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REVIEW ARTICLE

Transanal total mesorectal excision (TaTME): current status and future perspectives

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Abstract
Total mesorectal excision (TME) is the gold standard surgical treatment for mid- and low rectal cancer; however, it is associated with specific technical hurdles. Transanal TME (TaTME) is a new procedure developed to overcome these difficulties, through an enhanced visualization of the dissection plane. This potentially could result in a more accurate distal dissection with a lower rate of positive circumferential resection margins, increasing the rate of sphincter-saving procedures. The indications for TaTME are currently expanding, despite not being yet standardized, and structured training programs are ongoing to help overcome the steep learning curve related to the technique. The procedure is feasible and safe with similar intraoperative complications and readmission rates when compared with conventional open or laparoscopic TME. Favorable short-term oncologic results have been reported: in particular, TaTME is associated with mesorectal specimen of a better quality and a longer distal resection margin that is established at the beginning of the procedure under direct view. Robotics, when available, will probably overcome the steep learning curve related to the complexity of TaTME. Long-term follow-up and ongoing RCT trials data are awaited regarding functional results, local recurrence and survival, and to facilitate the comparison with standard laparoscopic or robotic rectal resections. The present review is focused on critically analyzing the theoretical benefits and risks of the procedure, its indications, short- and long-term results and future direction in the application of TaTME.

Keywords Rectal cancer · Total mesorectal excision (TME) · Transanal total mesorectal excision TaTME · Robotics

Introduction

The surgical approach to tumors located in the medium and lower rectum is often a challenge for the surgeon and, consequently, for the patient. In the last 20 years, much progress has been made, and following the introduction of the concept of TME, an increase in the rate of sphincter-saving procedure and a significant reduction in the local recurrence rate from 16% to less than 5%, has been reported [1]. Unfortunately, in the presence of bulky tumors, narrow male pelvis, or obesity, the surgical scenario is more challenging with reported high morbidity rates and lower rates of clear surgical margins [2, 3]. The idea of an alternative approach, a 'bottom–up' technique from the distal to the proximal mesorectal plane, was suggested by the introduction of new minimally invasive devices and relative innovations by Natural Orifice Transluminal Endoscopic Surgery (NOTES), Transanal Endoscopic Microsurgery (TEM), which made the concept possible [4]. After an initial experience on animal and cadaveric models in the year 2010, Patricia Sylla and Antonio Lacy published the first human clinical case of transanal total mesorectal excision (TaTME) [5]. Apparently, the new procedure seems to include all the major surgical innovation of the last three decades in the treatment of rectal cancer such as TME, laparoscopy and NOTES [6]. TaTME may result in a more accurate distal complete excision of the mesorectum with wider resection margins, lower rate of positive CRM, and could increase the rate of sphincter-saving procedures [6–9]. After an initial phase of enthusiasm, with small case series and few prospective studies showing low or no conversion rate and equivalence or superiority in terms of short-term outcomes [10–14], some rare complications of open

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or laparoscopic TME, such as urethral injuries and bladder dysfunction, were reported as the most common major complications following TaTME [11, 12, 15].

These findings emphasized the need for technical standardization of the procedure, for proper patient selection and correct surgical indication. The purpose of the present review is to evaluate the current status of the TaTME in terms of perioperative morbidity, short- and long-term outcomes according to the available literature, and to imagine the possible future scenarios.

