Transanal total mesorectal excision for rectal cancer: a review

Ido Mizrahi, Dana R. Sands

Department of Colorectal Surgery, Cleveland Clinic Florida, Weston, Florida, USA

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Correspondence to: Dana R. Sands, MD. Department of Colorectal Surgery, Cleveland Clinic Florida, 2950 Cleveland Clinic Blvd, Weston, Florida 33331, USA. Email: sandsd@ccf.org.

Abstract: Low anterior resection (LAR) with total mesorectal excision (TME) can present a technical challenge in patients with middle or lower third rectal tumors. The challenge increases in obese male patients, those with a narrow pelvis, and following neo-adjuvant chemo-radiation. These factors may hamper the quality of the TME specimen, increase laparoscopic to open conversion rates, consequently influence oncological outcomes, and decrease the rate of reconstructive surgery. Transanal TME (taTME) was developed to overcome the abovementioned technical difficulties through enhanced visualization of the dissection planes in the distal most difficult portion of the TME procedure. The transanal approach may facilitate a clearer distal and circumferential resection margin (CRM), offer more patients sphincter-preserving surgery, and serve as a natural orifice extraction site of the specimen. Recent publications report an acceptable perioperative and short-term oncologic outcomes when comparing taTME to open or laparoscopic LAR. The aim of this review is to summarize the available current literature on taTME and to propose future perspective of training, quality control, and clinical research.

Keywords: Low anterior resection (LAR); total mesorectal excision (TME); rectal cancer; transanal TME (taTME); sphincter-preserving surgery; natural orifice extraction site

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Introduction

Rectal cancer is one of the most common types of cancer worldwide with an annual incidence of approximately 40,000 new cases diagnosed in the United States alone (1). Total mesorectal excision (TME) was first described by Heald *et al.* in 1982 and since then has been considered the gold standard for the surgical treatment of rectal cancer (2). TME results in lower rates of positive circumferential resection margins (CRMs) with subsequent reduction in locoregional recurrence and improved oncological outcomes (3).

Despite its endorsement for colon cancer, laparoscopy for the treatment of rectal cancer is still under debate. Randomized controlled trials such as the COLOR II, COREAN and CLASICC, comparing laparoscopic to open low anterior resection (LAR) with TME have shown comparable short and long term oncological results (4). However more recently, the ACOSOG Z6051 and ALaCaRT trials failed to show the non-inferiority of laparoscopic LAR in comparison to open surgery (5). The utility of laparoscopic LAR can be extremely challenging when dealing with low rectal tumors and especially in patients with the following characteristics: deep and narrow pelvis, male gender, obesity, following neo-adjuvant chemo-radiation, and those with a bulky tumor. The technical challenges derived from these characteristics include a limited exposure of the TME surgical planes and difficulty stapling across a low rectal tumor. These may lead to breaches in the quality of the mesorectal fascia and incorrect identification of the distal resection margin (DRM). The distal transection in the deep and narrow pelvis using the currently available laparoscopic or robotic staplers can be difficult and may require multiple linear stapler firings which is associated by some authors with increased rates of anastomotic leak (AL) (6). The above-mentioned challenges result in considerable laparoscopic to open conversion rates as high as 34%, consequently linked to increased post-operative morbidity and worse oncologic outcomes (7).

Based on these concerns, the concept of transanal TME (taTME) utilizing a "bottom up" approach has been proposed. The technique has become possible due to recent advances in minimally invasive transanal surgery. Transanal endoscopic microsurgery (TEM) via a wide bore rigid proctoscope was initially reported by Buess *et al.* in 1983, for resection of rectal adenomas and early stage rectal cancer (8). Marks *et al.* presented the laparoscopic transanal abdominal transanal proctosigmoidectomy with sphincter preservation and colo-anal anastomosis (TATA) for low lying rectal tumors (9). Subsequently, transanal minimally invasive surgery (TAMIS), using a single-incision laparoscopic port, was introduced by Atallah *et al.* (10). Finally, the development of the Natural Orifice Transluminal Endoscopic Surgery (NOTES) approach allowed surgical access through natural orifices and, when applied to rectal surgery, is even more attractive since the target organ for transluminal access houses the pathology.

