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RESEARCH ARTICLE

Technologies, technical steps, and early postoperative results of transanal TME

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ABSTRACT

Introduction: First described in 1982, TME overcomes most of the concerns regarding adequate local control after anterior rectal resection. TME requires close sharp dissection along the so-called Heald's plane down to the levators, with distal dissection often cumbersome. In recent years, Transanal TME was introduced with the aim to improve distal rectal dissection and quality of mesorectal excision.

Material and methods: A prospective, non-randomized study, started in 2013, is currently ongoing in two Italian Centers. Study objectives were assessing the safety of TaTME and TME quality. TaTME technique and technologies as performed in these centers and cumulative results at ≤30 postoperative days of the first 102 patients are reported.

Results: Early postoperative morbidity and mortality rates were 33.3% (34 pts, 16 Clavien-Dindo I + II and 18 Clavien-Dindo III + IV + V), and 1.96% (two deaths), respectively. The quality of mesorectal excision according to Quirke was: complete in 97.1% and nearly complete in 2.9% of the cases.

Conclusions: The results confirm the effectiveness of TaTME, especially regarding the quality of the mesorectal dissection. Open questions regarding standardization, anatomical landmarks, indications, morbidity (with special regard to local infection and sepsis), learning curve and oncological outcomes require further answers from larger studies and RCTs before definitive validation of this procedure.

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Introduction

Total mesorectal excision (TME) is the gold standard surgical treatment of rectal cancer. First described by RJ Heald in 1982 (1), TME overcomes most of the concerns regarding adequate local control after anterior rectal resection, the technique of which almost did not change since Claude Dixon reported the results of this restorative procedure in 1948 (2). TME entails the removal of the rectum along with the surrounding mesorectum and an intact overlying fascia down to the level of the *levator ani* muscles. To accomplish that, TME requires a close sharp dissection along the space between the mesorectal fascia and the endopelvic fascia.

Dissection of the distal rectum according to TME principles may be somewhat cumbersome in cases of narrow pelvis, bulging tumors, and obese patients. Transanal TME (TaTME) was introduced in 2010 with the aim to cope with all these limits and improve the quality of mesorectal dissection even in the most challenging cases (3). TaTME, an evolution of the transanal-abdominal-transanal (TATA) procedure with bottom-up dissection of the distal rectum (4), is the ultimate match point of several minimally invasive surgical approaches, where laparoscopy merges with the principles of transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS), with those of natural orifice transluminal endoscopic surgery (NOTES), natural orifice specimen extraction (NOSE), single access laparoscopy and endoluminal surgery (5) (Table 1).

Technique of and technologies for TaTME and cumulative results at 30 days of the patients treated in two Italian Centers are herein reported and discussed.

Material and methods

A prospective non-randomized dual-institutional trial is currently ongoing at Rummo Hospital, Benevento and San Giovanni Hospital, Rome. In the short-term, objectives of the study are: assessment of surgical, early postoperative and histopathologic outcomes; in the long-term the objectives of the study will be

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assessment of functional and oncologic outcomes. The present study deals with the short-term objectives of the study.

Prospective data collection included gender, age, American Society of Anesthesiologists (ASA) score, BMI, length of surgery, postoperative stay, morbidity rate and mortality rate (early postoperative complications at ≤30 postoperative days), tumor location and size, tumor stage, lymph node harvest, specimen length, margins of clearance (distal and radial margin, the latter assessed as circumferential resection margin - CRM), integrity of mesorectal fascia. Postoperative complications were graded according to the Clavien-Dindo (CD) contracted classification, completeness of mesorectal excision was evaluated according to the Quirke criteria (6) (Table 2). CRM ≤1 mm was considered positive for an involvement/infiltration of the mesorectal fascia (7). Among postoperative complications, infections and anastomotic leaks were specially analyzed, the latter being categorized according to the ISREC scheme (International Study Group of Rectal Cancer definition and severity grading of anastomotic leakage) (8–9).

There were no actual exclusion criteria: Patients who had undergone previous local resections (i.e. endoscopic resection or TEM) were included in the study, as well as patients with synchronous metastatic disease. Preoperative tumor assessment included rectal exploration, colonoscopy with biopsies and CT scan in all cases; patients with tumor located in the mid and distal rectum also underwent MRI. Patients with tumors of the mid and distal rectum staged as T3-T4 or N+ at preoperative imaging assessment received either standard neoadjuvant chemo-radiation therapy or radiation therapy alone. These patients were re-staged after eight weeks and prior surgery with colonoscopy/proctoscopy, repeated biopsies and histology, CT scan and MRI. Tumor regression grading according to Mandard was assessed at final histology in all these patients (10). Patients with tumors involving the intra-peritoneal portion of the rectum and patients with tumors of the mid and lower rectum staged at preoperative imaging as T1-T2, N- did not receive any neo-adjuvant treatment. All patients included in the study signed an informed consent and were treated according to the principles of good clinical practice.

