**ΜΕΤΑΠΤΥΧΙΑΚΟ ΠΡΟΓΡΑΜΜΑ ΣΠΟΥΔΩΝ:**
**‘‘ΕΛΑΧΙΣΤΑ ΕΠΕΜΒΑΤΙΚΗ ΧΕΙΡΟΥΡΓΙΚΗ,**
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**ΕΘΝΙΚΟ ΚΑΙ ΚΑΠΟΔΙΣΤΡΙΑΚΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ**
**ΙΑΤΡΙΚΗ ΣΧΟΛΗ**

# ΔΙΠΛΩΜΑΤΙΚΗ ΕΡΓΑΣΙΑ

# ΘΕΜΑ:

# “LAPAROSCOPIC LOW ANTERIOR RESECTION, TaTME. REVIEW OF THE LITERATURE”

**ΜΕΤΑΠΤΥΧΙΑΚΟΣ ΦΟΙΤΗΤΗΣ:**
**ΚΑΛΑΤΖΗΣ ΒΑΣΙΛΕΙΟΣ**
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**ΠΡΑΚΤΙΚΟ ΚΡΙΣΕΩΣ**
**ΤΗΣ ΣΥΝΕΔΡΙΑΣΗΣ ΤΗΣ ΤΡΙΜΕΛΟΥΣ ΕΞΕΤΑΣΤΙΚΗΣ ΕΠΙΤΡΟΠΗΣ**
**ΓΙΑ ΤΗΝ ΑΞΙΟΛΟΓΗΣΗ ΤΗΣ ΔΙΠΛΩΜΑΤΙΚΗΣ ΕΡΓΑΣΙΑΣ**
**Του Μεταπτυχιακού Φοιτητή Βασιλείου Καλατζή**

***Εξεταστική Επιτροπή***

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Η Τριμελής Εξεταστική Επιτροπή η οποία ορίσθηκε από την ΓΣΕΣ της Ιατρικής Σχολής του Παν. Αθηνών Συνεδρίαση της.....ης ..... 20.... για την αξιολόγηση και εξέταση του υποψηφίου κου Βασιλείου Καλατζή, συνεδρίασε σήμερα .../.../....

Η Επιτροπή διαπίστωσε ότι η Διπλωματική Εργασία του Κου Βασιλείου Καλατζή με τίτλο: «LAPAROSCOPIC LOW ANTERIOR RESECTION, TaTME. REVIEW OF THE LITERATURE», είναι πρωτότυπη, επιστημονικά και τεχνικά άρτια και η βιβλιογραφική πληροφορία ολοκληρωμένη και εμπεριστατωμένη.

Η εξεταστική επιτροπή αφού έλαβε υπ' όψιν το περιεχόμενο της εργασίας και τη συμβολή της στην επιστήμη, με ψήφους ..... προτείνει την απονομή του Μεταπτυχιακού Διπλώματος Ειδίκευσης (Master's Degree), στον παραπάνω Μεταπτυχιακό Φοιτητή.

Στην ψηφοφορία για την βαθμολογία ο υποψήφιος έλαβε για τον βαθμό «ΑΡΙΣΤΑ» ψήφους ....., για τον βαθμό «ΛΙΑΝ ΚΑΛΩΣ» ψήφους ....., και για τον βαθμό «ΚΑΛΩΣ» ψήφους ..... Κατά συνέπεια, απονέμεται ο βαθμός «.....».

Τα Μέλη της Εξεταστικής Επιτροπής

- Νικόλαος Ι. Νικητέας, **Επιβλέπων** (Υπογραφή) _____
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*Την κάτωθι εργασία θα ήθελα να την αφιερώσω στην αγαπημένη μου οικογένεια , και σε όλους όσους με τον δικό τους τρόπο με βοηθούν τα χρόνια των σπουδών μου.*

**TABLE OF CONTENTS**

## 1. INTRODUCTION - BACKGROUND

Rectal carcinoma appears to be one of the most common types of carcinoma worldwide, with 1.36 million new cases annually diagnosed worldwide (1). During late 19$^{th}$ and early 20$^{th}$ century, most patients with rectal cancer were managed through rectal amputation, regardless of their location. Most rectal tumors were excised using the perineal approach, popularized by the British surgeon Lockhart-Mummery of St. Mark's Hospital. This two step approach enclosed a sigmoidostomy followed by a perineal resection after several weeks (2). It was William Ernest Miles, in 1908, with his article "A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon" published in Lancet, that first introduced the "cylindrical concept" .The observations he made, after the high number of local recurrence in lymph nodes at the and pelvic peritoneum, in patients that underwent perineal resection and sigmoidostomy led him to the "cylindrical concept". A theory that tumor spread, occurred in all directions, through the lymph nodes which were responsible for the locally recurrent disease. He then proposed the APR approach, which led in a new way of managing the rectal cancer (3). Nowadays it is scientifically accepted, that the technique of surgical complete total mesorectal excision - TME, is the gold standard in the surgical treatment of rectal cancer, as Professor RJ Heald has described in his publication in 1982 (4).

The treatment of rectal cancer has developed radically through the past years with the use of not only neoadjuvant chemoradiatherapy, but also new surgical approaches less invasive such as laparoscopic or robotic. Nevertheless the gold standard in the treatment of rectal cancer is the complete high quality total mesorectal excision-TME, with clear DRM (distal resection margin) and CRM (circumferential resection margin) which leads to low locoregional recurrence and high cancer free survival. (5-6).

The need to a obtain better TME specimen after rectal surgery, especially in difficult pelvic dissections, lead to the implementation of new advanced surgical approaches. TME has shifted from the open, to Laparoscopic, Robotic and Transanal approach.

Several studies mostly randomized prospective RCT's have shown that oncological outcome, in low rectal cancer, is not compromised with laparoscopic versus open surgery. (7-8). The CLASICC trial, in 2005, has demonstrated again that the short-term outcomes of laparoscopically assisted colectomy were similar to those of open and hypothesized that long-term outcomes would likely be similar (9). The COLOR II trial showed that the complication rate and the oncological outcome of the laparoscopic approach is similar to the open surgery especially in high and middle rectal tumors but also that the laparoscopic approach was superior in low rectal tumors, a result that probably can be explained from the fact that laparoscopy can provide a better view in this subset of patients (Affected margins in low rectal cancer in Laparoscopic Vs Open surgery 9% vs 22% $p<0.01$) (8). COREAN study showed that laparoscopic resection, for locally advanced rectal cancer after preoperative chemoradiotherapy, provides similar outcomes for disease-free survival as open resection, not only in short term, but also in long term which was also the aim of the study. The lapTME compared to open is found to have similar results in regard to quality of specimen, perioperative morbidity, number of resected lymph nodes, overall survival and surgical outcome (8, 10-14) .

Although the LapTME has been established as an approach non inferior to open surgery for the rectum cancer, a number of patient and tumor related factors can lead to a higher risk of positive CRM. Narrow pelvis, male sex, high body mass index, neoadjuvant chemo-radiotherapy, fixed anterior bulky low rectal cancer are associated with higher risk of positive CRM. The narrow pelvic canal with the fixed bony structures of the pelvis lead to extreme difficulty in the use of laparoscopic staplers especially in the matter of angulation of the tip of the instrument making the dissection in low cancers more strenuous. This may lead to multiple firings in order to fully transect the rectum most times in a "zigzag" manner which may multiply the risk of an anastomotic leakage. (15). All these difficulties, in the race to achieve intact TME speciments, led to a novel approach in the effort to achieve negative CRM in the TME procedure.

The "Bottom up TME", widely known as **TaTME** –Transanal TME is a new technique designed to manage difficult pelvic dissections, and has attracted much attention the last years. It is designed to be implemented in patients with low rectal cancer ,where a clear visualization and dissection of the holy plane can be easily achieved avoiding excess manipulation of the rectum and obtaining better oncological

outcomes considering not only CRM but also DRM. Additionally, TaTME can preserve better pelvic autonomic nerves leading to better urinary and sexual function.

TaTME is not a complete novel concept. Previous experience in rectal surgery with other techniques such as transanal endoscopic microsurgery –TEM, transanal transabdominal approach –TATA, natural orifice transluminal endoscopic surgery NOTES and transanal minimally invasive surgery TAMIS ,have helped this approach to be established and developed partly as a combination of previous mentioned techniques. (16-21)

The first published TaTME was reported in 2010 (22). In this case it was a 76year old women with a T2N2 rectal cancer treated with preoperative chemoradiation, that underwent transanal endoscopic resection with total mesorectal excision with laparoscopic visualization and assistance. From that time until now several efforts and studies have been conducted showing promising results regarding surgical oncological outcomes and mid term outcomes (23-25). It is now ongoing a multicenter clinical trial comparing TaTME vs LaTME for mid and low rectal cancer (COLOR III) (26)

Indications for TaTME approach have yet to be established and various opinions among surgeons exist. In 2014 after the International TaTME conference, consensus statements have been published (27).

- Patients with both benign and malignant disease should be included
- Male patients
- Obesity and/or BMI>30 kg/m2
- Narrow or/and deep pelvis
- Prostatic hypertrophy
- Tumor height less than 12cm from the anal verge
- Tumor diameter >4 cm
- Neoadjuvant radiotherapy that led to distorted planes
- Primary low tumors impalpable requiring accurate DRM

Contradictions to TaTME:

- T4 tumors
- Obstruction due to mass and emergency surgery

The aim of this paper is to analyze the literature, up to a certain time period, on Transanal Total Mesorectal Excision – TaTME with regards to:

- technical aspects,
- short term outcomes, like postoperative recovery, length of hospital stay, complications, conversion rate,
- oncologic safety, assessed primarily by the degree of lymphadenectomy, CRM , DRM and quality of the specimen.
- assess the potential advantages and/or disadvantages of this relatively new technique

## 2. MATERIALS AND METHODS

### *2.1 Articles Identification*

The database consulted to fulfill the search for relevant articles was Medline -PUBMED. Relevant articles related to the study topic were also reviewed. Keywords used were "((TaTME) AND RECTAL CANCER)" and related terms. References from retrieved articles were reviewed to broaden the search. The search was conducted until May 2017.

### *2.2 Articles selection*

Inclusion criteria were articles written in English language, case series, prospective or retrospective studies, systemic reviews, meta-analysis, adult human patients, colorectal surgery, without restriction of operative indication, or surgical procedure. Congress abstracts and technique reviews were also assessed.

Exclusion criteria were letters, experimental studies conducted in cadaver or animals.

## 3. RESULTS

### *3.1 Studies Selection and Characteristics*

The search in the previous mentioned database came with 100 results. Since TaTME is a rather new technique applied in rectal surgery, the published literature is not extended. For this literature review, the following were analyzed.

- Three systematic reviews of TaTME. The first included 36 studies (8 case reports, 24 case series and 4 comparative studies) totally 510 patients published in 2015. (28). The second one, published in 2016, included 33 studies (3 case reports, 25 case series, 5 comparative studies) totally 794 patients. (29) .The third one published in 2016 includes 449 patients from 15 studies.(49)
- four comparative meta-analysis LaTME vs TaTME , analyzing mostly short-term clinical outcomes of oncological and perioperative outcomes (30-32,48)
- 1 study analyzing 720 cases of TaTME from the International TaTME Registry for benign and malignant rectal pathology. (33)

The following table (table 1) shows the studies analyzed

| Author (ref) | Year | Number of patients | Number of studies | Type of study | Surgical indication | Theme |
|---|---|---|---|---|---|---|
| C.Simillis et al (28) | 2015 | 510 | 36 | Systematic review-retrospective | Malignancy | TaTME |
| C.L.Deijen et al (29) | 2016 | 794 | 33 | Systematic review – retrospective | Malignancy | TaTME |
| Arunachalam et al (49) | 2016 | 449 TaTME | 15 | Systematic review | Malignancy | TaTME |
| M. Fernandez-Hevia et al (30) | 2014 | 37 Ta vs 37 La | NA | Comperative retrospective | Malignancy | TaTME vs LaTME |
| W. Xu et al (32) | 2016 | 209 Ta vs 257 La | 7 | Comperative retrospective | Malignancy | TaTME vs LaTME |

| | | | | | | |
|---|---|---|---|---|---|---|
| B.Ma et al (31) | 2016 | 270 Ta vs 303 La | 7 | Comperative retrospective Meta-Analysis | Malignancy | TaTME vs LaTME |
| Perdawood et al (48) | 2016 | 25 Ta Vs 25 La | NA | Comperative retro-prospective Meta-Analysis | Malignancy | TaTME vs LaTME |
| M.Penna et al (33) | 2016 | 720 TaTME | NA | Retrospective Case Series | Malignancy and Benign | TaTME |

## 4. OPERATIVE TECHINQUE

As already described TaTME is a novel method in treatment of rectal cancer. The last years, this method gained the trust of many surgeons worldwide since it provides an oncological acceptable and easier way to access the low and middle rectum providing the surgeon a solution of known anatomical and technical difficulties encountered in not only laparoscopic but also open treatment of mid and low rectal cancer.