taTME has clear benefits over the laparoscopic or opens trans-abdominal TME in achieving a clear DRM as the dissection starts distal to the tumor and is developed proximally. Moreover, it enables better exposure of the mesorectal planes exactly at the point where the traditional approach struggles to, especially in the obese male patient. It also often allows for a single stapled anastomosis and when appropriate, a natural orifice for specimen extraction hence avoiding an abdominal scar and potentially reducing incisional hernia rates and adhesions.

Since the first taTME report by Sylla *et al.* in 2010, the procedure has grown in popularity reflected by the rising number of scientific publications (11). Reports have shown promising results regarding TME specimen quality, high rates of sphincter preservation while achieving a clear DRM, and comparable post-operative morbidity (12). Despite the potential benefits of the procedure there is concern for widespread and unmonitored adoption of taTME as it is a challenging operation even in the hands of an experienced laparoscopic surgeon and requires considerable comfort with other transanal techniques.

This review summarizes the current available literature on taTME and proposes future perspectives regarding its training and clinical research.

Pathology outcomes

The quality of the TME specimen defined by completeness of the mesorectum and uninvolved circumferential and DRMs has been shown to be the most important prognostic factor predicting local recurrence (13). A recent and most comprehensive systematic review by Deijen *et al.* of 33 studies that included 661 patients who underwent taTME showed TME quality to be 87.6% complete, 10.9% near complete, and 1.5% incomplete (14). The authors reported a 0.2% positive DRM and a 4.7% positive CRM. In 45.2% of the patients, a pT3 or pT4 tumor was found on final pathology. Five of the studies included in their review compared laparoscopic TME to taTME and a sub-analysis of these studies showed a complete TME in 75.2% in the laparoscopic TME group and 82.8% in the taTME group, (P=0.72). Involvement of CRM was 7.6% and 3.2% in the laparoscopic TME and taTME groups, respectively (P=0.37). Nearly similar outcomes were reported in an earlier systematic review by Simillis *et al.* of 36 studies and 510 patients (15). TME quality was described as complete in 88% of cases, near complete in 6% and incomplete in 6%. The CRM was positive in 5% of cases and the DRM in 0.3%. On final pathology, 48% of patients had a pT3 tumor and 4% had a pT4. Recently, Lelong *et al.* published their results of a single institution study, not included in the reviews above, comparing laparoscopic (n=38) to taTME (n=34) (16). In the taTME group the mesorectal quality was classified as complete in 56% and near complete in 44% while in the traditional laparoscopic group 52.6% of patients had complete TME, 42.1% near complete, and 5.3% (two patients) incomplete (P=0.66). The CRM was positive in 5.9% and 10.2% in the taTME and laparoscopic group, respectively (P=0.29). All 34 patients who had taTME had a negative DRM and one patient who had laparoscopic resection had a positive DRM (P=1). Another recent single center study by Meillat *et al.*, not included in the reviews above, describes combined taTME and single-incision laparoscopy (17). The authors report a 75% complete and 25% near complete TME, a 4.9% positive CRM and 0% positive DRM. Finally, Penna *et al.* reported results of the first 720 cases on behalf of the taTME International Registry (18). This is the largest published study, although short or long-term oncologic data are unavailable. The registry shows an 86% complete and 11% near complete TME, a 2.4% positive CRM and 0.3% positive DRM.

These data clearly show that pathologic quality indicators after taTME compare favorably to the published laparoscopic TME studies, especially when considering that most of the data are obtained from patients with middle and lower third rectal tumors whereas the large laparoscopic studies also include high rectal tumors (4).