Table 1. Minimally invasive surgical approaches.

TEM	Transanal Endoscopic Microsurgery
TAMIS	Transanal Minimal Invasive Surgery
NOTES	Natural Orifices Transluminal Endoscopic Surgery
NOSE	Natural Orifice Specimen Extraction
SAL	Single Access Laparoscopy

Study endpoints were: safety of TaTME assessed by analyzing surgical outcomes and postoperative complications at ≤30 days, and quality of the mesorectal excision with a transanal down-to-up endoscopic approach assessed by analyzing the histopathologic outcomes. Consecutive variables were expressed as mean ± SD, median value and range, whereas categorical variables were expressed as count and percentage. Analysis of data was performed using XLSTAT 2015.1 software for Excel.

Perioperative management

Perioperative management of all patients undergoing surgery for rectal cancer in this study was according to the enhanced recovery after surgery (ERAS) protocol (11), with a few exceptions regarding bowel preparation and pelvic drainage. ERAS perioperative management in uncomplicated patients included all of the following: preoperative counselling, preoperative carbohydrate load, prophylaxis against thrombo-embolism, prophylactic antibiotics starting one hour before surgery, avoidance of long-acting sedation, anesthetic protocol with epidural analgesia, use of short-acting opioids and ventilation with high oxygen concentration, prevention of intra-operative hypothermia, perioperative fluid infusion with a near-0 balance, prevention of postoperative nausea and vomiting (PONV), immediate removal of the naso-gastric tube, immediate postoperative diet, early removal of the urinary catheter (on postoperative day 2), immediate mobilization. Patients with a complicated postoperative course were treated with a case-by-case policy and the postoperative management changed accordingly. Bowel preparation in early patients of this series consisted in a low pressure 1 to 2 liter enema on the day prior to surgery, whereas most patients required oral consumption of either 4 l high-volume Polyethylene glycol-electrolyte solutions (PEG-ELS) or 2 l low-volume

Table 2. Grading of quality and completeness of the mesorectum in a total mesorectal excision specimen from Ref. [6].

	Mesorectum	Defects	Coning	CRM*
Complete	Intact, smooth	Not deeper than 5 mm	None	Smooth, regular
Nearly complete	Moderate bulk, irregular	No visible muscularis propria	Moderate	Irregular
Incomplete	Little bulk	Down to muscularis propria	Moderate–marked	Irregular

*CRM: circumferential radial margin.

PEG-ELS. Furthermore, these patients followed a clear liquid diet on the day before surgery, and a low-residue diet during the previous days, whenever possible.

Surgical technique and technologies

TaTME was performed by a single team with a sequential approach (laparoscopic first or transanal first), the order of which has changed over the study period. The described technique is the one performed in the last year and at the present time. In both institutions surgeons were highly experienced in laparoscopic colorectal surgery and TEM. Low anterior resection with TME was performed for tumors of the mid and lower rectum, while a partial mesorectal excision (PME) with $\geq$5 cm distal safety margin was performed for tumors of the upper rectum (7).

TaTME sequential steps were: (1) Transanal, (2) Laparoscopic approach to left colonic dissection, central vessel ligation/division and upper mesorectal excision, (3) Transanal approach to mid and lower rectum mesorectal excision, completion of anterior resection with specimen removal (NOSE) and anastomosis.