### *4.1 Preoperative assessment*

Patients the day before surgery are being administrated mechanical bowel preparation, and oral antibiotics. Potential stoma is being designed, prior to surgery, and IV antibiotics are given to prevent surgical site infection (Cephazolin and Metronidazole or Ertapenem or Ciprofloxacin). Precaution to avoid deep venous thrombosis is been taken with the use of low molecular weight heparin, and leg pneumatic compression devices are activated prior to induction to anesthesia. The patient is placed in position (lithotomy - Trendelemburg) and arms are tucked with chest tape placed to prevent movement from the operation table.A Rectal enema with iodine is been administrated and the rectum is irrigated with a proctoscope to evacuate remaining stool if necessary. A urine catheter is placed.

### *4.2 Equipment used in TaTME operation*

- Insufflation Systems

The insufflation system used is very critical in the success of TaTME operation. Insufflation systems, such as AirSeal system (SurgiQuest, CT, USA), that provides continuous CO2, and rapid smoke extraction are been used, making the operation easier and quicker. Without this continuous CO2 insufflation with rapid smoke evacuation devises, removing the smoke created in narrow fields, such as the pelvis or the mesorectal plane during the Transanal mesorectal excision, leads to collapsing the working place and disturbing the visualization.

- Transanal platform

There are two types of platforms being used. Rigid or Flexible.

-Transanal endoscopic operation (TEO) proctoscope (Karl Storz, Tuttlingen, Germany)
-Endorec Trocar (Aspide Medical)
-GelPOINT Path Transanal Access Platform (Applied Medical)
-Transanal access port (PAT, Developia Inc., Spain) closed on the back with GelPOINT (Applied Medical) ,
-SILS Port (Covidien)
-Single-channel colonoscope (Olympus,Tokyo, Japan)

There are no data comparing rigid vs flexible platforms . Rigid platforms although they are more expensive to buy, they are reusable, providing a steady environment, with no need of a camera-man. Flexible platforms allow a better manoeuvrability and are easier to be fitted in the anal canal. They apply less traumatic retraction, and less impact on the anorectal function. (21, 28, 34)

Camera used in TaTME are a 5mm 30 degree scope or a flex camera 5 mm Endoeye (Olympus,Center Valley ,PA ,USA)

### *4.3 Operative Technique*

Most of the times, two surgical teems perform simultaneously the operation. One team perform the abdominal operation and the other the perineal phase of the operation. (Fig.1) It is described the operation to be performed with one team, beginning usually from the abdominal phase. From the literature reviewed we present the technique as described by Maria Clara Arroyave, F. Borja DeLacy , and Antonio M.Lacy in October 2016 . (35), and Justin A. Maykel in July 2015 (36)

Fig 1 : a Room setup showing two laparoscopic setups for abdominal and perineal fields. (Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

- Abdominal phase: Pneumoperitoneum 12 -15 mmHg is being installed using a Verres niddle. Four laparoscopic ports are being inserted. A 12 mm or 5mm trocar above the umbilicus, and three 5mm ports in left –right flank and right iliac fossa. The distal sigmoid is been clamped and simultaneously the perineal team inserts the purse –string in order to exclude the rectal lumen. After that both teams start working in a simultaneous way.

The approach chosen is medial to lateral. After appliance of traction to the Inferior Mesenteric vessels, with the use of electrocautery to the peritoneum the avascular plane is recognized and dissected. Initially identification of the left ureter and hypogastric nerves is critical. High ligation, with the use of a vessel sealing device, is being applied to the IMA (Inferior Mesenteric Artery) 1 cm after originated from the aorta. Using also a sealing device, IMV ( Inferior Mesenteric Vein) is being ligated at the level of the low border of the pancreas. Told's fascia is taken down and thus the dissection of the

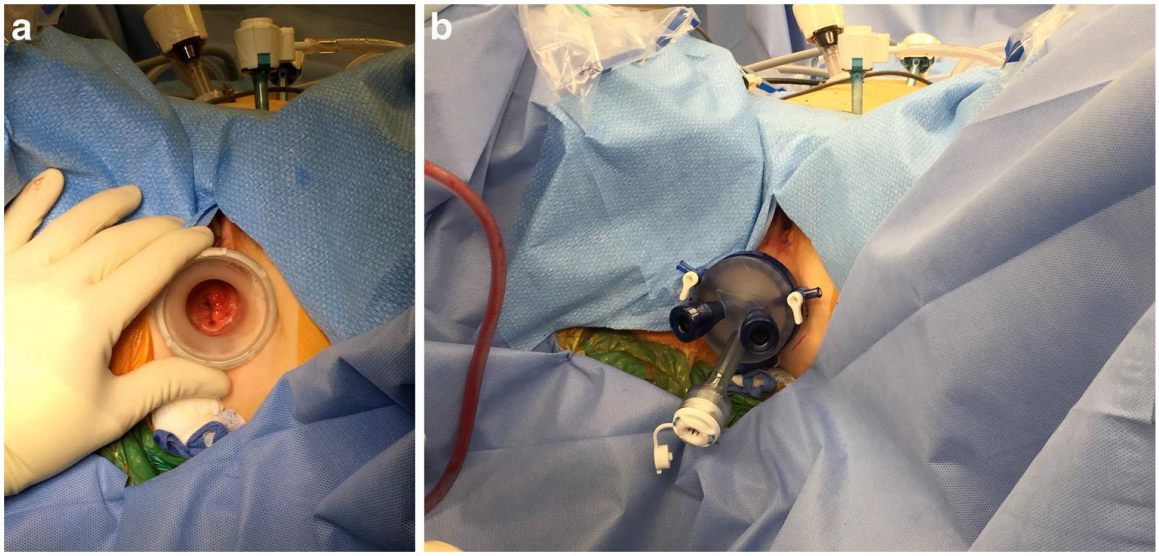
descending colon is finished. Ligation of superior hemorrhoidal vessles is performed. Rectal dissection begins following the posterior plane. Circumferential plane follows, and finally the anterior plane, respecting Denonvillier's fascia, leading to a meet-point with the perineal team. Splenic flexure mobilization is performed when needed so as to achieve a tension free coloanal or stappled anastomosis.

- Transanal phase: Clear identification of the dental line with the use of a self retaining retractor is the first step (LoneStar , Cooper surgical , Trumbull , CT ,USA) . The transanal platform is then inserted in an, as possible, atraumatic way. Reversed triangle scope is advised to be used with the scope at the lower trocar. (Fig 2). It has to be noted that during the transanal phase, transanal pressure has to be higher than the abdominal pressure to obtain a clear plane. A 0 polypropylen suture with a 26mm rounded needle is used to place the purse-string so closure of the distal rectum is achieved. With this maneuver DRM is achieved. It is essential that the suture is placed at the same distance circumferentially from the transanal device , including the same "amount" of tissue , avoiding capturing essential surrounding structures (ex vagina). It is advised to start from the anterior wall (12h), and move clockwise. It is also very important that closure of the purse-string is air tight to avoid not only contamination and tumor spillage, but also CO2 loss intraluminal.(Fig 3).This step can also been done with standard open technique if the distance from the anal verge is accessible or laparoscopically if the string site cannot be reached transanally. It is recommended to use iodine solution to dilute the rectum to wash out cancer cells during this procedure.

Another variation to this step is the initial use of electrocautery, prior inserting the purse string, 1 cm lower of the distal macroscopic end of the tumor to mark the exact place of the area that the suture will be placed (Fig 4). Inserting the purse-string suture as previously described follows.

Next step is marking the dissection line using an electric hook "tattooing the mucosa" (Fig 3). Full thickness perpendicular dissection of the rectal wall is then carried out using monopolar hook in a circumferential progressive manner before moving deeper. Next step is the dissection, following the "holy plane" down to up avoiding a cone shape specimen so as to ensure the whole mesorectal envelope is obtained. Posterior and anterior planes are easier to dissect than the laterals. Recommendation is to proceed to

lateral dissection after the posterior and the anterior, by cutting the imaginary line that completes the circumference, of the already dissected anterior and posterior mesorectum. Better plane for the dissection by pushing the specimen cephalad rather than retracting it through the anus can be achieved. This is one of the most important steps of the transanal procedure because it is essential to enter the correct plane. It is important to start from the posterior plane between the muscular wall of the rectum and the presacral plane. Caution is needed not to enter the intermesorectal plane at the beginning, and staying exteriorly of the fascia propria of the mesorectum. . During the lateral planes it is essential to stay medial to the lateral sympathetic nerves (Fig 5).




Pic 2 : a, b Gelpoint PATH access channel in place, providing visualization of the tumor and access to the low rectum. When the cap is placed, insufflation is possible and allows the transition to laparoscopy (Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

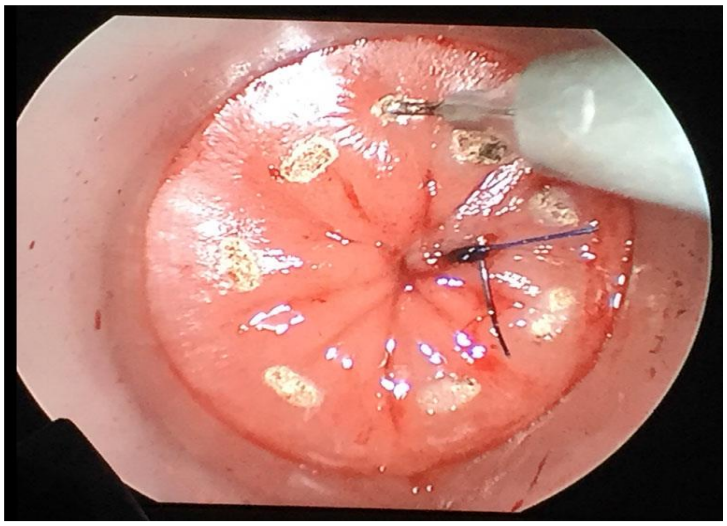


Fig 3 The rectum has been marked circumferentially between the closed
prolene suture and the top of the access channel, defining the level of full thickness rectal transaction.
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

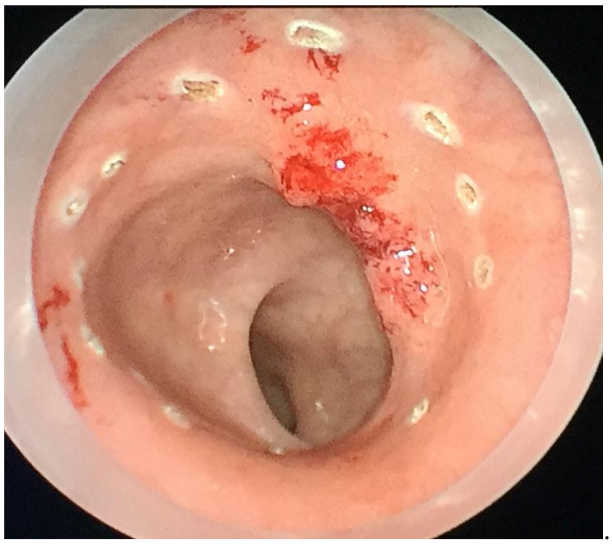


Fig 4 : Rectal lumen marked laparoscopically with cautery for subsequent placement of purse string suture for rectal closure. This prevents stool spillage, CO2 infiltration of the rectum and colon and isolates the tumor from the dissection plane.
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