Oncologic outcomes

There are currently no published data with a complete 3-year follow up to calculate the 3-year disease-free survival. In the most recent systematic review by Deijen *et al.* only 5 of 33 studies (including 302 patients) reported follow-up of more than 12 months (14). Overall time of follow-up was 18.9 months. The local and distant recurrence rates were 4% and 8.1%, respectively. Meillat *et al.* reported their experience showing that at a median follow-up of 29 months, overall and disease-free survival rates were 97.5% and 80.5%, respectively (17). Lelong *et al.* showed a 5.3% *vs.* 5.7% local recurrence rate after a follow up of 31.9 months, in the laparoscopic *vs.* taTME group, respectively (P=1) (16). All patients experiencing local recurrence in the taTME group had resectable synchronous metastasis at the time of diagnosis. However, when considering patients with curative resections (those without metastasis at diagnosis) local recurrence rates were 5.7% *vs.* 0% for the laparoscopic *vs.* taTME groups, respectively. The disease free and overall survival rates at 24 months, were 88% *vs.* 86% (P=0.91) and 95% *vs.* 100% (P=0.52) for the laparoscopic *vs.* taTME groups, respectively.

Long term follow up is required before drawing definitive conclusions regarding the long term oncological outcomes of taTME. Short term results are promising and certainly at least comparable to the standard open or laparoscopic approach (4).

Complications

Safety is of paramount importance when introducing a new and technically challenging surgical technique such as taTME. The overall peri-operative complication rate of 35% seems comparable to the open, laparoscopic, and robotic approaches as shown by recently published systematic reviews and meta-analysis (12). However, there are new and specific complications that should be evaluated and understood. Urethral injury is a serious complication related specifically to taTME and is uncommon during open, laparoscopic, or robotic TME. During the transanal dissection, the prostate may unintentionally be incorporated into the plane of dissection resulting in a urethral injury. This is especially true for ultra-low tumors when the dissection starts at or just above the dentate line. Simillis *et al.* reported a 1.1% rate of urethral injury in their systematic review of 36 studies and 510 patients (15). Results from the taTME International Registry of the first 720 cases showed a urethral injury rate of 0.7% (18). Other visceral injuries during the perineal dissection in this study included bladder injuries (0.3%), vaginal perforations (0.1%), resection of hypogastric nerve (0.1%), and rectal perforation (0.3%).

The transanal dissection commences with placement of a purse-string suture thereby securing the distal margin. A rectal incision is then made that can theoretically create a contaminated field. This raised initial concerns for higher rates of pelvic abscesses. Indeed Velthuis *et al.* found a positive pelvic culture in 39% of patients, during taTME (19). However, these concerns are not supported by the published data. Deijen *et al.* reported a pelvic abscess in 18 of 794 patients (2.3%) in their systematic review (14). Wolthuis *et al.* reported a rate of 3.4% in their systematic review including 20 studies and 323 patients (12). A nearly similar rate of 2.4% (17/720) was reported from the international taTME registry (18). To reduce contamination, we routinely perform a rectal washout with povidone-iodine just before the procedure and after the rectal purse-string closed prior to rectotomy. We also regularly order a full bowel preparation with addition of oral antibiotics.

Other procedure-specific complications include pelvic sidewall injury and bleeding which result from dissecting too lateral. The pneumo-pelvis serves as an aid during the pelvic dissection but it might also create false areolar planes and mislead the surgeon. This is especially true during the lateral dissection at the level of the mid-rectum and during the posterior dissection at the level of the mid and upper rectum. Bleeding may originate from the pre-sacral venous plexus posteriorly, or from pelvic side wall vessels laterally. Pelvic bleeding reported as problematic and difficult to control was reported in 6.9% of 720 patients in the taTME international registry (18).