Indications to TaTME

Early studies and consensus paper on TaTME indicate that ideal candidates to transanal approach are patients with narrow pelvis, prostate hypertrophy, visceral obesity or body mass index (BMI) > 30 kg/m^2, tumor diameter > 4 cm, distorted tissue planes due to neoadjuvant radiotherapy and difficult recognition of the distal resection margin. TaTME should be reserved to this cohort of patients for resettable tumors located less than 12 cm from the anal verge including very low cancer (i.e., less than 5 cm from the anal verge) [9, 16, 17]. Recently, international consensus guidelines strongly recommend the adoption of TaTME for low rectal tumors [18]. Nevertheless, inclusion criteria in terms of distance of the tumor from the anal verge have not yet been standardized. In the largest monocentric series on 140 cases, reported by Lacy in 2015, in 29 (20.7%) cases, the tumor was located in the proximal rectum [11]. Similarly, 38% of patients included in the International Registry had mid- or proximal third rectal cancer with a distance up to 13 cm at rigid sigmoidoscopy [15]. This point is of concern, since in these cases, the complete excision of the mesorectum is not indicated, with potential functional disadvantages of coloanal anastomosis. Moreover, since TaTME is still in its infancy, the nature of the surgical candidates best suited to taTME treatment is still under continuous evolution. The recently published multicenter RCT trial (COLOR III), which aims to compare TaTME with laparoscopic TME, has outlined new strict criteria for patient selection: in particular clinical T3 tumors with margins < 1 mm from the endopelvic fascia, tumors with ingrowth in the internal sphincter or in the levator ani muscle, and all T4 tumors as staged prior to neoadjuvant therapy have been excluded from this approach [19]. Beyond the classical surgical indication for cancer, other indications have recently emerged [18]. Table 1 reports the current indications and ideal candidates for a TaTME approach. In particular TaTME can be offered to inflammatory bowel disease patients both for a completion proctectomy and for a proctocolectomy. In these patients, the operation is really challenging due to the chronic inflammation obscuring tissue planes, and in surgeons who are experienced in laparoscopic and transanal rectal resection, TaTME could represent a valid alternative to conventional or laparoscopic abdominal surgery. Other unusual indications are the dissection/removal of a neorectum in cases of chronic anastomotic sinus or anastomotic leak, and proctectomy for rectovaginal fistula.

Learning curve

TaTME is a complex operation, mainly due to the anatomical landmarks which are different from those encountered during standard laparoscopic or open TME. The experts recommend that the procedure should be performed by certified colorectal surgeons who have extensive experience in laparoscopic or robotic TME, in transanal minimally invasive surgery (TAMIS) or intersphincteric resection (ISR) with an annual case volume of at least 20 procedures. Moreover, they also suggest to reserve initial cases to female patients, with benign disease and no history of prior pelvic irradiation [9, 20]. Training is a crucial point. Currently, there are

Table 1 Current indications to TaTME

Nature of the disease	Indications	Ideal candidates and potential advantages
Rectal Cancer	TME or pTME Middle and distal rectal tumor (< 10 cm from anal verge) Tumor stage: T1–T3 (excluding T1 tumors amenable to local excision and T3 tumors with margins < 1 mm to the endopelvic fascia) Diameter (any diameter)	Male with narrow pelvis Patients with prostate hypertrophy Bulky tumor (4 cm in diameter) Obese patients (BMI > 30) Better recognition of the distal resection margin Avoid dissection in distorted planes due to neoadjuvant therapy
Inflammatory Bowel Disease	Restorative proctocolectomy or completion proctectomy (with or without an ileal pouch anastomosis) Dissection or removal of the neorectum in presence of rectovaginal fistula, chronic anastomotic sinus or leak	Avoid dissection through scar tissue and obscured or inflamed planes

TaTME transanal total mesorectal excision, *TME* total mesorectal excision, *pTME* partial total mesorectal excision several recognized centers worldwide organizing specific training for TaTME in lab or on cadaveric model. Practice on cadaver is strongly recommended to acquire knowledge and technical skills to enable the attendees to start performing TaTME [16, 21]. Previous experiences have shown a significant decrease in operative time and an increase in specimen length after the first five cadavers [21]. The importance of following a formal course on cadaver has also been stressed by the results from the first training workshop on TaTME, raising to a minimum of 14 procedures per year which have to be performed to assure optimal quality and mantain competence [16]

However, there is paucity on data on learning curve available in the current literature. Bucks hypothesized that approximatively 20–25 cases are needed, providing that the surgeon is experienced in laparoscopic low anterior resection and in TEM [22]. Koedam specifically addressed the issue of learning curve in TaTME utilizing Cumulative Sum analysis in 138 consecutive patients operated by colorectal surgeons with extensive experience in mini-invasive and transanal surgery. The authors reported an improvement in postoperative outcome after the first 40 patients, also showing a decrease in major postoperative complications from 47.5 to 17.5% and a decrease in leakage rate from 27.5 to 5%. Moreover, transition to a two-team approach resulted in a decrease in operating time and conversion rate [23]. However, more papers specifically addressing the issue of learning curve are needed to quantify the number of procedures necessary to be proficient in TaTME.