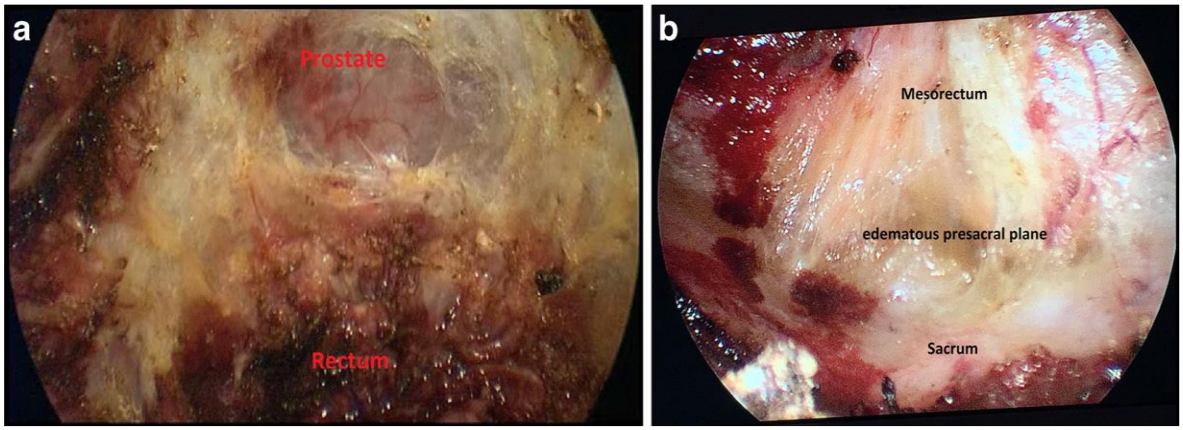



Fig. 5 a, b The anterior and posterior planes are easiest to develop early in the dissection and are followed around circumferentially to perform the totalmesorectal excision (TME)
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

Before communication of both teams is achieved, a second purse-string (2-0 polydioxanone) is placed in the free open edge of the distal rectum. It is important that the distal rectum cuff is mobilized and not attached to the levators or the vagina/prostate anteriorly so that the stapler can be easily inserted for the anastomosis . (Fig 6)

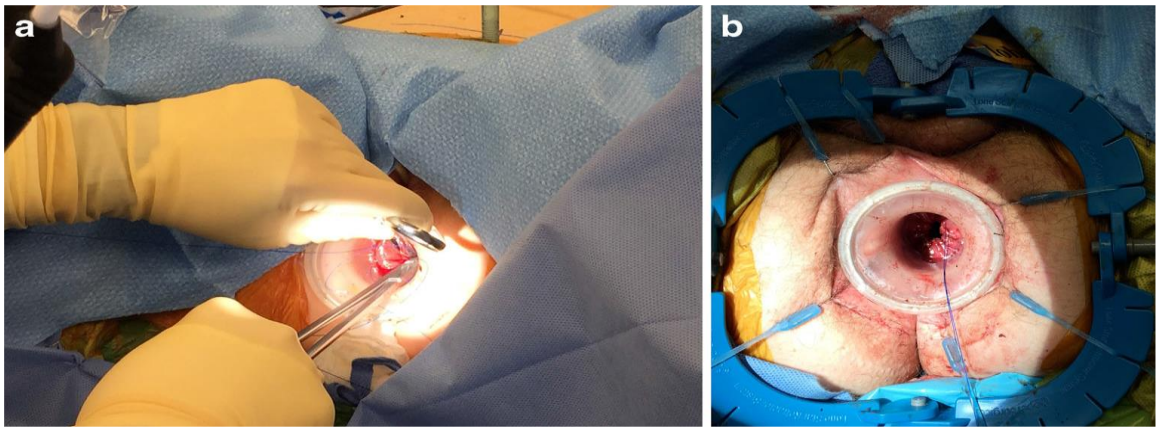



Fig. 6 a, b The distal 2–0 Prolene purse string suture is placed in a hand sutured fashion through the access channel
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

When “rendez-vouz” of the transanal and perineal team is achieved at the peritoneal reflection, and when this reflection is been dissected the two teams work simultaneously until rectum and sigmoid are fully free to be extracted. The communication of the two teams can be achieved either on the anterior plane in the cul-de-sac or posteriorly in the presacral plane.

Extraction can be done either from the abdomen (Pfannestiel incision, ileostomy marked site, or by extending the infraumbilical port site) or from the anus. In cases of big bulky tumors, or narrow pelvis, a Pfannestiel incision is needed for the specimen to be removed through the abdomen. (Fig 7)

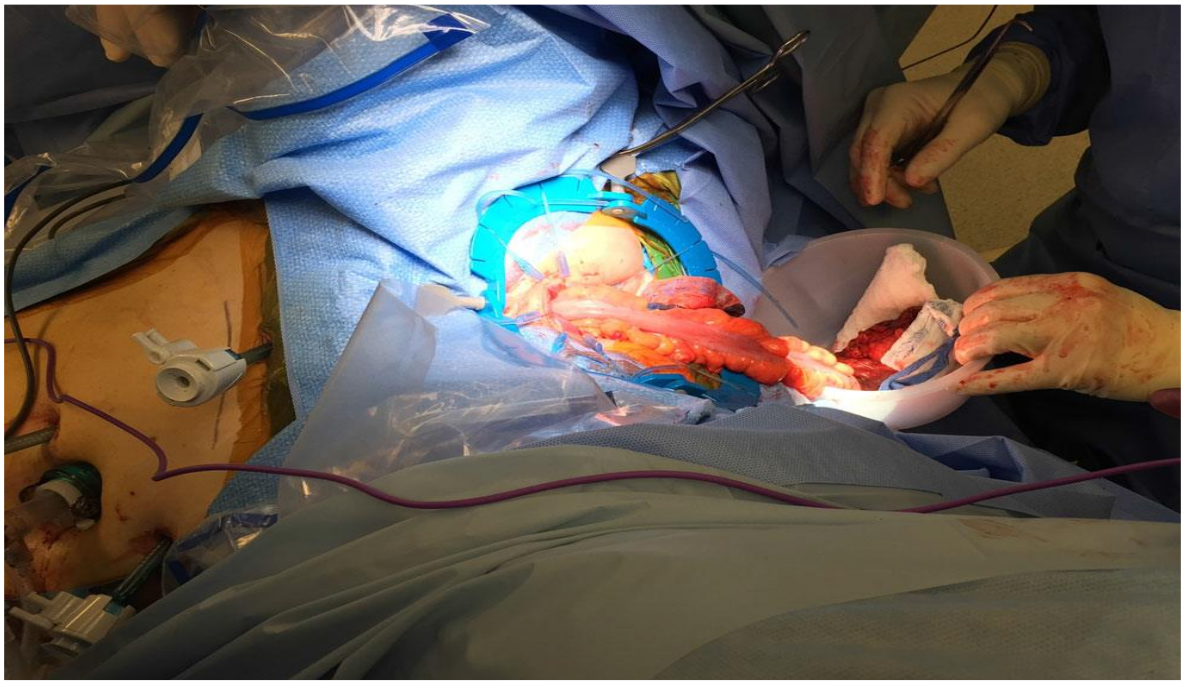


Fig. 7 The mobilized and devascularized rectum is exteriorized through the access channel where it is resected, and the EEA anvil is placed in the proximal colon in preparation for the anastomosis
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

In case of very low rectal tumors that internal sphincter is involved, the transanal operation begins with a standard intersphincteric open approach after the appliance of a self retaining retractor such as the LoneStar system. The rectal wall is then divided circumferentially and after the intersphincteric plane is found the procedure continues using standard open surgery equipment as far as proximal is possible so that the

transanal platform can be inserted. After that the distal rectum is sutured closed, so as to avoid air leak and spillage of the area and the previous mentioned procedure of mesorectal excision continues.

### *4.4 Anastomosis*

The types of anastomosis depending the length of peripheral rectum are either stapled or hand-sewn colo-anal.

- Stapled technique: If the specimen is extracted through the abdomen, the abdominal team places and secures the anvil in the proximal colon, and then guides it to be placed in the pelvis. A drain (suction type) then is inserted from the anus inside the pelvis and the distal end of the drain is attached in the head of the stapler (Fig 8), The distal placed purse string, already mentioned, then is tied and secured around the drain using it as a guide for the circular stapler to be entered through the pursed distal rectum cuff. The drain tube attached to the spike of the anvil helps lengthen it and makes its manipulation easier. (Fig 8).

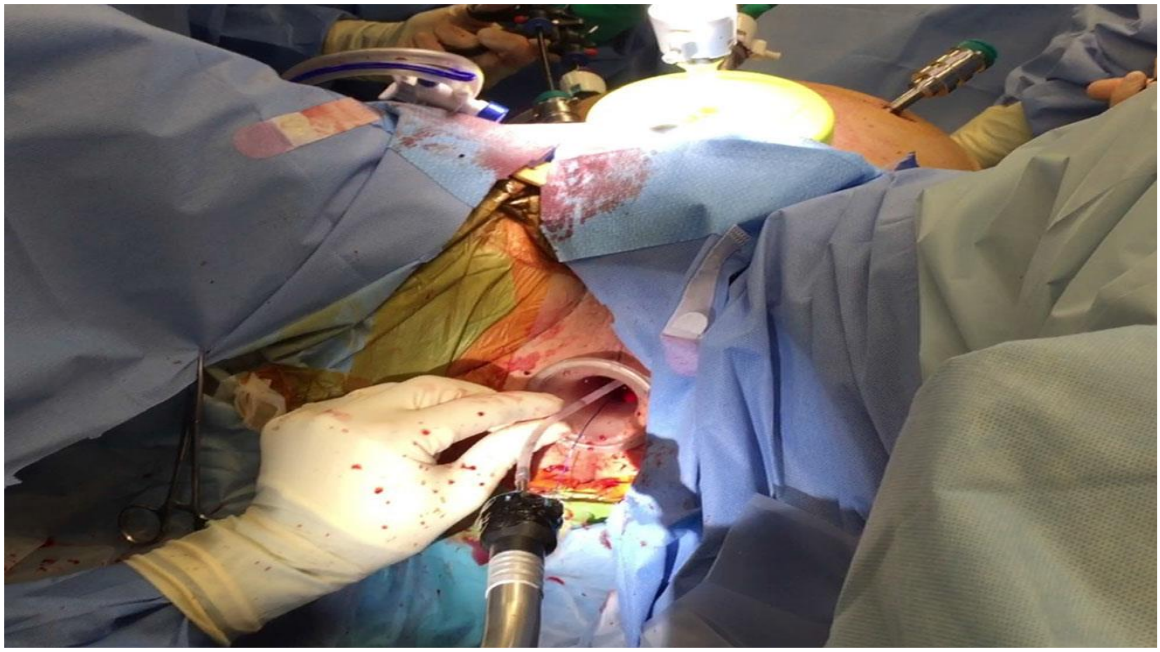


Fig 8 The Blake drain is used to guide the EEA stapler trocar through the purse string closure of the distal rectum and stapler head through the anal canal
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

The abdominal team then detaches the inserted drain and matches the anvil of the proximal colon to the rod of the staplers head. (Fig 9) The stapler closes from the transanal team with the abdominal team monitoring from above. After firing the anastomosis is completed.

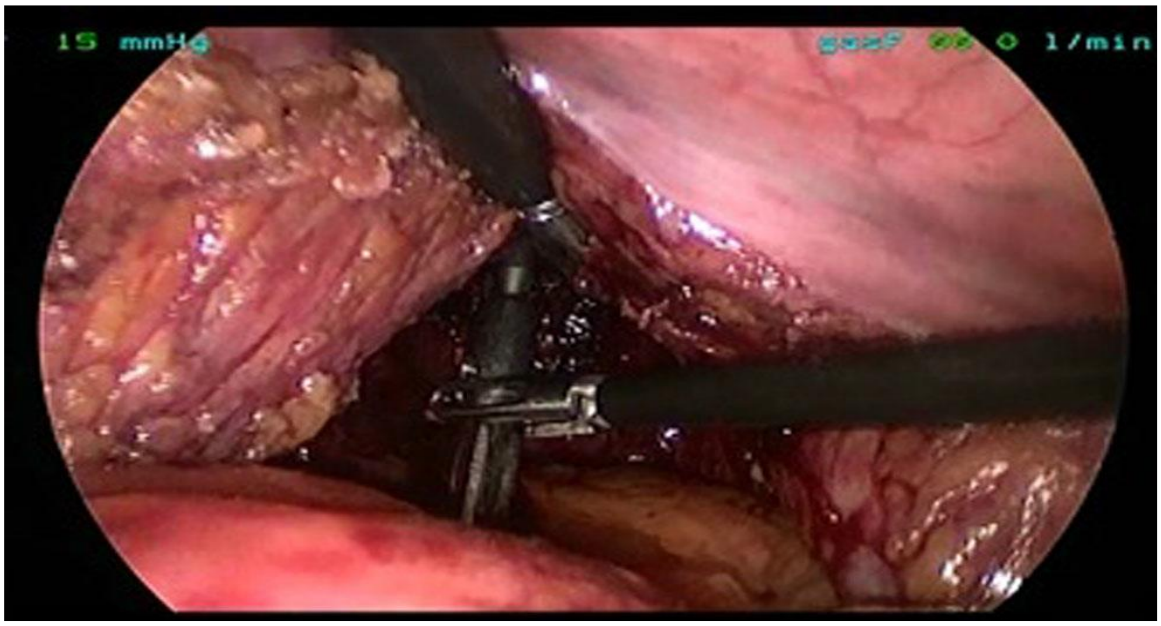



Fig. 10 The abdominal surgeon exposes the pelvis and mates the anvil to the EEA trocar (which has been guided through the purse string closure of the distal rectum). Proper retraction and exposure allow the abdominal surgeon to watch the EEA stapler close, free of surrounding structures such as the vagina
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

When the specimen is extracted from the anus, the transanal team places the anvil and then reintroduces the proximal colon to the pelvic canal. In both cases the rod and the anvil are connected and the circular stapler is fired to create the anastomosis as described before. The transanal platform is then placed again in the anal canal and the anastomosis is inspected from inside the rectum to check for completeness and possible bleeding. In case needed, extra sutures are placed. .