Two complete and separated sets of instruments including optics are used. The skin is prepared on both the abdominal and the perineal field as usual. The patient lies on the table in the lithotomy position. After anal dilation, the rectum is rinsed with 1 liter povidone-iodine solution; thereafter, a self-anchoring anal retractor, either disposable (Scott retractor, Lone Star Medical Products, Houston Texas, USA) or reusable (Figure 1) is positioned for better anal exposure and the device for transanal surgery is introduced. Either rigid reusable operation rectoscopes as the one designed by Buess for TEM (Richard Wolf GmbH, Knittlingen, Germany) (12) and the TEO rectoscope (Karl Storz, Tuttlingen, Germany), or a disposable platform for transanal minimal invasive surgery - TAMIS may be equally used. In the large majority of cases the Gel-point path® transanal platform (Applied Medical, Rancho Santa Margarita CA, USa) was used (Figure 1). Surgery is carried out under endoscopic guidance provided by the Visera Elite imaging platform supporting a 3CCD full HD camera head and a 30° angle view scope (Olympus Europe, Hamburg, Germany). Three cannulas are inserted through the Gel-point sealing cap, in a triangular fashion: the upper one for the optic and the lower two for the working instruments. CO_2 insufflation is started, at a pressure >15 mm Hg at this stage. Either a standard hi-flow insufflator or one provided with a roller pump is used. The tumor is visualized and, depending on its location, a purse-string suture is fashioned and tied 1 to 5 cm below the distal tumor margin. This maneuver should warrant a better control of bacterial and tumor cell spillage from the rectal lumen. Thereafter, a circumferential dissection line at 1 cm distal to the purse-string is marked with the HF monopolar hook and the full thickness dissection of the rectal wall is started following this line, first on the posterior and the anterior side, then on the lateral sides, until the perirectal space is entered. In case of low rectal cancers (tumors located at the level of the ano-rectal ring or below), a transphincteric dissection is performed and both the purse-string and the full-thickness dissection of the wall are carried out under direct view, inserting the Gel-point path only after the perirectal space is entered circumferentially. CO_2 is left flowing through the retroperitoneal space: This will enhance the visualization of the correct dissection plane during the laparoscopic step of the procedure. At this point the surgeon switches from the perineal field to the abdominal field.

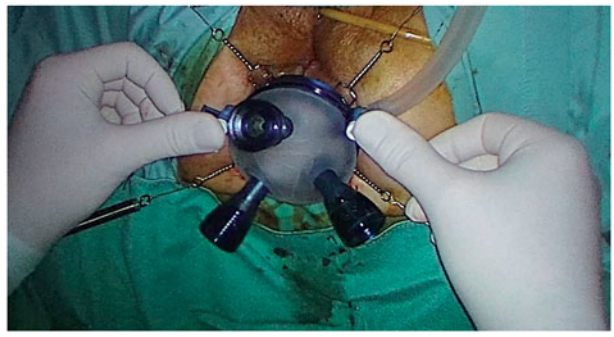

Figure 1. Patient set-up for transanal TME: with the patient lying in a lithotomic position, the anus is stretched with self-restraint hook retractors and the Gel-point path® transanal platform (Applied Medical, Rancho Santa Margarita CA, USA), a disposable device for transanal minimally invasive surgery – TAMIS, is inserted into the anal canal to provide access to the rectal lumen above the anorectal ring. Three ports are usually inserted through the sealing cap (for the optic and the working instruments) to accomplish the procedure.

The laparoscopic step of the operation is accomplished through a standard three-port approach with complete mobilization of the splenic flexure, division of the inferior mesenteric vein at the level of Treitz, high tie ligation/division of the inferior mesenteric artery, complete dissection of the left colon along the plane between Toldt's and Gerota's fascia and dissection of the proximal rectum down to the level of peritoneal reflection anteriorly, and along the Heald's *holy plane* posteriorly. The peritoneal reflection is always opened, allowing completion of the upper rectum mesorectal excision. In a few cases low section of the inferior mesenteric artery was performed, dividing the vessel right caudal to the origin of the left colic artery. During the laparoscopic step, it is important to divide

the left mesocolon medial-to-lateral, following a line from the point of vessel dissection to the colon, at the level of the desired proximal section: This trick allows marking out where the blood supply to the colon is interrupted and, once the bowel will be extracted transanally, makes the recognition of the exact level of the proximal section easier. During laparoscopy, either radio-frequency or ultrasound energized dissection devices are equally employed. Nevertheless, most procedures are accomplished using an advanced bipolar sealing and cutting device (Caiman®5 – B. Braun Aesculap AG, Tuttlingen, Germany).

At this stage, the surgeon switches again to the perineal field and starts transanal mesorectal excision. Initial dissection, when the surgeon is looking for the right plane, is likely the most challenging part of this procedure. Three anatomical details must be taken into account during dissection:

- the anal canal, which is at a steep angle with the pelvic floor
- the curvature of sacrum, and
- the presence of neurovascular structures on both lateral sides, the injury of which may cause intraoperative bleeding and, much worse, damage to the autonomic nerve supply to urogenital organs.