Intraoperative complications

The issue of safety is of paramount importance when introducing a new technique for validation by the surgical and academic communities. The reported incidence of conversion rate to open surgery following TaTME varies between 0 and 9.1% [10, 12, 22–25], which is lower when compared to standard laparoscopic TME [1], and might further decrease with increasing experience. Dejien who compared low-volume centers performing TaTME (< 30 cases) to high-volume centers (> 30 cases) reported conversion rates of 4.3% and 2.7%, respectively [26]. Of note, in most of the series, the causes of conversion were due to intraoperative complications, while tumor or patient's characteristics did not affect the operation's outcome.

When a new procedure is introduced, the risk of encountering rare and unexpected complications should not be underestimated. Ruanet in an early series reporting on high-risk patients with unfavorable anatomical tumor characteristics or recurrent rectal tumor reported the occurrence of urethral injury in 2 of 30 patients (6.6%) [8]. The latest data on this subject were reported by the largest multi-institutional series including 720 patients, in which the reported incidence of urinary injuries was 0.7% (urethral) and 0.3% (bladder) [15]. This a serious concern directly related to the transanal phase of the operation (urethral lesions have not been reported with abdominal approach), and is an important risk factor for TaTME; it will probably be overcome with increased experience and standardization of the surgical procedure. In addition, recently a reliable method has been described to intraoperatively identify the urethra with fluorescence imaging, which could be beneficial with this new technique [27]. Another matter of concern is the damage of the pelvic side wall and subsequent bleeding [28] which has been variously reported with figures ranging from 1 to 3%, which did not significantly differ when laparoscopic or open TME is considered [29]. The risk of opening areolar planes beyond the scope of dissection caused by C02 as well as the risk of extensive pneumatosis have also been reported and represent another possible complication directly related to this new technique. Two distinct areas are generally involved: laterally at the level of the mid rectum, and posteriorly at the level of the mid- and upper rectum [26]. Going off planes during perineal dissection could result in inadvertent injury to the pelvic sidewall autonomic nerves laterally and to the sacral venous plexus posteriorly. To avoid these potential damages, a mapping of the key zones for autonomic nerve injury has been proposed by Kneist [30]. Image-guided real-time navigation and fluorescence-guided surgery represent other promising tools to maintain an appropriate plane of dissection, to avoid injuries to key anatomic structures and to evaluate the progress of the surgical dissection [31, 32]. At present time, the application of these devices to the daily clinical practice is hampered by the need of dedicated OR, costs and increased operating time, but in a near future, there will be probably an integrating part of the multimedia OR.

Postoperative complications

One of the major concerns in rectal surgery is the occurrence of postoperative complications. The safety of TaTME in terms of postoperative complications has been extensively investigated by various authors with retrospective small series or cohort studies with figures ranging from 27 to 35% [12, 13, 33, 34]. Data from the international TaTME registry including 720 patients reported an overall morbidity of 32.5% [22]. Similar results were also reported by means of other large monocentric TaTME series [33, 34]. These figures are comparable with data coming from large RCT on conventional laparoscopic or open TME [35, 36]. Similar conclusions were reached by Perdawood in a comparative case-matched study, reporting no differences in terms of postoperative morbidity according to Clavien–Dindo classification when laparoscopic, open or transanal TME was compared [37]. Conversely, Ma in a pooled analysis comparing laparoscopic vs TaTME reported significantly lower rate of postoperative complications in the TaTME group (OR = 0.65, 95 CI = 0.45–0.95, $p = 0.03$). The interpretation of these results, however, deserves some caution, since data on postoperative outcome were reported in six studies only for a total of 245 patients [25].