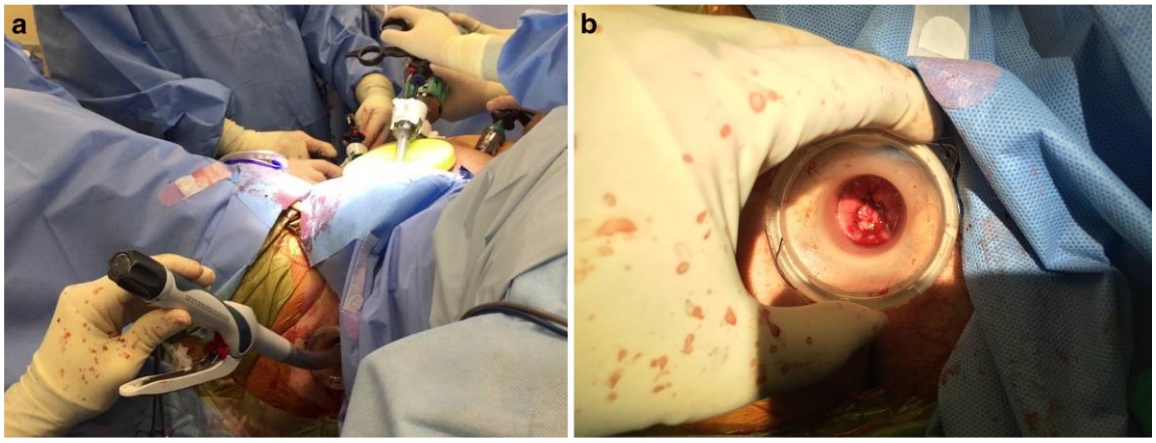



Fig. 11 a, b With the EEA stapler advanced through the access channel, the perineal surgeon fires the EEA stapler to create the low colorectal anastomosis. In b, the circular coloanal anastomosis can be directly visualized, leak tested, and accessed through the rigid channel of the GelPOINT Path device
(Picture and description used after request and under license from Maykel JA , originally published in the artcle : Laparoscopic Transanal Total Mesorectal Excision (taTME) for rectal cancer , published in J Gastrointes Surg , July 2015 (36))

In an article of M Penna et al published in March 2016 (37) , four anastomotic techniques are described . The traditional hand sewn coloanal anastomosis and 3 stapled. All three stapled techniques use the pattern of the purse-string to the distal rectal cuff.
1) EEA haemorrhoid stapled anastomosis: The first analyzed is with the use of the 33 mm, AutoSuture EEA ,haemorrhoid and prolapse DST series, Covidien. Due to the extended reach of the center rod of the anvil (13.5 cm) the use of the "drain technique" described above is not necessary. (Fig 12)

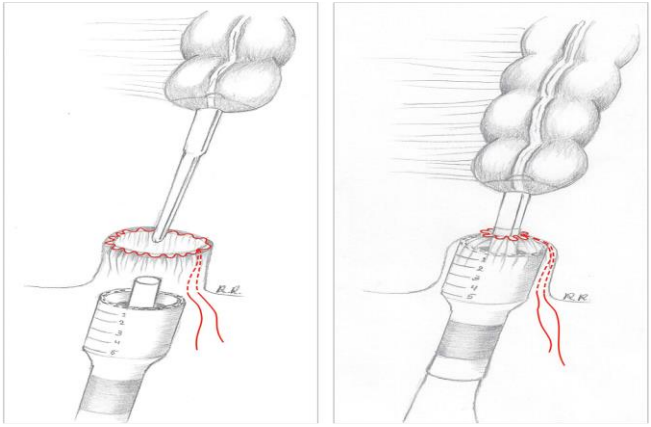


Fig 12 . Pursestring placed distal rectal. The long spindle of the circular EEA stapler is brought transanally through the centre of the pursestring suture (left image). The anvil is connected to the centre shaft of the stapler, and the pursestring is then tightened around the centre rod (right image) ( Pictures by Mrs Ria Raijmakers and description retrieved from the article of M Penna , Penna M, Knol JJ, Tuynman JB, Tekkis PP, Mortensen NJ, Hompes R.Four anastomotic techniques following transanal total mesorectal excision (TaTME). Tech Coloproctol. 2016 Mar;20(3):185-91)

2) Modified circular stapled anastomosis 28–31 mm with abdominal view: The second one describes the technique analyzed previously with the use of the drain as a guiding catheter so the rod of the stapler head is inserted through the distal rectum and the purse string attached captures the drain. The drain acts as a guide to ensure that the rod is entered in the center of the distal rectum (Fig 13). After abdominal removal of the drain from the abdominal surgical team the anastomosis is conducted.

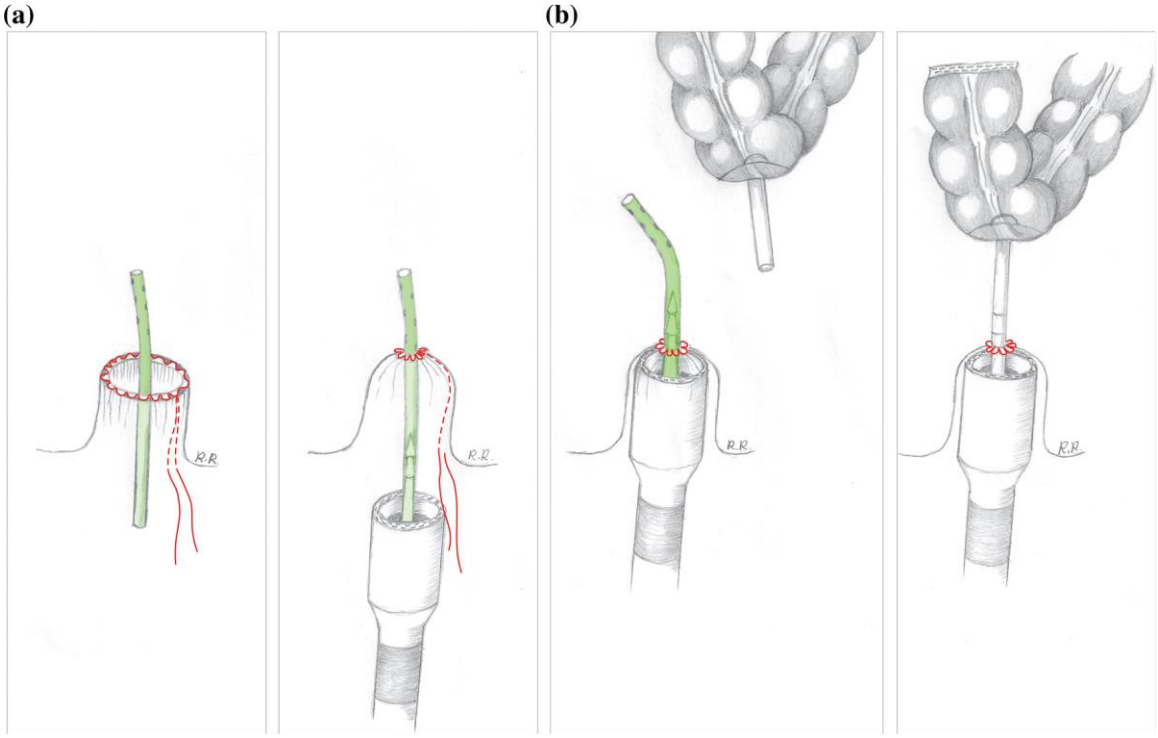



Fig.13 A 10Fr redivac drain is inserted through the central opening of the pursestring and secured by tying the pursestring (a). The spindle of a standard 28- or 31-mm AutoSuture CEEATM circular stapler is attached to the distal end of the drain (a) and advanced into the pelvis (b). With the assistance of the laparoscopic graspers, the drain is removed, and the anvil is connected to the spindle ready to form the anastomosis (b)
( Pictures by Mrs Ria Raijmakers and description retrieved from the article of M Penna , Penna M, Knol JJ, Tuynman JB, Tekkis PP, Mortensen NJ, Hompes R.Four anastomotic techniques following transanal total mesorectal excision (TaTME). Tech Coloproctol. 2016 Mar;20(3):185-91)

3) Modified pull-through circular stapled anastomosis 28–31 mm with transanal view: In this technique the colon with the anvil is extracted down to the pelvis using a 2-0 multifilament suture attached in the anvil of the stapler where the white plastic cup is attached. The anvil is retracted through the open distal rectum carefully so that the previously placed but not tightened string of the distal rectum is placed at the base of the anvil. Once this is completed the purse string is then tightened around the anvil. Using a

laparoscopic instrument the anvil is extracted from the anus and the white cup is removed using an open surgery instrument (curved Roberts artery forceps). The stapling gun is being attached to the anvil so the anastomosis is performed under direct vision. (Fig 14)

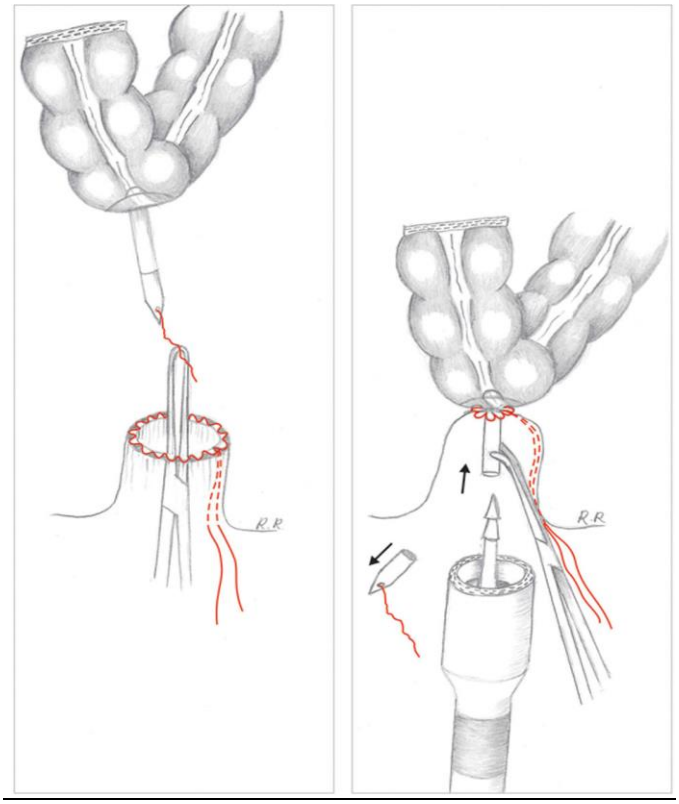


Fig. 14 A multifilament suture is attached to the white plastic cap that is connected to the anvil which has been secured with a pursestring in the bowel. A laparoscopic grasper passed transanally grasps the multifilament suture and guides the anvil down to the rectal opening in order to tighten the second pursestring around the anvil. Whilst the anvil is held in place with a curved Roberts artery forceps, the white cap is removed, and the stapling gun attached allowing the anastomosis to be performed under direct vision.
(Pictures by Mrs Ria Raijmakers and description retrieved from the article of M Penna , Penna M, Knol JJ, Tuynman JB, Tekkis PP, Mortensen NJ, Hompes R.Four anastomotic techniques following transanal total mesorectal excision (TaTME). Tech Coloproctol. 2016 Mar;20(3):185-91)

- Hand-sewn technique (side to end): In case of hand-sewn anastomosis , four reference sutures are placed to the distal rectum (purse-string is not used in this case) to guide the colonic conduit down. A colotomy in the antimesenteric border of the proximal colon is made, and these four sutures are placed to the wall of the colon .Alternative a Foley catheter 14fr can be inserted via the anus inside the antimesenteric border of the colon to prevent twisting of the colon as this is pulled to the anus. The colon is then

properly descended without tension and positioned in the pelvic canal. Avoiding tension and twisting of the proximal colon is essential to reduce the risk of post operative anastomotic leak and ischemia of the anastomosis. The anastomosis is then completed with the use of simple 2-0 or 3-0 polyglycolic acid interrupted sutures. Each suture includes the mucosa of the rectal cuff with a portion of the proximal internal sphincter and full thickness muscular layer of the colon. The anastomosis can be created as side-to-end , colonic J-pouch , or straight (end-to end).