Hence, full-thickness sharp dissection with the HF hook starts as perpendicularly as possible and then, when the avascular plane was developed posteriorly, upward dissection is furthered anteriorly and on the lateral sides in a circumferential fashion. During this step, CO_2 insufflation pressure is diminished, as well as the gas flow volume (down to 10–12 mm Hg and 1 l/m respectively), to avoid establishment of a severe retropneumoperitoneum and the "*soffietto*" effect caused by high-flow volumes. The risk and major pitfall during down-to-up TME is to dissect the rectum along a plane external to the mesorectal plane. Deepening the posterior dissection excessively may lead to bleeding of presacral vessels. Careful lateral and upper-lateral sharp and blunt dissection, always keeping on the bright avascular plane described by Heald, minimize the risk of injuring the neurovascular bundles of Walsh. Anterior dissection is carried out avoiding entering through the rectovaginal or the retroprostatic fascia. Down-to-up TME is far more challenging after radiation therapy, which causes fibrosis and inflammation of perirectal tissues (Figure 2(A,B)). Once the upper plane of dissection is reached, the last attachments of the rectum are divided and TME is accomplished. The transanal platform is removed, the mobilized rectum and the sigmoid colon with their vascular pedicle are withdrawn through the anus and the anterior resection is completed dividing the colon at the previously demarcated level. Vascularization of the colonic stump is checked before fashioning the anastomosis. In cases of bulky tumors, thick mesorectum and very narrow pelvis, the specimen is extracted through a supra-pubic mini-laparotomy with abdominal wall protection, thus avoiding stressing the sphincter or causing visceral damage.

Either a stapled or a hand-sewn colo-anal anastomosis are performed afterwards, the latter after resection of low and very low rectal tumors. When a stapled anastomosis is performed, the anvil of a circular stapler sized 29 to 33 mm in diameter is fixed to the proximal colonic stump by a purse-string. A second purse-string is fashioned on the distal rectal stump, either under direct view or through the transanal platform. This purse-string is tied around the spike of the stapler anvil, which is then connected to the

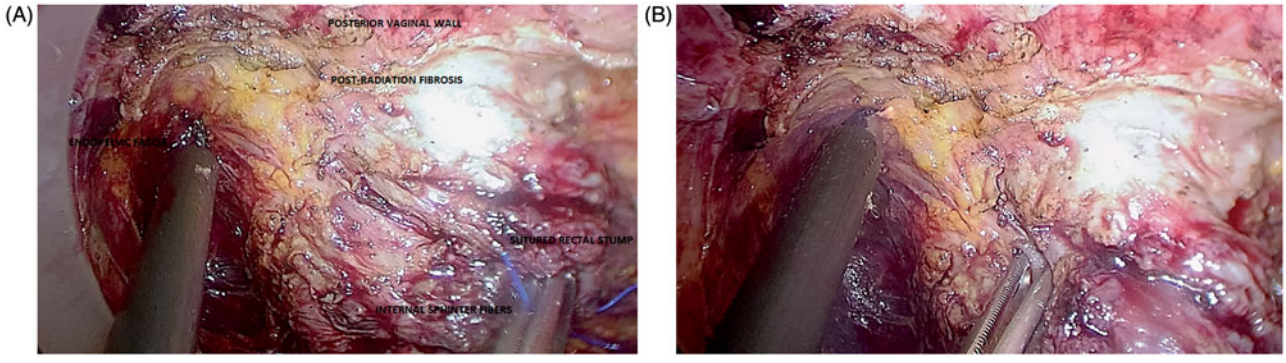

Figure 2. Careful transanal right side rectal dissection with a HF hook along the plane between the mesorectal fascia and the endopelvic fascia in a patient with anterior/right lateral cancer of the lower third of rectum treated by neo-adjuvant chemo-radiation therapy. The extra-rectal space is entered after inter-sphincteric dissection, first incising the anal canal right above the dental line, then introducing the TAMIS device (A). Dissection is furthered through the post-radiation fibrotic tissue between the posterior vaginal wall and the anterior aspect of rectum (B).

stapler shaft, and finally, the anastomosis is fired. Correct orientation of the colonic stump is checked by laparoscopy, while an endoscopic check of the anastomosis is possible through the platform. In case of any defect the anastomosis itself may be reinforced transanally with one or more interrupted sutures passed through the Gel-point path platform. When a hand-sewn colo-anal anastomosis has to be performed it is done according to the standard technique under direct vision with anal canal exposure achieved with the hook anal retractors. At the end a loop ileostomy on the right flank is always performed for protection of the anastomosis.