In terms of safety, anastomotic leak represents the most dreaded complication after a low anterior resection of the rectum, which could seriously affect length of stay, early and long-term anorectal function, and long-term oncologic outcome [38, 39]. A low incidence of anastomotic leak rate following TaTME has been reported by several authors in large TaTME series and meta-analyses [22, 24–26, 34, 37]. In particular, data from the two largest meta-analyses currently available in the literature including 510 and 794 patients report figures of 5.7 and 6.1%, respectively [24, 26]. Moreover, recent data from the International TaTME registry on 1594 patients operated over a 30-months period in 107 surgical centers reported an overall 30-day anastomotic leak rate of 7.8% and a delayed leak rate of 2.0% [40]. The reported anastomotic leak rates favorably compare with the figures ranging between 10 and 20% reported by large RCT and large monocentric series on laparoscopic, open and even robotic TME [41, 42]. Finally, an overall incidence of 2.2% of pelvic presacral abscess has been reported in a large review paper including almost 800 patients [26]. This could be related to the increased bacterial load which has been reported to be present in the pelvis after TaTME [43].

Functional results

Quality of life following proctocolectomy represents another important issue. Sphincter function following TaTME is a reason for concern. Several factors specifically related to this procedure could potentially interfere and impair functional outcomes such as the increased rate of coloanal anastomosis, the sacrifice of the internal sphincter or the prolonged anal dilatation related to the use of a wide anal platform which is maintained throughout the whole procedure. At present, functional outcome following TaTME has been poorly investigated in small series (ranging from 8 to 30 patients) and in a review paper with short follow-up and high heterogeneity among the scores and methods used to evaluate functional outcome [44–47]. Moreover, in the majority of the available studies, functional results of low colorectal, coloanal and intersphinteric anastomoses after TaTME, (the latest two carrying the theoretical risk of impaired continence) are not analyzed separately [44, 45]. No solid conclusions can, thus, be made in this regard at present. Nevertheless, preliminary results show that TaTME is associated with acceptable quality of life and functional outcome comparable to published results after conventional laparoscopic low anterior resection with TME [44–50].

With respect to urinary dysfunction following TaTME, data are scarce. In the current available literature, the incidence of urinary dysfunction after laparoscopic or open TME is 0–26% [48]. A lower incidence has been reported after TaTME when compared to conventional surgery [47]. In particular, Tuech reported the occurrence of postoperative urinary retention in 5 of 56 (8.9%) patients following a TaTME procedure. At a 3-month follow-up period, all patients reported normal urinary function with no incontinence [49]. A possible explanation could be the better visualization of the pelvic nerves obtained with the technique, but further studies are needed to confirm this hypothesis. With respect to sexual function following TaTME, few data mainly on male patients are currently available. Tuech and Kneist who examined male sexual function reported a 11–22% incidence of impotence, 22% worse erectile function and 33% decreased ejaculation [49, 50]. Similar results in terms of failure to ejaculate and impotence were reported after conventional or laparoscopic TME [46, 48].

Oncological outcome

The better visualization of the distal rectum, the better deep pelvic dissection without the need for traction on the rectum, and an easier identification of the plan of dissection, are theoretically reported advantages of TaTME which could determine a higher quality TME specimens, and a reduction in CRM positive and DRM rate [5, 8–10, 14].

In an earlier systemic meta-analysis reporting data on 510 patients, a complete TME specimen according to Quirke classification was reported in 88% of cases and near complete in 6%, while CRM was positive in 5% of cases and the DRM in 0.3% cases [24]. Similar results in terms of quality of mesorectum, CRM and DRM rates were reported by the international TaTME registry [40]. De Lacy in the largest single-cohort study focused on pathological results following TaTME,reported an overall complete mesorectum in 95.7%, a positive CRM in 8.1% and positive DRM in 3.2% [51]. The higher efficacy of TaTME in terms of quality of the mesorectum have been recently reported by Hu et al., who showed that complete mesorectal excision rate was 1.93 higher in the TaTME when compared to the laparoscopic TME. A lower positive circumferential resection margins rate was also reported in the TaTME group, while positive DRM rate failed to reach statistical difference, probably due to an heterogeneity in tumor location of the included studies [52].In the same direction goes a recent study showing a significant lower residual mesorectal tissue assessed by postoperative magnetic resonance imaging after TaTME when compared to Lap TME (3.1% vs 46.9%; $P < 0.001$) [53].