It has to be noted that the use of the 33 mm, AutoSuture EEA ,haemorrhoid and prolapse DST series by Covidien has the disadvantage of higher risk for damaging essential circumferential structures such as the anal sphincters or the vagina, when the anastomosis is made, due to its large diameter , and also that a sufficient rectal cuff is needed so the head of the stapler fits. On the other hand the long length of this instrument allows passing from the purse string without the need of the "drain technique". The third technique described, (Modified pull-through circular stapled anastomosis 28–31 mm with transanal view) is useful only in heights of rectal cuff up to 4 cm due to the fact that the anastomosis is done very low and under direct vision.

It is suggested from M. Penna et al (37) , that if the tumor lies in the anorectal junction the TaTME to start without a platform and the anastomosis to be coloanal hand-sewn , if the tumor is higher to initiate the transanal operation with the use of the platform, and depending the height of the tumor the anastomosis to be conducted with the three previous mentioned ways in a manner of : 2-3 cm with the use of the transanal pullthrough technique , 3-4 cm with the abdominal technique (use of "drain technique) , and if 4cm and higher with the EEA Haemorrhoid Stapler.

A diverting ileostomy is then made in high risk patients, such as patients with colonal anastomosis , obese patients ,or previously irrigated . Suction –drain is inserted in the pelvis and a soft rectal tube is placed to minimize pressure intraluminal in the rectum where the anastomosis is established.

## 5. LITTERATURE REVIEW

### *5.1 Systematic reviews*

As mentioned before TaTME is a rather new method in the treatment of colorectal cancer. Not many systematic reviews or prospective studies have been published. It is now ongoing an international multicentre randomised study comparing short- and long-term outcomes of TaTME and laparoscopic TME for rectal cancer (COLOR III) (26) ,
Three systematic reviews, four meta-analysis comparing laparoscopic to transanal approach, and 1 case series of 720 patients are being analyzed (28-33,48,49). Quality of life and functional outcome after TaTME is reviewed in an article published in 2016 by T.W. Koedam et al. (38) .

The first review presented by Simillis et al (28) in October 2015, consists of 36 studies (8 case reports, 24 case series and 4 comparative studies) of total 510 patients. Search period was January 2007 until 8 December 2014. Rectal adenocarcinoma was the main indication for surgery (16 patients with benign disease). The following table (table 2) shows patient characteristics.

**Table 2: Patient characteristics**

| | |
|---|---|
| Age | Range: 23 to 87<br>Mean 43-80 ,<br>Most frequent 65 |
| Male/female ratio | 2:1 |
| BMI | Range:16 to 42 kg/m2<br>Mean: 21.7 to 31.8 kg/m2,<br>Most frequent: 26 kg/m2 |
| Neoadjuvant therapy | 71% chemoradiotherapy<br>7% radiotherapy<br>1% chemotherapy<br>21% no neoadjuvant |
| Tumor distance from anal verge | Range: 1-15 cm<br>Mean : 4 -9.7 cm<br>Most frequent :5 cm |
| Tumor size | Range: 0.6-9.3 cm<br>Mean: 2.5-3.7 cm |

| | |
|---|---|
| Preoperative clinical tumor size (among studies reporting it) | T1 : 6% T3 : 65%<br>T2: 21% T4: 8% |
| Preoperative Lymph node staging (among studies reporting it) | Nx : 2% N1 : 29%<br>N0 : 52% N2 :17% |

TaTME was performed purely transanally or with laparoscopic assistance (hybrid TaTME). When purely transanal approach was conducted, with no abdominal assistance, not only the mobilization of splenic flexure and left colon, but also the ligation of the vascular pedicle of the inferior mesenteric vessels was performed transanally. In hybrid TaTME , the abdominal approach was either laparoscopic ( multiple port , mini laparoscopy-three port , single port) , robotic or with open approach.

The operation time range was 76 to 495 min, with mean operation time 143-450 min. Blood loss range was from 0 – 600 ml, mean 22-225ml. Twelve conversions were reported to open surgery. The reasons for these were: obesity, urethral injury, high bulky tumor, adhesions caused by prior abdominal operations, and posterior fixity of the tumor. Intraoperative complications reviewed were a small tear of the rectal wall ,rectal perforation, intraoperative pelvic bleeding that was managed with a 24h paching, urethra injury managed with transanally suturing, air embolism , accidently opening of the Douglas leading to air leakage prior completion of the TaTME, and pneumatosis of the retroperitoneum and mesentery of the small bowel.

The length of stay ranged from 2-29 days, mean 4.3-16.6 days. There was no 30 days mortality and 1 death reported due to pulmonary embolism eight weeks post op. In the following table (Table 3), post-operative complications reported are analyzed.

**Table 3: Post-operative complications**.

| | | | |
|---|---|---|---|
| Anastomotic leakage | 26 | Anastomotic fistulae | 1 |
| Pelvic abscess formation | 16 | Urine incontinence | 1 |
| Urinary retention and transient urinary disfunction | 15 | Ascites | 1 |
| Ileus small bowel | 15 | Sepsis requesting critical care | 1 |
| Anastomotic stenosis | 7 | Acute renal failure | 1 |

| | | | |
|---|---|---|---|
| H20 and Na depletion due to high ileostomy output causing renal failure | 5 | Rectovaginal fistulae | 1 |
| Bowel obstruction | 4 | Haemorrhage | 1 |
| Pelvic hematoma | 3 | Stoma dermatitis | 1 |
| UTI | 3 | Cerebral infraction | 1 |
| Fever | 3 | Pertonitis secondary to ileal injury | 1 |
| Wound infection | 2 | | |
| Pneumonia | 2 | | |
| Transient paraesthesia due to positioning | 2 | | |
| Post Op RBC transfusion | 2 | | |
| Pulmonary embolism | 2 | | |

Reoperation rate of 3.7 % (14 cases) were reported. Reasons for reoperation were abdominal abscesses, small bowel obstruction and anastomotic leaks related to proximal colon necrosis due to ischemia.

The histopathological results reviewed showed a complete or intact or satisfactory TME in 88% of the cases reported. CRM margin negative more than 1mm was reported in 95%. DRM in 99.7% was negative. (Table 4)

**Table 4 : Histopathological results reviewed**

| | |
|---|---|
| Lymph nodes | -Range 5 to 81 ,mean 11.5 to 33<br>-N0 72%<br>-N1: 19 %<br>-N2 :9 % |
| Tumor size (T) | -T0: 11% -T3: 48%<br>-Tis: 1% -T4: 4 %<br>-T1: 10 %<br>-T2: 26% |

| | |
|---|---|
| TME Description (462 reports) | -Complete-Intact-Satisfactory-G3: 88%<br>-Nearly complete-G2 : 6 %<br>-Incomplete- inadequate- G1 : 6% |
| CRM (455 reports) | -Negative margin >1mm : 95 %<br>-Tumor infiltration <1mm<br>from resection margin : 5 % |
| DRM (326 reports) | - Negative : 99.7 %<br>- Positive : 0.3 % |

In this systematic review, six studies reported follow-up in matter of oncological outcomes. No long term outcomes have been analyzed. (Table 5)

**Table 5 : follow-up results**

| **Study – author** | **Follow up-No of patients** | **Results** |
|---|---|---|
| Rouanet et al (39) | -Range:10-41 months<br>-Median: 21 months<br>-30 pt | • 4 cancer related deaths<br>• 12 patients with locoregional or distal recurrence (treated)<br>• 4 locoregional recurrence only<br>• Survival rates in 12 months: 96.6%<br>in 24 months: 80.5 %<br>• Recurrence-free survival rates<br>12 months : 93.3%<br>24 moths : 88.9% |
| Atallah et al (40) | -Median : 6 months<br>-20 Pt | No locoregional recurrence<br>One distal metastasis |
| Sylla et al (41) | -Mean 5.4 months +/- 2.3<br>-9 pt | All disease free |
| Chouillard et al (42) | -9 months<br>-16 Pt | No recurrence distal not local |
| Tuech et al (43) | -Range:18-52 months<br>-Median 29 months<br>-56 Pt | • Overall survival rate : 96.4%<br>• 1.7 % local recurrence<br>• Disease free 5 year 94.2 |
| Lelong et al (44) | 24 months<br>34 Pt | • Comperative La vs Ta<br>• Comperative Survival rates between laparoscopic and transanal<br>• Local recurrence : 3% transnal<br>6% laparoscopic |

The oncological outcomes from this systematic review are comparable to those of open and laparoscopic approaches.

The positive CRM margins were in 5% of cases, compared to open surgery where positive CRM is from 1.3 to 18% , and to laparoscopic from 1.2 to 18.1 %. For DRM, positive margin was 0.3%, compared to reported incidence in open from 0 to 1.2% and laparoscopic from 0 to 1.3%. Grade 3 –complete TME is in this study 88% and G2-nearly complete 6% resting only 6% as incomplete.

Analyzing lymph nodes in this systematic review the mean number was 11.5 to 33 compared to open and laparoscopic approaches.

The peri-operative morbidity rate was 35%, including new types of serious complications such as urethral injury, uncommon in open or laparoscopic operations. Also the augmented need for coloanal anastomosis with the TaTME approach raises the related morbitity of this type of anastomosis. The anastomotic leak of 6.1% reported is comparable to rates of laparoscopic (1.2 – 10%) and open (1.4-12 %). Another relevantly common complication reported was urinary disfunction and retention in 5% of cases. After laparoscopic or open surgery, rates of sexual and urinary dysfunction reported incidence is from 11-38 % and 0-26% respectively. It appears that with the better planes achieved during the transanal approach through the presacral plane, preserving the sacral autonomic nerves can lead in lower incidence of urinary and sexual dysfunction. On the other hand the prolonged time of the transanal platform causing anal dilatation, has to be analyzed in terms of anal sphincters damage and incontinence.

Four of the thirty-six studies reviewed in this systematic analysis are comperative studies between La and Ta approaches. The results follow on table (Table 6)

**Table 6 : Results of comperative studies in this review**

| Author – study | Results |
|---|---|
| Velthuis et al (45) | • 25 patients<br>• Statistical significant difference in number of Pt with Complete TME in Ta Vs LA : 96% vs 72 %<br>• CRM , DRM ,Length of specimen the same |
| Fernández-Hevia M et al (30) | • No difference in 30 day complication<br>• 37 vs 37 patients<br>• Ta group : - Lower readmissions<br>- Lower operative time<br>- More frequent coloanal anastomosis<br>- Longer DRM |
| Marks et al ( 46) | • 17 patients<br>• No difference perioperative or Histopathological |
| Lelong et al ( 44) | • 34 patients<br>• Lower conversion rates in Ta<br>• Shorter hospital stay<br>• Comparable oncological outcome<br>• 24 months intermediate – outcome comparable survival rates and local recurrence Ta vs La |

Although there are not clear indications, contradictions and patient selection criteria for the TaTME technique, based on this review it can be said that patients with low and middle rectal cancer obese male with narrow pelvis are suitable. T4 tumors, or with threatened CRM or possible involvement of sphincters should not be candidates.