Results

A total of 102 patients underwent TaTME for rectal cancer from 2013 to date. Demographics and tumor characteristics of the patients included in this study are reported in Table 3. Table 4 summarizes the surgical outcomes and type of early (at ≤30 days) postoperative complications. Tumors were located in the mid or lower rectum in 87 cases (85.3%); in 58.2% of cases the tumor stage was 0-II: the stage 0 case was one patient with a large sessile villous adenoma (>8 cm in diameter) with multiple foci of *carcinoma* in situ. Thirty-four patients (33.3%) received neo-adjuvant chemo-radiation therapy or RT alone. Anterior rectal resection was performed in all cases. The mean operative time was 185 ± 87.5 min (range 60–480), median 167.5 min. A stapled anastomosis was fashioned in the majority of cases (72, 70.6%), a hand-sewn colo-anal anastomosis was preferred in most cases with tumors located in the lower rectum. A protective ileostomy was performed in all cases. There was no conversion to open surgery in this series of patients.

The early postoperative morbidity rate was 33.3% (34 out of 102 cases). Infections, with no x-ray evidence of anastomotic dehiscence, developed in 5.9% (six out of 102) of cases, with a wide range of severity, from mild to life-threatening. Anastomotic leaks with x-ray evidence of contrast medium spillage and clinical symptoms occurred in 4.9% (five cases) of patients. According to the ISREC classification, anastomotic leaks were graded B in three cases and C in the remaining two. The distribution of complications according to the Clavien-Dindo contracted classification is shown in Table 5. Postoperative complications were minor (CD I + II) in 16 (15.7%) patients, and

Table 3. Patient demographics and tumor characteristics/staging.

Characteristics		Data
Age (y, range)	Mean ± SD	67.6 ± 11.3 (35-87)
	Median	67.5
Gender (*n*, %)	Male	56 (54.9)
	Female	46 (45.1)
BMI* (Kg/m^2)	Mean ± SD	25.3 ± 4.1
	Median	25
ASA** score (*n*, %)	I	3 (2.9)
	II	37 (36.3)
	III	62 (60.8)
Tumor location (*n*, %)	Upper rectum	15 (14.7)
	Mid rectum	57 (55.9)
	Lower rectum	30 (29.4)
Tumor stage*** (*n*, %)	0*****	1 (1.0)
	I	18 (18.4)
	II	38 (38.8)
	III	38 (38.8)
	IV	3 (3.0)
Neo-adjuvant treatment**** (*n*, %)		34 (33.3)

*Body Mass Index.
**American Society of Anesthesiologists.
***Pathological stage, according to AJCC 2010 classification (pTNM – four patients with no residual disease after local resection and/or neoadjuvant CRT not included).
****CRT, RT.
*****pTis in a large villous adenoma (>8 cm).

Table 4. Surgical outcomes and early (≤30 days) postoperative complications.

Outcome		Data
Length of surgery (min)	Mean ± SD (range)	185 ± 87.5 (60-480)
	Median	167.5
Type of anastomosis (*n*, %)	Stapled	72 (70.6)
	Colo-Anal	30 (29.4)
Postoperative stay (d)	Mean ± SD (range)	9.6 ± 9.2 (4-69)
	Median	7
Morbidity rate (*n*, %)		34 (33.3)
Mortality rate (*n*, %)		2 (1.96)
Type of complications		
CD* I	Fever	1
	Urinary retention	2
	Pleural effusion mild	1
	Hematoma conservative treatment	1
	Hematuria mild	1
	Delated bowel movements	1
CD II	Leak mild conservative treatment	1
	Leak with anastomotic abscess	1
	Pelvic collections: Blood	2
	Abscess	1
	Fever	1
	Urinary infection	1
	Angina	1
	Prolonged hypoglycaemia	1
CD III	Intra-abdominal bleeding	1
	Intra-abdominal abscess	1
	Ileostomy obstruction	2
	Bowel obstruction	1
	Leak	1
	Leak with anastomotic abscess	1
	Pelvic abscess	1
	Colonic Ischemia	2
	Jejunal perforation	1
CD IV	Intra-abdominal abscess with leak, Atrial fibrillation sever bedsore/ICU	1
	Pneumonia severe/ICU	2
	Peritonitis severe/ICU	1
	Bowel obstruction, Compartment syndrome/ICU	1
V	Peritonitis/ICU	1
	Pulmonary embolism	1

*CD: Clavien-Dindo.