TaTME resulted in the lowest rate of incomplete specimen and involved CRM margin, in a recently published paper comparing short-term results of total mesorectal excision in 300 patients who underwent transanal, laparoscopic or open resection [29].

The quality of the excised mesorectum evaluated through CRM and DRM positivity rates is both surgeon- and patient related. In this respect, it should be emphasized that TaTME is still a procedure under development and thus, case volume and learning curve factors should be considered. Better-quality TME specimen has been reported in high-volume (> 30 cases) when compared to low-volume centers (< 30 cases), and this seems to confirm the hypothesis of a learning curve and surgeon's effect [26]. With respect to the second point, CRM and DRM positivity are influenced by several factors such as narrow pelvis, large tumors and lower distance of the tumor from the anal verge It might be considered that the majority of TaTME studies include patients with middle- or lower third rectal tumors, whereas data from laparoscopic studies also included high rectal tumors. The better performance of TaTME in terms of lower rate of CRM and DRM, if confirmed by further studies, will play a determining role when choosing the best approach for low rectal cancer.

Long-term oncological outcomes

Data on oncological outcomes are reported in Table 2. Few studies are currently available in the literature and none of the included studies has a complete 3-year follow-up; thus, no definitive conclusions can be drawn at present [7, 11, 22, 49, 54–58]. Nevertheless, the results are promising. In the most recent review on the subject, Dejjen et al. stated that among 5 of the 33 studies included in the analysis, only 5 had a follow-up period longer than 12 months [26]. With a median follow-up period of 18.9 months, the pooled, local and distal recurrence rates were 4% and 8.1%, respectively, which are within the range of the reported percentages in large RCT studies dealing with laparoscopic TME or open TME. Again, all those reported results must consider the learning curve that impacts with worst outcomes in the early phase of every new technique.

The similar short-term outcomes following laparoscopic or TaTME have also been confirmed by Lelong in a comparative series including 72 patients [54]. The author reported a 5.3% vs 5.7% local recurrence rate in laparoscopic and TaTME, respectively, with a median follow-up period of 31.9 months. However, when considering only patients with curative resections (no metastases at diagnosis), local recurrence rates were 0% vs 5.7% in the TaTME and LAP groups, respectively. This study failed to give any information about distant metastases.

Table 2 Short- and mid-term oncological outcomes

References	Study design	No. of cases	Positive CRM (pts)	Positive DRM (pts)	Follow-up (months)	Disease-free survival			5-years survival	
						Local recurrence	Systemic recurrence	Local + systemic recurrence	Cancer related deaths	Non cancer related deaths
Buchs et al. [22]	Observational	40	2 (5%)	0 (0%)	10.7 (MEDIAN)	0 (0%)	6 (15%)	0 (0%)	NA	NA
Burke et al. [55]	Observational	50	2 (4%)	1 (2%)	15.1 (7–23.2)	2 (4%)	7 (14%)	0 (0%)	NA	NA
Dumont et al. [7]	Observational	4	NA	NA	4.3 (3–9)	0 (0%)	0 (0%)	0 (0%)	NA	NA
Lacy et al. [11]	Observational	140	9 (6.4%)	NA	15	1 (2.3%)	8 (7.6%)	2 (1.5%)	NA	NA
Muratore et al. [57]	Observational	26	0 (0%)	0 (0%)	23	0 (0%)	2 (7.7%)	0 (0%)	1 (3.8%)	1 (3.8%)
Tuech et al. [49]	Observational	56	3 (5.3%)	NA	29 (18–52)	1 (1.8%)	2 (3.6%)	0 (0%)	2 (3.6%)	0 (0%)
Yao et al. [58]	Observational	19	0 (0%)	0 (0%)	12 (2–20)	0 (0%)	0 (0%)	0 (0%)	NA	NA
Lelong et al. [54]	Comparative	34	2 (5.9%)	0 (0%)	31.9 (29.3–42)	2 (5.7%)	0 (0%)	0 (0%)	NA	NA
Marks et al. [56]	Comparative	17	0 (0%)	0 (0%)	19.5	1 (5.9%)	0 (0%)	0 (0%)	NA	NA