A second systematic review presented by C.L. Deijen et al in November 2016 (29) analyzed thirty-three studies (three case reports, twenty-five case series, five comperative studies (30,47,49,60,61)) including 794 patients. Search period was 1 January 2005 until 1 July 2016. The aim of this review is to analyze data concerning surgical oncologic perioperative outcome with specific focus on adverse effects .Thirteen reviews for this systematic review were also included in the review of Simillis et al (28), previously mentioned. In this review a comparison between high and low volume centers was analyzed.

In total 794 patients included. Patient and Tumor data are presented in table 7, and operative –surgical details and outcomes reviewed in table 8

**Table 7 : Patient and tumor characteristics**

| | |
|---|---|
| • Age (years) | Range: 48-80 y.o<br>Mean : 63.4 |
| • Male / female | 67% / 33 % |
| • BMI (kg/m2) | Range : 20-32<br>Mean: 26.1 |
| • ASA score | Range :1-3<br>Mean :2 |
| • Tumor distance from anal verge (cm) | Range: 2-8.4<br>Mean: 6.3 |
| • cT3-T4 (%) | Range: 40-100<br>Mean : 71.6 |
| • Neoadjuvant therapy (%) | Range 28-100<br>Mean: 72.5 |

**Table 8 : Operative details and surgical outcomes**

| | |
|---|---|
| Conversion (%) | Range: 0-22<br>Mean: 3 |
| Post operative complications (%) | Minor: 0-100 , mean 28.8<br>Major :0-100 , mean 11.5 |
| Operative time ( %) | Range: 166-369<br>Mean: 243.9 |
| Hand-sewn coloanal anastomosis (% pt with anastomosis) | Range 0-100<br>Mean **53.9** |
| Ileostomy (% total pt) | Range :25-100<br>Mean : **90.3** |
| Colostomy (% total patients) | Range : 0-28<br>Mean : 4.7 |
| Two –team approach (%) | Range 0-100<br>Mean: **37.5** |
| Hospital stay (days) | Range 4.5-14<br>Mean: 8.4 |
| 30 day mortality(%) | Range: 0-3.8<br>Mean : 0.3 |

Intraoperative compilations: 12 studies reported complications, 18 reported no intra-operative complications, in 2 studies the number of complications were not reported, and in 1 no major complications were reported.

The following complications were reported in 12 studies reviewed:

- 5 cases of urethral and 5 cases of side wall damage
- One case of C02 leakage,
- One case of extensive pneumatosis of the retroperitoneum and small bowel mesentery
- One case air embolism with oxygen desaturation ,
- Ten cases of bleeding
- One case of bladder injury.

Urethral damage was managed with suturing (2pt) or not operative (1pt), not defined (3pt). In cases of bleeding, five of them the pelvic side wall was the cause, and in one patient the iliac vessels.

For the assessment of TME specimen, the studies used the Quirke's classification, and the results are the following: 87.6% (mean) Complete, 10.9% nearly complete. DRM positive found only in 0.2%, CRM involvement was in 4.7% of the cases. Mostly half of the patients (45.2%) had a pT3, pT4 tumor. Recurrence in a median follow up of 18.9 months was local 4% and distant 8.1%.

Establishing a conclusion about long term results is not safe from this review, thus none of the studies had a 3 year complete follow up. Five studies (302 patients), reported follow up more than 12 months, with mean 18.9 months. Recurrence was locoregional and distal 4.0 and 8.1 % respectively.

From five comparative studies included in this review (30,47,49,60,61) . The following results are presented in matter of conversion, postoperative complications, CRM, and TME completeness is involved. Mean conversion rate in TaTME was 1.4 %, compared to Laparoscopic TME 5.4 %. (p=0.33). Complications were in TaTME group 30.4% and in Laparoscopic group 34%, (p=0.22). TME completeness was reported in 82.8% of Transanal group versus 75.2% of the laparoscopic (p=0.72) and finally CRM was involved in 3.2% of the TaTME versus 7.6 % of the LaTME (p=0.37).

Interesting in this review is the comparison between low and high volume centers regarding surgical details, operative time, number of teams involved, conversion rates, TME completeness, CRM involvement, overall complications, local recurrence, and distant recurrence. (Table 9)

**Table 9: comparison of low vs high volume centers on taTME**

| | Low volume (< 30 cases) ,weighted mean | High volume (> 30 cases), weighted mean |
|---|---|---|
| Conversion (%) | **4.3** | 2.7 |
| Post operative complications (%) | Minor 21.9<br>Major 12.2 | 25.2<br>10.5 |
| TME quality (%) : Complete<br>Nearly Complete<br>Incomplete | 80.5<br>15.1<br>4.0 | **89.7**<br>9<br>1.3 |
| DRM(%) | 0.4 | 0.3 |
| CRM (%) | 4.8 | 4.5 |
| pT3 –pT4 (%) | 44.3 | 45.1 |
| Gender Male (%)<br>Female (%) | 65.8<br>34.2 | 67.4<br>32.6 |
| BMI (kg/m2) | 26.1 | 26 |
| Age (years) | 62.3 | 63.8 |
| Tumor distance from anal verge(cm) | 6.0 | 6.5 |
| cT3 –cT4 (%) | 71.3 | 69 |
| Neoadjuvant therapy (%) | 69.8 | 73 |
| Operative time (min) | 282.5 | 222.2 |
| Hand-sewn anastomosis (%) | **62.6** | 46.8 |
| Ileostomy (%) | 89.8 | 88.8 |
| Colostomy(%) | 6.8 | 4.8 |
| Two- team approach (%) | 13.7 | **51.3** |
| Hospital stay (days) | 6.6 | 6.5 |
| Mortality 30 days (%) | 0.4 | 0.2 |
| Recurrence Local (%)<br>Distant (%)<br>(data only >12 months.) | **8.9**<br>7.7 | 2.8<br>8.1 |
| Follow up (months) | 21.9 | 18.3. |

Although the systematic review doesn't mention any statistically significant comparison between high and low volume centers, it has to be mentioned that local recurrence was higher in low volume centers compared to high, Two team approach was more often in high volume centers (51.3% < 13.7%), conversion rate was higher in low volume and TME quality was better in high volume centers (89.7% < 80.5%).

Another systematic review by Arunachalam et al (49) published in 2016, reviewed fifteen retsospective studies including 449 patients. Mean age, 64.3 years; 64.1% men. The mean distance from the anal verge was 5.6 cm Neoadjuvant therapy was

received in 72% of the patients. Operative time varied from 91 to 495 minutes, with a median time of 254. During the abdominal phase of the operation 90% of patients splenic flexure had to be mobilized. And almost every patient (98%) had a diverting stoma. Anastomotic leak was 9.1%, higher than the Similis et al (28) which was 6.1 (%), and also reoperations were higher. CRM was negative in 98% of the cases. Mean DRM and CRM were 2.5 and 1.1 cm respectively. The resected mesorectum was grade III in 87% of patients .There were no long term 5 year overall study included for disease free survival rates.

### *5.2 Comperative studies Laparoscopic (LaTME) versus Transanal (TaTME)*

Although a rather novel approach in the management of rectal cancer especially mid and low, comperative studies of the transanal technique versus laparoscopic have been published. Most of them are retrospective meta-analysis of cases and one is prospective.

Fernandez et al (30) reported in 2014 , a prospective cohort of 37 consecutive patient all with middle or low rectal cancer treated by taTME from November 2011 until March 2013 , compared to a retrospective cohort of 37 consecutive patients with identical characteristics treated the immediate chronological time before by Laparoscopic TME (period August 2010 to October 2011)

Patients rectal cancer was not higher than 10 cm from the anal verge. All patients with T3-4 NO , T1-4 N1-N2 staged tumor according to preoperative assessment, were treated with Neoadjuvant Chemoradiaton (protocol :total dose 45 Gy , 1,8 daily 5days , 5 days continuous infusion of 5-FU ,225 mg/m2/d ).

- Laparoscopy group: A 0 or 30 degree camera and four or five ports were used. Splenic fixure was not always mobilized, All anastomosis conducted with stapler, and most of the times a diverting ileostomy was made. Specimen extraction was most of the time a Pfannestiel incision. Drain was placed in the pelvis. No hand-assisted was described in the laparoscopy group.

- Transanal group: These cohorts operations were conducted by two separate teams. An abdominal and a perineal. A 3D flex camera was used. In case of very low tumors (<3 cm from the anal verge), an intersphinteric dissection was done originally after cutting

the dental line by electrocautery. After inserting the Ta platform, the surgeons proceeded with the dissection circumferential of the Transanal mesorectal plane. Specimen was extracted transanally, and hand-sewn anastomosis was performed between the proximal colon and the rectal cuff. In case of middle and low cancers, the operation starts with the placement of the transanal platform after positioning the LoneStar retractor. Anastomosis was performed with a stapler (EEA 33mm single use stapler with 4.8mm staples-Autosuture Covidien) ,or hand-sewn coloanal , or lateral/end to end stapled. If specimen was large with a bulky mesentery, the specimen was extracted from the abdomen using a Pfannenstiel incision. Ileostomy was decided on table considering the height of the anastomosis and previous irradiation of the pelvic area.

In matter of age, sex, BMI, previous abdominal surgery, ASA score, Tumor size and location, lymph nodes, positive CRM, pTN, there was no statistically significant differences between Ta and La group. It was though statistical significant the number of patients receiving neoadjuvant chemoradiation in the Ta group than those in the La group. Quality of specimen was equally evaluated as complete in 35 patients of the La group and 34 of the Ta group.

Operation characteristics from this analysis, showed that the time of operation was higher in the La group compared to Ta (252+- 50 vs 215 +- 60 min, $p<0.01$). Colonanal anastomosis was more frequent in the Ta vs La (43% >16 %). More patients in Ta needed splenic flexure mobilization (37.8% in Ta > 13.5% in La, $p=0.02$), and DRM was higher in the Ta group compared to the La (2.7+- 1.7 mm vs 1.8+-1.2 mm, $p<0.01$).

Short term outcomes: There were no statistical significant differences between the two groups. Length of stay and starting diet period were shorter in the transanal group. 30-day post-operative complications were higher in the laparoscopy group than the transanal, 51% La vs 32 % Ta $p=0.16$). Anastomotic leaks were also higher in the La group (11%), compared to Ta (5.4%) $p=0.39$. Fluid Collections, acute urinary detention and readmissions were higher in the laparoscopic group. Readmissions in Ta group were 2 pt (6%) when in the La group were 8 pt (22%) $p=0.03$. On the contrary higher was the incidence of post-operative ileus in the transanal group (11% Ta vs 5% La, $p=0.39$.)

As a conclusion we can say that TaTME is associated with similar oncologic results, fewer readmissions and shorter operative time. It has to be mentioned that in this

metanalysis no data is provided on anal functioning post-operative in matter of continence.

Bin Ma et al (31) reported in July 2016, a systematic review and meta-analysis of Transanal compared to Laparoscopic TME. It is based on seven studies included 573 patients, (270 Ta group and 303 in La group).Indication was low and middle rectal cancer. The oncological outcomes of this metanalysis showed:

From five out of seven studies, that included data on the quality of the specimen , grade of quality of the mesorectum was higher in the Ta group compared to the La ( 140/169 Ta vs 125/169 La , p=0.04) . All studies provided info regarding lymph nodes, CRM and DRM. Equivalent number of harvested lymph nodes between Ta and La were found. Concerning DRM comparable data was found between the two groups .Greater CRM though, was found in the Ta group ($p<0.01$).Six studies provided data on positive CRM and three on positive DRM. The meta-analysis showed that lower number of patients in the TaTME group had a positive CRM (10/220 Ta vs 21/203 La, p=0.02), but the involvement of DRM was comparable (7/133 Ta vs 4/116 La, p=0.67)

Perioperative outcomes were provided after meta-analysis of six studies providing data.

TaTME showed: shorter operation time ($p<0.01$), lower conversion rate (p=0.02), and comparable hospital stay (p=0.19). From three studies data, splenic flexure was needed more on the Ta group (p=0.05). From four studies analyzed no difference in intra-operative complication rate was found. Contrary, post –operative complications, (after analyzing six studies), were lower in the Ta group ( 83/245 Ta vs 107/278 La , p=0.03) .Anastomotic leakage , urinary morbidity and post operative ileus were equal between Ta and La. ( Anastomotic leakage : 26/245 Ta vs 30/278 La , p=0.41 , Urinary morbidity : 11/194 Ta vs 23/244 La , p=0.06 , Ileus 12/194 Ta vs 13/244 La , p=1.00) . The analysis showed also a tendency to fewer readmissions after TaTME but not statistically significant.