major (CD III + IV + V) in the other 18 (17.6%) patients, the latter requiring interventional radiology management, surgical management and, in some cases, ICU management. In more detail, percutaneous drainage under US or CT guidance was requested for treatment of one sub-hepatic abscess and three pelvic/anastomotic abscesses. Surgery was needed to treat eight additional cases: one laparoscopic control of intraperitoneal bleeding, two laparoscopies for the management of ileostomy obstruction, one laparoscopic adhesiolysis and reduction of an internal hernia with obstruction, one laparoscopic suturing, lavage and drainage of jejunal perforation with mild peritonitis, one laparoscopic lavage and drainage for anastomotic leakage, two open Hartmann procedures, for colonic stump ischemia and adhesive obstruction with abdominal compartment syndrome, respectively. In the latter case, vacuum-assisted closure (VAC) treatment was established successfully. Complications that required ICU management are reported in Table 4. There were two deaths within the first 30 days (mortality rate 1.96%): one patient with sepsis and multi-organ failure died from acute peritonitis, and one patient died due to pulmonary embolism three hours after surgery.

Table 6 summarizes the histopathology of the surgical specimens. Mean (±SD) and median number of lymph nodes harvested including patients who underwent neoadjuvant CRT or RT were 20 ± 11.7 and 19, respectively. CRM was found: > 1 mm in 94.6% and ≤1 mm in 5.4% of cases. Completeness of mesorectal excision according to Quirke classification was assessed in all specimens examined and was found complete with integrity of the mesorectal fascia in 99 out of 102 cases (97.1%), whereas in 2.9% of cases it was nearly complete.

Table 5. Distribution of complications (at ≤30 days) according to the Clavien-Dindo contracted classification.

Grade	#	%
I	7	6.9
II	9	8.8
III	11	10.8
IV	5	4.9
V	2	1.9
TOTAL	34	33.3

Table 6. Histopathology of surgical specimens including Quirke grading of completeness of the mesorectal excision.

Pattern		Data
Tumor size (cm)	Mean ± SD	3.21 ± 2.99
	Median	3
Specimen length (cm)	Mean ± SD	22.6 ± 6.7
	Median	22
Distal margin (mm)	Mean ± SD	37.1 ± 28.5
	Median	30
CRM* (mm)	Mean ± SD (range)	15.1 ± 9.1 (0–30)
	Median	15
Node harvest (*n*)	Mean ± SD	20 ± 11.7
	Median	19
Quirke grading** (*n*, %)	Complete	99 (97.1)
	Nearly complete	3 (2.9)

*Circumferential resection margin.
**Completeness of mesorectal excision.

Discussion

The possibility of combining the laparoscopic and the transanal endoscopic approaches through a rigid platform for colorectal resection, with transanal specimen extraction, was first described by Lirici and Buess who reported the results of an experimental trial in 1993 (13). In 2011 Lacy reported the first totally transanal TME through a TEM platform with laparoscopic assistance on a human being (14). In the following years several studies on transanal TME with laparoscopic assistance have been published, all showing the feasibility and safety of this new approach to rectal cancer surgery according to the Heald's principles (15–26).

The described technique and technologies vary among authors, especially regarding: sequence of surgical procedure, transanal platforms, and dissection during transanal TME, making evident the present lack of standardization. Table 7 resumes the main technical aspects of TaTME as from the largest series reported from 2013 to 2015.

In the majority of cases, the sequence of operative steps was transanal approach first, followed by laparoscopy. During the transanal step of the procedure a down-to-up TME is performed until the peritoneal reflection is opened. Carbon dioxide insufflation in the pelvic space opens the dissection plane, making TME easier. Moreover, the transanal first approach may make the abdominal step faster by creating a retropneumoperitoneum, which opens the embryonic fusion plane between Toldt's and Gerota's fascia. On the other side, the abdominal first approach may decrease the risk of peritoneal contamination. This approach was chosen by a few other authors (17,19,21,24); Veltcamp Helbach et al., e.g., switched from a transanal first approach, performed in the first patients, to a transabdominal first approach to avoid severe retroperitoneal pneumatosis (17). A concurrent, dual team abdominal and transanal approach to TME (Lacy's Cecil approach) has been described by three groups (16,19,26). The main advantage of this simultaneous approach is that carrying on dissection, traction and counter-traction maneuvers at the same time from above and below not only accelerates the whole procedure but may facilitate mesorectal excision along the

Table 7. Technical aspects of TaTME as from the largest series reported from 2013 to 2015.