TaTME transanal total mesorectal excision, *CRM* circumferential resection margin, *DRM* distal resection margin

Role of robotics

After successful implementation in other surgical fields, robotic colorectal surgery has gained considerable interest. Robotic technology seems to offer a better maneuverability of the instruments with optimal stability of the platform. These potential advantages are related to the ability of robotics to enable ambidextrous movements, decrease tremor and improve dexterity allowing a more precise dissection in force of the 3D visualization of the surgical field, especially when a confined space is considered. All these variables would potentially help to overcome the steep learning curve related to the complexity of TaTME [59, 60].

Small case series reporting the use of robotic technology in performing TaTME is currently published, and robotic single-site surgery is also being explored clinically. Despite there being little data available, results are promising in terms of mesorectal integrity, resection margins, number of intraoperatively harvested lymph nodes, and conversion rate [61–68].

Current limitations are mainly represented by costs, and the fact that the majority of published studies refer to a hybrid procedure that incorporates an abdominal phase to achieve proximal colonic mobilization and inferior mesenteric vessel division. Nevertheless, robotics in surgery is under continuous innovation. The development of new platforms and longer flexible instruments, such as the flexible robotic system arms recently described by Atalllah [67], will push toward the next phase of the procedure which will be the combination of an abdominal robotic single-site procedure with robotic transanal TME, i.e., robotic natural orifice transluminal endoscopic surgery. The recently published paper by Kuo et al., applying robotic technology to a combined transanal and transabdominal approach in 16 patients with low rectal lesions with the use of a single-site plus one-port for the abdominal phase of the operation, seems to go in this direction [65].

Future scenarios and conclusions

Current studies show that TaTME has a low conversion rate, similar postoperative complications when compared to standard laparoscopic or open TME, excellent pathologic effectiveness and promising oncologic results. Nevertheless, some caution in the interpretation of the results is mandatory, since the majority of the published series is coming from highly trained surgeons in high-volume centers with results that are difficult to reproduce. In addition, some studies include the same patients in different reports and randomized trials on this issue are lacking [68, 69].

Standardization of the technique is mandatory, since there is great heterogeneity among studies with respect to the surgical procedure performed and the type of platform and instruments used.

A high heterogeneity has also been reported with respect to indications, patient selection, and distance of the tumor from anal verge. All these variables could have influenced the results and the interpretation of the data in particular when meta-analyses are taken into account. As a matter of fact, meta-analyses represent a good tool to draw scientific conclusions about controversial subjects or about studies based on narrow sample sizes, but they always reflect the literature, being, therefore, influenced by its limitations. In case of TaTME the main limitation is represented by the lack of high-quality,well designed and randomized studies.

According to these remarks, the acceptance and implementation of TaTME by the surgical and academic community should depend on several factors:

1. Agreement among experts on the proper definition of indications and standardization of the technique (materials, devices, methods).
2. Establish a learning curve and assess a minimum case volume per center and per surgeon. At present time, there are no papers specifically addressing this issue.
3. Despite promising short-term oncologic results, data on long-term follow-up of oncologic outcome, with particular emphasis to local recurrence rate, are pending ongoing RCT trials. These results, and quality of life and long-term functional outcomes, will help the surgical community to properly evaluate the procedure.
4. Moreover, in the era of cost-effectiveness, an analysis of the cost related to the procedure is mandatory in particular when a two-team operation is considered.
5. Implementation of detailed national training programs which have been initiated in the US will assure a safe expansion and standardization of the technique.

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Compliance with ethical standards

Conflict of interest All authors mentioned in this study do not have any competing interest. This specific report does not endorse any specific Company.

Research involving human participants and/or animals This article does not contain any studies with animals performed by any of the authors.

Informed consent The informed consent does not apply since this is a meta-analysis study.

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