This meta-analysis concluded that patients after TaTME had a significant higher rate of complete specimen TME, longer CRM, and less positive involvement of CRM, shorter operation times and lower conversion rates, and lower post-operative complications compared to Laparoscopic TME. Achievement of complete or near complete specimen in Ta was 95.3% versus 88.2% found in the laparoscopic group.

Comparable results on readmissions and hospital stay, and shorter operation time and conversion rate was found. Comparable rate concerning intra-operative complications and significant lower incidence of post-operative complications in Ta vs La were analyzed. It has to be noticed that data for long term outcomes were not provided.

Another meta-analysis conducted by Wei Xu et al (32) published in December 2016, used seven studies including 209 TaTME and 257 LaTME patients. Four of the seven studies included in this meta-analysis are also included in the meta-analysis of Bin Ma et al (31) .

Compared with LapTME, TaTME showed

- a longer CRM
- lower rate of positive CRM
- more specimen with complete TME ,
- less operative time
- Harvested lymph nodes, conversion, DRM, complete remission, intra-operative complications, were not significant different.

There was no significant differenced in matter of anastomotic leakage, reoperation, postoperative complications, readmissions and hospital stay. No data on long term oncological or functional outcomes were provided to be analyzed.

Perdawood et al published in 2015 a study comparing 50 patients who underwent TaTME for rectal cancer studied in a prospective way from December 2013 to April 2015, with 50 patient treated for rectal cancer with laparoscopic TME the preceding period February 2013 to November 2013. Patients had rectal carcinoma up to 10 cm from the anal verge. Group and tumor stage demographics were comparable. Oncological outcomes: CRM positive was found in four patients in the laparoscopic cohort compared to one patient in the Ta one. All patients undergone Transanal approach had complete or nearly complete TME specimen, in contrast to the La group were four patients had incomplete. Intra –operative complications were not different and shorter hospital stay and operation time was found in the Ta cohort. Readmissions were the same. Two anastomotic leakages were observed in the Ta group compared to four in the La group

without statistical significance. In more cases splenic flexure mobilization had to be performed during the Ta cohort. No long term information was presented.

### *5.3 Case series and other reviews*

A study by Penna M et al (33), published in 2016, analyzed data from 66 registered units in 23 countries, from july 2014 until December 2015. Data was retrieved from the international transanal total mesorectal excision (taTME) registry for benign and malignant rectal pathology. 720 patients were analyzed including 634 patients with rectal cancer and 86 with benign pathology. The aim of this study is to show initial short term outcomes of the international registry. The data set of the registry included:

-Patient demographics

-Staging

-Neoadjuvant treatment or not

-Operative details

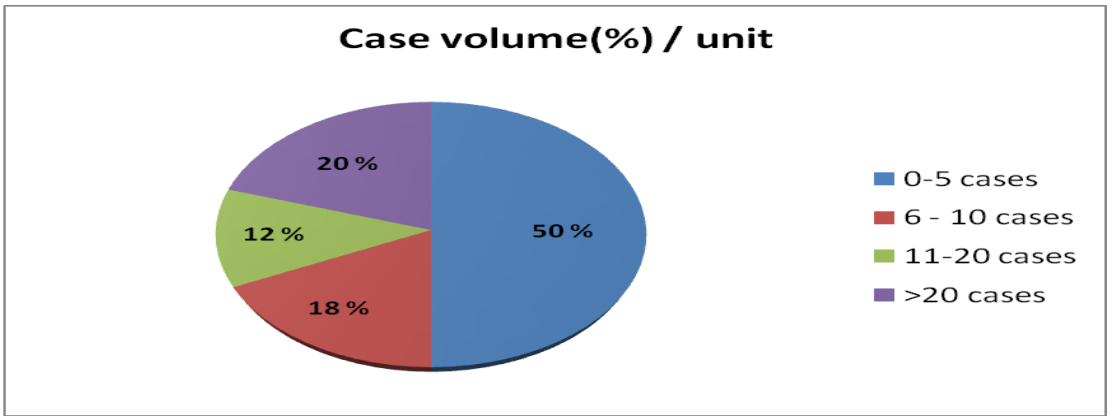
-Outcomes post operative and histological

-Readmissions

-Morbidity and long term oncologic outcome.

Results from this study came up with a volume of 720 patients in a period of time 18 months. 88.1% of them 634 patients were treated for cancer, and the resting 11.9%, 86 patients for benign diseases. Male to female was 67.9% to 32.1% , mean age was 62.4+-13 years old, Mean ASA was 2 ,Mean BMI was 26.5+-4.3 , previous abdominal surgery in 185 patients. Case load per unit was as follows:

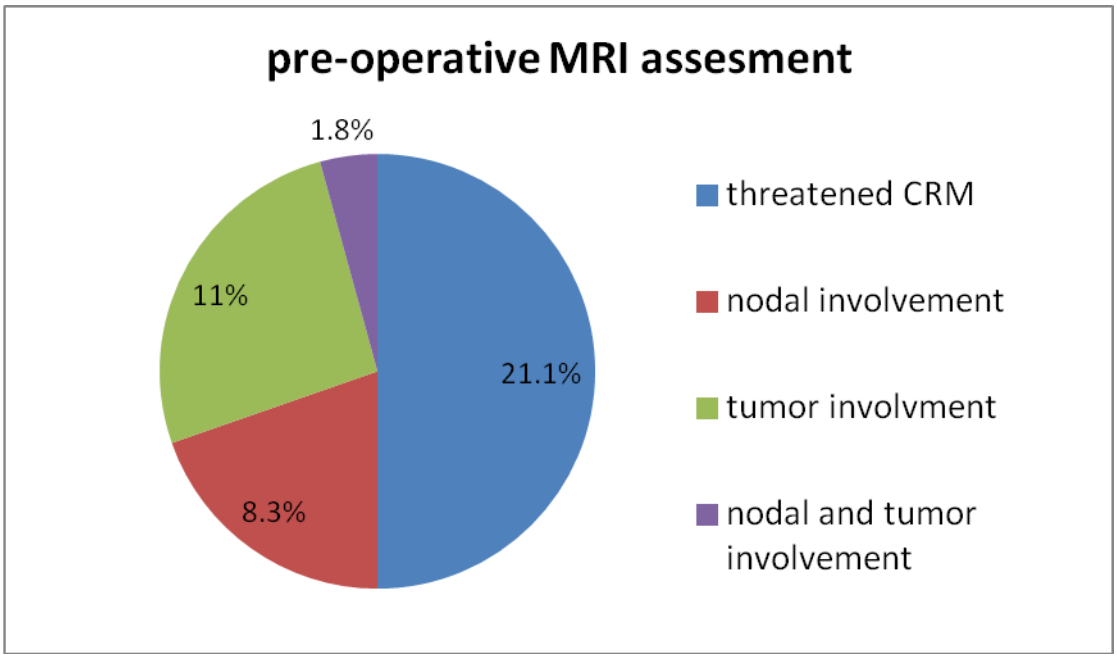
| | |
|---|---|
| 0-5 cases | 33 units (50%) |
| 6-10 cases | 12 units (18%) |
| 11-20 cases | 8 units (12%) |
| >20 cases | 13 units (20%) |




For the cancer related cases: Tumor location was in - **62% of cases <6cm** ,

- 37% of cases 7-10 cm ,
- 1% of cases > 10 cm.

Pre operation **MRI staging** revealed the following data :




MRI staging results concerning tumor staging :

| | | |
|---|---|---|
| T stage | T1- T2<br>**T3**<br>T4 | 185 cases (33.1%)<br>**343 cases (61.4%)**<br>31 cases (5.5%) |
| N stage | **NO**<br>N1<br>N2 | **232 cases (41.8%)**<br>221 cases (29.8%)<br>102 cases (18.4%) |
| M stage | Synchronous metastatic disease | 40 cases (6.6%) |

Tumor location was in 43.3% anterior and 41.5 % posterior. Neoadjuvant therapy was admitted to 355 patients (57.1 %), Preoperative CRM involvement from MRI was in 115 patients (21.1%).

Operative details: Regarding the abdominal phase of the operation: 650 patients underwent minimal invasive approach (96.9%), 72% of the patients underwent splenic flexure mobilization. It was analyzed the extent of abdominal resection during the up to down procedure. The results follow:

- Anterior extent in Cancer patients:

| | |
|---|---|
| Male patients | Pouch of Douglas → **53%**<br>Seminal vesicles →38%<br>Prostate →9% |
| Female patients | Pouch of Douglas → **67%**<br>Mid-vagina →7.1 % |

- Posterior extent in Cancer patients :

| | |
|---|---|
| Level of 8-10 cm | **56 %** |
| Level of 5-7 cm | 31% |
| Level < 5 cm | 13% |

In benign diseases it is notable that the surgeons proceeded lower than the cancer patients .Anterior resection reached in male patients the seminal vesicles in 53 % (compared to 38% in cancer patients), and posterior resection reached <5 cm in 20% (compared to 13% in cancer patients) 91% of the patients underwent a diverting ileostomy.

Concerning perianal phase of the operation, both rigid and flexible platforms were used (14.4% to 85.6 % respectively) .Rectal purse string technique was used in 62.5 cases of cancer and 52.6% of benign patients, Medial purse string location was mean 4 cm from anal verge, and in 66.7% of the patients with anterior tumor, the anterior resection was performed anterior to Denonvilliers fascia.

Anastomosis was manually conducted in 252 cases (43.6%) , and stapled in 327 cases (56.5%).

**Stapled** anastomosis

| | | |
|---|---|---|
| Stapled in cancer patients | • **Side-to-end**<br>• End-to-end<br>• Colonic J pouch<br>• Ileal pouch-anal anastomosis(IPAA) | **49.2%**<br>46.9%<br>3.3%<br>0.7% |
| Staplers used in cancer patients | 28/29 mm<br>31 mm<br>**33 mm** | 30.6%<br>12.4%<br>**57%** |

**Manual** anastomosis in cancer patients:

| | |
|---|---|
| **- End –to-end →67.9%** | - Colonic J-pouch → 4.4% |
| - Side-to-end →27.3% | - IPAA→ 0.4% |

For benign cases, stapled anastomosis was in the majority of the patients with most of them performed as IPAA (89.5%), manual were referred in 3 patients only.

Intraoperative events and complications are also analyzed. 40 cases of conversion are referred (6.3%). Intra –operative events recorded, consisted of ureter transections, iatrogenic small bowel enterotomy on insertion of laparoscopic instrument, splenic injury, and bladder injury. Perineal conversion was also reported in 20 cases (2.8%). Reasons for that was difficulty maintaining appropriate pneumopelvis, failure of purse string closure, excessive smoke, incorrect planes and uncontrolled pelvic bleeding. Most common was the maintaining the air. It has to be noted that these cases didn't use continuous air supply and smoke evacuation systems. Vaginal perforation, unilateral resection of hypogastric nerves and rectal tube perforation were reported. Blood loss was less than 100 ml in 61.7% of the cases.

Postoperative outcomes came with a morbidity of 32.6% and mortality of 2.4 %( 17 cases). Median time of deaths was 248 days. 6 deaths were cancer related. Anastomotic leaks occurred in 40 cases (6.7%). 32 of them (5.4%) of those were early identified and 8 cases were identified >30 days. 14 cases were treated surgical or radiological. Reoperations were done due to left colon ischemia, fecal peritonitis, exams for anastomotic leak under anesthesia, heamatomas, and hernia. Readmissions were up to 6.9%, 50 patients. 60% of them (30 patients) where treated conservatively.

Histopathology results from 634 cases analyzed showed R0 resection in 97.3% of the cases, and R1 resection in 2.7% of the cases (16 cases).Reasons for R1 were positive DRM in 2 patients, positive CRM due to tumor in 10 patients, and positive CRM due to lymph node involvement in 4 patients. TME was described as poor in 24 cases (4,1%).

What was interesting from this review was the fact that after multivariate analysis **three** factors were described to have significant risk for a poor oncologic outcome:

- Posterior pelvic dissection to be performed by the abdominal team to a high less than 4 cm from the anal verge. This upraised the risk up to 6 times for a poor outcome compared to the operation been done by the transanal team
- Tumor lying less than 2 cm from the anal verge.
- Pre-operative positive CRM on staging MRI.