Author	# Patients	Approaches	Platform	Trans-anal dissection technique	Abdominal approach	Insufflation/ pressure	Dissection technology	Anastomosis
Lacy et al. (16)	140	Simultaneous (Cecil), meeting point peritoneal reflection trans-anally entered	Lone star, GelPOINT (Applied Medical)	Anterior and posterior first then lateral	4 or 5-port laparoscopic	9 mmHg	HF monopolar hook/US Harmonic ace (Ethicon,J&J)	Handsewn stapled EEA 33 (Covidien)
Veltcamp Helbach et al. (17)	80	Trans-abdominal first with peritoneal reflection incision laterally from above	SILS port (Covidien)/ GelPOINT (Applied Medical)	Posteror as high as possible, then anterior, then lateral	4-port laparoscopic/SILS	10-14 mmHg	HF monopolar hook	EEA Hemorrhoid stapler (Covidien)
Tuech et al. (18)	56	Trans-anal first entering the peritoneal cavity	Lone star, GelPOINT (Applied)/SILS (Covidien)/ Endorec (Aspide)	Anterior then posterior then lateral	4-port laparoscopic/SILS/ Robotic	10 mmHg	Bipolar and US Harmonic ace (Ethicon,J&J)	Handsewn coloanal with colonic J-pouch, end-to-side, straight and DCA
Serra-Aracil et al. (19)	32	Trans-abdominal first with peritoneal reflection incision	TEO 15mm rectoscope (Karl-Storz)	First posterior entering peritoneal cavity then lateral then anterior	4-port laparoscopic	14 mmHg	US Harmonic ace (Ethicon,J&J)	Handsewn/mechanical stapler
Muratore et al. (20)	26	Trans-anal first then laparoscopy with incision of peritoneal reflection from above	Lone star, SILS port (Covidien)	Circumferential dissection from posterior to lateral and anterior	3-port laparoscopic	10-12 mmHg	RF Ligasure 5mm (Covidien)	Handsewn with J-Pouch/end-to-side/straight
Velthius et al. (21)	23	Trans-abdominal first then TAMIS entering peritoneal cavity trans-anally	Lone star, SILS port (Covidien)	First posterior, then anterior then lateral	3 or 4-port laparoscopic/SILS	14 mmHg	RF Ligasure (Covidien)	Handsewn with J-Pouch/EEA Hemorrhoid stapler
Atallah et al. (22)	23	Trans-anal first then laparoscopy with incision of peritoneal reflection from above	Lone star, GelPOINT (Applied medical)	First posterior and lateral then anterior	Robotic/ Laparoscopic/ Open	15 mmHg	HF monopolar hook/Robotics instruments	Handsewn straight or end-to-side J pouch/stapled
Chouillard et al. (23)	16	Trans-anal first entering the peritoneal cavity from the bottom	SILS port (Covidien)/ GelPOINT (Applied medical)	First posterior entering peritoneal cavity, then posterior then lateral	Pure NOTE/SILS	NR*	RF Ligasure (Covidien)	Handsewn straight
Knol et al. (24)	10	Trans-abdominal first then TAMIS entering peritoneal cavity trans-anally	SILS port (Covidien)	First posterior then anterior then lateral	4-port laparoscopic	8-12 mmHg	HF monopolar hook	Handsewn straight or end-to side/ 33mm-EEA circular stapler (Covidien)
Zorron et al. (25)	9	Trans-anal first entering the peritoneal cavity from the bottom	Triport (Olympus, Japan)	First posterior then lateral then anterior entering peritoneal cavity	3-port laparoscopic	8-10 mmHg	US Harmonic ace (Ethicon,J&J)/HF monopolar hook	Handsewn/mechanical stapler with or without colonic pouch
Elmore et al. (26)	6	Concurrent TAMIS and laparoscopy	Triport (Olympus, Japan)	Anterior and posterior first then lateral	4-port laparoscopic	8-10 mmHg	HF monopolar hook	mechanical stapler

*NR: not reported.

proper plane. Main pitfalls of the simultaneous approach are the significantly increased costs of personnel for doubling the surgical team and the loss of staff energy. Mean operative time for the concurrent two-team technique in the largest series published was 166 minutes (range, 60—360 minutes) (16), which compares favorably with the 185 minutes (range, 60–480 minutes) operative time of our series of patients treated with a sequential approach. Opposite to other sequential procedures, the sequence we adopted in our series of patients is similar to that described by J. Marks for the TATA procedure: Transanal-Abdominal-Transanal (27). Our average operative time is shorter than that reported in the laparoscopic arm of the COLOR II RCT: 185 vs. 240 min (28)

Performing TaTME through a rigid metal operation rectoscope such as the TEM and the TEO ones gives the advantage of working with a stable platform. Furthermore, there is no need for the assistant to hold

the camera throughout the procedure, thus avoiding conflict between surgeons' arms in a restricted space. Drawbacks of rigid platforms are the small room left for instruments which run almost parallel and significantly restrained movements. Even though several flexible transanal platforms are available, the Gel-point path is the most versatile and the only one specifically designed for TAMIS. This flexible platform provides a much better instrument maneuverability with reduced collisions, which entirely compensates both the higher risk of air loss through sealing cap and cannulas, resulting in an impairment of pneumorectum, and the fixed length of the access channel that sometimes cannot adapt to that of the anal canal.

