (21.1)	1	37.5 (27.0)	1	33.7 (28.7)	6	1.000	1.000
Urinary incontinence	9.7 (20.8)	0	8.0 (14.5)	0	11.1 (21.8)	1	1.000	1.000
Abdominal pain	8.3 (14.7)	0	11.1 (18.8)	1	12.0 (23.1)	4	1.000	1.000
Dysuria	1.4 (6.8)	0	2.7 (9.2)	0	2.8 (9.3)	2	1.000	1.000
Buttock pain	13.9 (21.8)	0	25.3 (30.9)	0	15.7 (23.4)	1	1.000	0.357
Bloating	16.7 (22.0)	0	16.0 (21.8)	0	23.3 (25.4)	2	0.783	0.632
Dry mouth	8.3 (14.7)	0	20.0 (28.9)	0	13.2 (20.3)	4	1.000	0.622
Hair loss	0.0 (0.0)	0	8.0 (17.4)	0	5.6 (17.3)	4	0.431	1.000
Taste	6.9 (24.0)	0	16.0 (32.1)	0	5.7 (18.8)	5	1.000	0.262
Flatulence	38.9 (21.2)	0	43.1 (20.8)	1	41.3 (26.5)	6	1.000	1.000
Fecal incontinence	16.7 (22.0)	0	36.2 (30.0)	2	21.7 (27.4)	6	1.000	0.111
Sore skin	8.3 (14.7)	0	29.2 (34.5)	1	15.9 (20.8)	6	0.625	0.091
Embarrassment	30.6 (32.5)	0	40.3 (31.1)	1	25.2 (22.7)	7	1.000	0.101
Impotence (men)	47.6 (38.6)	3	36.4 (34.8)	5	42.9 (39.3)	5	1.000	1.000
Dyspareunia (women)	8.3 (16.7)	3	6.7 (14.9)	4	25.5 (34.4)	9	0.942	0.689
Functional								
Body image	9.3 (15.3)	0	11.6 (14.5)	2	16.8 (22.5)	3	0.354	0.832
Anxiety	26.4 (26.0)	0	23.6 (20.8)	1	25.9 (22.8)	3	1.000	1.000
Weight	13.0 (16.7)	1	12.0 (21.3)	0	17.4 (27.0)	6	1.000	1.000
Sexual interest (men)	31.4 (22.0)	0	28.2 (26.7)	3	38.0 (30.0)	6	1.000	0.832
Sexual interest (women)	26.7 (27.9)	2	16.7 (18.3	3	33.3 (31.3)	3	1.000	0.654

*The symptom as well as the functional scale range from 0-100. 1 Comparison of the laparoscopic group with the robot-assisted group. 2 Comparison of the transanal group with the robot-assisted group. * Significant after the Bonferroni correction.*

Table 10: FSFI

	Robot-assisted (n=10)	
Domain	**μ (SD)**	**M**
Desire	5.6 (1.0)	0
Arousal	1.9 (2.6)	0
Lubrication	1.6 (2.0)	0
Orgasm	1.5 (1.9)	0
Satisfaction	1.5 (1.1)	4
Pain	2.2 (3.0)	2
Overall score	17.9 (8.6)	4

Domain scores have a range of 0-6 except desire (range 1.2-6.0) and satisfaction (range 0.8-6.0). The overall score ranges from 2.0 to 36.0.