Although there are various studies that analyze the short term oncologic and intra-operative and peri-operative outcomes of TaTME procedure, there are no data on long term outcomes. Reviewing the literature, a study of Koedam et al (38), assessed the effects on patients of TaTME, concerning patient-reported quality of life and functional outcome, in a study published in January 2017. This prospective study conducted from January 2014 until January 2016 in VU University Medical Center in Amsterdam, reviewed patients presenting rectal cancer and being operated under Transanal approach with primary construction of anastomosis. The trigger for this study was the need to study whether patients who are submitted to the transanal approach hamper functional outcome compared to laparoscopic operation.

The fact that the transanal platform cause prolonged dilation of the anal canal , that the anastomosis are closer to the anal sphincters , and the fact that the resections could be more radical which could cause damage to the innervation of elevators ani, led Koedam et al ,to perform this study.

All patients 6 weeks after operation were submitted to a CT scan with a contrast enema, and sigmoeidoscopy to exclude patients with anastomotic problems. In case of diverting ileostomy , stoma was reversed.

Questionnaires were collected prospectively in 1 week prior to surgery, 1 and 6 months post-operative. Questionnaires used were:

| |
|---|
| EuroQol five dimensions (EQ-5D-3L) |
| EORTC QLQ-CR29 |
| EORTC QLQ-C30 version 3.0 |
| Low anterior resection syndrome LARS |

Totally in this period of time 140 patients underwent rectal procedure. 30 patients underwent TaTME with primary anastomosis. 21 males, with a median age 65 years, mean BMI 26kg/m2, ASA I-II 90% of patients. Tumor height median 6 cm. Neoadjuvant therapy was received by 22 patients. No ileostomy was conducted in 6 cases. Although deterioration in all variables was present at 1 month after surgery, most of them returned to baseline 6 months post-operative. Anal function and social function remained worse in 6 months. 6 months post operative, major LARS score was 33% when in 1 month was 80%. These results are comparable to LAR.

## 6. DISCUSSION

Management of rectal cancer has been a "synonymous" with the TME approach since Professor RJ Heald described total mesorectal excision in his publication in 1982 (4). Gaining an en-block complete and intact mesorectum specimen via sharp dissection from pelvic strictures, led to decrease of local recurrence from more than 30% to less than 10%, making TME the gold standard of rectal cancer. Neoadjuvant therapy and intact mesorectum with negative DRM and CRM improve cancer-free survival and local recurrence rates (50-52). Since the boost of laparoscopic surgery, laparoscopic anterior resections have been analyzed through a lot of RCT's comparing them to open surgery. COLOR II has demonstrated that LaTME has the same oncologic results as the open, and decreases local recurrence. In major trials such as the CLASICC trial, COREAN trial, COLOR II, for laparoscopic surgery implied in rectal cancer, local recurrence rate for low and mid cancers was approximately 5% three years after surgery. For low rectal cancer though, the number of specimen described as incomplete with higher rates of CRM positive margins have been higher compared to tumors of the higher rectum. (7-9, 53-56). On the contrary there are two RCT's, ACOSOG Z6051 (57) and ALaCaRT (58), that failed to show non-inferiority of LaTME in comparison to open surgery.

A new approach to rectal cancer, TaTME was initially presented by Patricia Sylla, David W Rattner, Salvadora Delgado and Antonio M.Lacy in 2010. (22). TaTME as a bottom-up approach through a transanal platform to rectal cancer, has since then, been implemented in many hospitals around the world. This technique may overcome the known technical difficulties of low and middle rectal cancer. Male sex, narrow pelvis, obesity, advanced T stage bulky tumors, anterior fixicity of the tumor, neoadjuvant radiotherapy are prognostic factors that increase difficulty in laparoscopic low anterior resections and open surgery. TaTME is expected to overcome these difficulties and improve the oncologic results in terms of negative CRM, DRM and good quality of TME specimen.

Possible **advantages** of TaTME from the literature reviewed:

- Direct vision of the mesorectum resection plane even in narrow low pelvis ,which can improve CRM and DRM margins
- DRM is determined not at the end of the operation as in laparoscopic but at the beginning and under direct vision (with the placement of the purse-string), gaining a negative DRM.
- Avoiding the multiple cross stapling firing of the rectum, for the resection of the specimen as in Laparoscopy leading to potential fewer anastomotic leaks.
- Capability of avoiding permanent stomas by resecting low tumors even when internal sphincters are being involved.
- Resection of bulky tumors T4 , with minimal invasive techniques
- Extraction of the specimen by natural orifices ,decreasing the possibility of SSI's
- Most important the direct view of the surgical planes , can lead to better preservation of parasympathetic ,sympathetic nerves of bladder , and the neurovascular bundles of the seminal vesicles. .
- Diminishing the operative time , especially when the operation is conducted with a two-team approach
- Reviews until now have shown small conversion rate , Deijen et al (29) mean 3%

- Tissue dissection of the mesorectal planes is facilitated with the use of constant pneumopelvis and the pneumodissection

This new approach came with new possible disadvantages and complications. Urethra injuries have been reported, an injury not usually experienced in Laparoscopic and open surgery. Urethra injury can be the result of a following a wrong anterior plane in the TaTME dissection and dissecting more anteriorly than needed. The need of more colo-anal anastomosis with TaTME either hand sewn or stapled, accompanies with its morbidity and the higher need of diverting ileostomy. Damage of side walls of the pelvic canal have been also described. Pelvic abscesses have also been described, possibly due to the increased bacterial load present in pelvis after TaTME (59). Also the use of transanal platforms, rigid or flexible for a prolonged time during the operation has not been studied on matter of anal sphincter damage and therefore incontinence. The fact that during transanal approach especially in very low cancer an intersphincteric approach may initialize the operation, adding that the resections could be more radical which could cause damage to the innervation of elevators ani , further functional studies post operative need to be done.

What has to be noted is that from current literature, all data are from retrospective systematic reviews, case series, case reports and meta-analysis. To our knowledge until now a RCT comparing TaTME vs LaTME for low and middle rectal cancers is not available. It is now ongoing a randomized controlled trial COLOR III trial (26), focusing in long-term oncologic outcomes, functional outcomes and quality of life. COLOR III is an international multicenter superiority randomized trial comparing TaTME and LaTME for low and middle rectal cancers.

Eligible criteria are:

- Patients with a solitary rectal carcinoma up to 10 cm from anal verge on MRI scan.
- any BMI
- previous Neoadjuvant
- previous abdominal or pelvic surgery
- patients with downstaged tumors

Exclusion criteria:

- T1 tumors eligible for local treatment
- T3 tumors with margin <1mm to the ebdopelvic fadcia
- Tumor with ingrowth to elevator ani or internal sphincter
- All T4 tumors as staged in MRI scan prior to neoadjuvant
- Previous rectal surgery
- Pregnancy
- <18 years old
- ASA score >III
- Acute intestinal obstruction , or synchronous abdominal operation
- History of FAP coli , HNPCC hereditary non-polyposis colorectal cancer , Crohn's active disease , UC and other malignancies except of skin BCC and in citu cervix uteri carcninoma

COLOR III trial will consist of 1098 patients in a ratio of Ta:La , 2:1 A 5 year follow up will carried out in terms of local recurrence ,distant metastasis , and quality of life accessed by pelvic MRI , CT thorax and abdomen scans and EORTC questionnaires and LARS for functional outcome. Primary endpoint is involvement of CRM.

Clear indications for TaTME and contradictions are not available. During the Second International Trans-anal Total Mesorectal Excision (TaTME) conference held in Paris in 2014, a consensus was reached for indications and contradictions for TaTME (27) (Table 10)

**Table 10 : Indications and Contradictions of TaTME**

| Indications | Contradictions |
|---|---|
| Malignant and Benign disease | Obstructing rectal tumors |
| Failure to proceed to rectal excision during abdominal operation and conversion to transanal as the only way to avoid APR | Emergency presentation |

| | |
|---|---|
| Male gender | T4 tumors |
| Rectal Carcinoma <12 cm anal verge | |
| Narrow – deep pelvis | |
| Visceral obesity and/or BMI >30kg/m2 | |
| Prostatic hypertrophy | |
| Tumor diameter >4 cm | |
| Distorted mesorectal planes due to neoadjuvant radiation | |
| Impalpable low primary tumor requiring accurate placement of DRM | |

## 7. CONCLUSIONS

TaTME is a novel approach in the management of rectal cancer. It seems to be especially advantageous in middle and low rectal carcinomas. It appears that short term oncologic outcomes and postoperative recovery benefits seem to be comparable to that of traditional laparoscopic rectal and open surgery but RCT are necessary to prove that. Indications and contradictions are to be officially established. Appropriate training and standardization of the technique for surgeons who perform TaTME is essential, and a learning curve has to be established. RCT's defining long-term oncologic and functional outcomes are required to evaluate safety and efficacy of the transanal method for rectal cancer treatment.

## 8. ΠΕΡΙΛΗΨΗ

Η εξέλιξη στην αντιμετώπιση του ορθικού καρκίνου, αποτελεί ένα πού σημαντικό τμήμα έρευνας και προόδου. Η είσοδος της λαπαροσκοπικής χειρουργικής οδήγησε σε αποτελέσματα εξίσου αποδεκτά με αυτά της ανοιχτής χειρουργικής όσον αφόρα το ογκολογικό αποτέλεσμα στην αντιμετώπιση του ορθικού καρκίνου. Ωστόσο δυσκολίες όχι μονό στην λαπαροσκοπική αλλά και ανοιχτή χειρουργική στην αντιμετώπιση ασθενών με όγκους μέσου και κάτω τριτημορίου του ορθού, με ιδιαίτερα χαρακτηριστικά όπως υπέρβαρους, με στενή πύελο και μεγάλους ογκώδεις όγκους, οδήγησαν στην ανάπτυξη μιας νέας μεθόδου. Η διαπρωκτική ολική αφαίρεση του μεσοορθού αποτελεί μια αναπτυσσόμενη μέθοδο. Από την ανασκόπηση της βιβλιογραφίας φαίνεται πως τα βραχυπρόθεσμα ογκολογικά αποτελέσματα της μεθόδου είναι ικανοποιητικά και συγκρίσιμα με αυτά της λαπαροσκόπησης προσέγγισης. Ωστόσο μακροπρόθεσμα ογκολογικά αποτελέσματα αλλά και σαφή λειτουργικά αποτελέσματα δεν υπάρχουν.

Αναγκαίο είναι να υπάρξουν προοπτικές τυχαιοποιημένες μελέτες οι οποίες θα συγκρίνουν τις δύο χειρουργικές τεχνικές, προκειμένου να αναδείξουν πιθανά πλεονεκτήματα αλλά και μειονεκτήματα, εάν υπάρχουν, στην διαπρωκτική τεχνική έναντι της παραδοσιακής λαπαροσκοπικής αντιμετώπισης του ορθικού καρκίνου, καθώς και να καθοριστούν ακριβείς ενδείξεις και αντενδείξεις της μεθόδου. Η σωστή εκπαίδευση των χειρουργών και η δημιουργία καμπύλης εκμάθησης είναι αναγκαία ώστε η διαπρωκτικη προσέγγιση να προσφέρει σωστά ογκολογικά αποτελέσματα.

## 9. ABSTRACT

Treatment of rectal cancer constitutes an important part of research and development. The entry of laparoscopic surgery has led to results as acceptable as those of open surgery with regard to the oncological effect in the treatment of rectal cancer. However difficulties, not only in laparoscopic, but also in open surgery concerning the treatment of patients with tumors of middle and lower rectum, with specific features such as obesity ,narrow pelvis large bulky tumors, have led to the development of a new method. Transanal total mesorectal excision (TaTME) is an evolving method. From literature review, it appears that the short-term oncological results of the method, are satisfactory and comparable to those of the laparoscopy approach. However, there are neither long-term published oncological outcomes nor clear functional results.

It is necessary to have prospective randomized controlled trials, comparing the two surgical techniques in order to reveal possible advantages or disadvantages, if any, in the TaTME approach versus traditional laparoscopic treatment of rectal cancer. It is also essential to determine specific patient criteria, and indications and contradictions of this novel method. Proper training of surgeons and the creation of a learning curve is necessary to ensure that the transanal approach offers proper short and long term oncological results.

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Tech Coloproctol 123

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