What comes to light from most reports (16–17,21) is that down-to-up TME facilitates an excessive lateral and back dissection, which may result in bleeding and autonomic nerve injuries. For this reason dissection should start first dorsally and ventrally and only then along the lateral sides.

Certainly, the possibility of peritoneal contamination through an open rectum is a major concern and an argument against TaTME. In 2015 Velthuis published a prospective study on intra-abdominal bacterial contamination during TaTME, reporting positive abdominal cultures in 39% of the patients operated (29). Forty-four percent of these patients developed presacral abscesses with or without anastomotic dehiscence. Our data confirm the risk of extra-peritoneal and peritoneal contamination: Infections occurred in 5.9% of patients, including three with C-D grade III, two with C-D grade IV and one with C-D grade V. Therefore, maximum care should be taken in both preoperative bowel preparation and antibiotic prophylaxis. Even though there is no general agreement or high evidence of their benefits, perioperative management should include preoperative low-residual diet and thorough lavage of the rectum with a povidone-iodine solution before starting the transanal step of the procedure. A chlohrexidine-gluconate solution may be a better alternative with an improved endoluminal bactericidal effect compared to povidone-iodine (29).

Early postoperative outcomes are equal to those reported in other TaTME series of similar size (16–17), but postoperative mortality was zero in both Lacy's and Veltcamp's series and 1.9% in the present study. When compared to the-short term outcomes of the COLOR II randomized trial, no significant differences in postoperative morbidity and mortality rate at $\leq$30 days were found (40% and 1% in the laparoscopic arm, 37% and 2% in the open arm of COLOR II vs. 33% and 1.9% of present study) (28).

Both macroscopic and microscopic specimen assessment are of paramount relevance in rectal cancer surgery. The quality of the mesorectal excision highly influences the local recurrence rate (7, 30). The CRM is a surgically-created plane of dissection produced during rectal removal from the surrounding tissue. Tumor involvement of the CRM is the single most important factor for predicting the risk of local recurrence in rectal cancer patients, and is an important predictor of distant metastasis and overall survival as well. Tumors at $\leq$1 mm of the surgically created margin have a significantly increased risk of recurrence: One study reported a high incidence of recurrence with a cutoff for CRM tumor involvement at 2 mm, but this finding has never been confirmed in subsequent studies (7). Mesorectal excision according to Quirke quality grading in the resected specimens of the present study was recorded as complete in 97.1% and nearly complete in 2.9% of cases. These data match with those of the other largest series of TaTME published to date and seem better than the results of the COLOR II CRT (88% completeness in the laparoscopic arm vs. 92% in the open arm (16–17, 31). Our data are significantly better than the data reported in the 2012 metanalysis on the quality of mesorectum in open surgery where a complete mesorectal excision was found in only the 56.4% of specimens (30). In 94.6% of our patients CRM was $>$1 mm and these data are similar to those reported by Lacy concerning his own series and COLOR II trial (93.6% vs, 93% laparoscopic arm and 91% open arm, respectively).

TaTME has been proven feasible and safe by a number of authors since its first description in 2010 (15), yet there are still some concerns about possible contamination of the peritoneal cavity and damage of the autonomic nerve supply to urogenital organs during down-to-up dissection of the mesorectum. Our results confirm the effectiveness of such a procedure, especially regarding the quality of the mesorectal dissection. Given the relative novelty of the procedure, long-term five-year survival, functional data and standardization of the surgical technique are lacking. Therefore, some main questions are still open, concerning the standardization of the approach, the definition of anatomical landmarks and optimal indications, the morbidity rate with special regard to local infection and sepsis, the learning curve and, last but not least, the oncological outcomes. Long-term results from multicenter randomized trials, systematic reviews and metanalyses are necessary before definitive validation of this technique.

Disclosure statement

All Authors have nothing to disclose nor conflicts of interest

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