AL is a devastating postoperative complication after LAR. Specifically, leak rates may reach 10–20% in "high-risk" anastomosis (<10 cm from anal verge and/or following neo-adjuvant radiation therapy) (20). Patients suffering from an AL are at risk for increased morbidity and mortality, prolonged length of stay, impaired functional outcomes, and increase in local recurrence rates in patients with rectal cancer (21). A consistently low AL rate following taTME has been reported by various authors. In the largest systematic review published to date including 661 patients, Deijen *et al.* report a 5.7% leak rate (14). In another large systematic review including 510 patients, Simillis *et al.* report a leak rate of 6.1% (15). A nearly similar leak rate of 6.7% (40 of 720 patients) is reported by Penna *et al.* (18). A slightly higher leak rate of 10% (26 of 245 patients) is shown by Ma *et al.* in their systematic review and meta-analysis (22). These leak rates compare favorably with those reported after open, laparoscopic, and robotic LAR and certainly encourage further adoption of this novel procedure (23).

Despite recent technical advances, a high conversion rate (range 0–34%) from laparoscopic to open surgery is still being reported with an associated increase in the morbidity and functional outcomes (24). The reported conversion rate during taTME in the three largest systematic reviews published to date is 1.4–2.3% (15). The reasons for conversion described in the systematic review by Simillis *et al.* include morbid obesity, posterior fixity of tumor, bulky and high tumor, urethral injury, and adhesions after prior laparotomy (15). Ma *et al.* found a lower conversion rate for taTME *vs.* standard laparoscopy (1.6% *vs.* 6.1%, P=0.02, respectively) (22). A similar conversion rate in favor of taTME was reported by Deijen *et al.* (1.4% *vs.* 5.4%, P=0.33) (14). Penna *et al.* reported conversion during the perineal phase of taTME to a more extensive abdominal dissection in 2.8% of patients (18). The seemingly low conversion rate is a definite advantage of taTME over open, laparoscopic, or robotic LAR especially for low rectal cancers. This may be attributed to better visualization in obese patients and/or in patients with a deep and narrow pelvis. It is also the result of the "bottom up" approach initiating the dissection just distal to the tumor, hence neglecting the difficulty of stapling across the rectum as performed in the other approaches.

Re-operation after taTME is reported in 44 of 720 patients (6.1%) in the International taTME Registry (18). A slightly lower re-operative rate of 3.7% was published in the systematic review by Simillis *et al.* (15). These acceptable re-operative rates are reassuring from a patient safety perspective.

Functional outcomes

LAR syndrome (LARS), which is often reported at approximately 50% after conventional TME, is associated with an immense decrease in quality of life and is considered one of the most important functional outcome measurements after proctectomy (25). In recent years, the acceptance of a shorter DRM, an increased interval after neo-adjuvant chemo-radiation, and the ability to perform an inter-sphincteric dissection have increased the rates of sphincter saving procedures in patients with low and ultra-low rectal cancers, however, with a clear impact on functional outcomes. More often these patients require an end-to-end hand-sewn anastomosis that is a known risk factor for worse functional outcome in the short term after proctectomy (26). Another factor that may influence function particularly after taTME is the prolonged anal dilation by the wide anal platforms taking place throughout the procedure. Recently, Koedam *et al.* reported on the functional outcome and quality of life 6 months following restorative taTME in 15 patients (26). Five patients did not have a diverting ileostomy and in 10 patients the function was recorded after closure of the ileostomy. Seven patients had no LARS (47%), 3 had minor LARS (20%), and 5 had major LARS (33%). The authors reported no change in urinary function after taTME and that the sexual function in males returned to baseline 6 months after the initial surgery. Kneist *et al.* were the first to report on LARS after taTME in 10 patients and showed that 40% of patients experienced no LARS, 50% minor LARS, and only 10% major LARS at 6 months after stoma closure (27). Worse functional outcomes have been published by Pontallier *et al.* (28) showing major LARS 12 months after stoma closure in 82% of patients with colo-anal anastomosis. Future studies should focus on the long-term functional outcome and LARS after taTME with specific concern for patients who have had inter-sphincteric dissection and a hand-sewn colo-anal anastomosis.

Technical considerations

It is beyond the scope of this review to describe in detail the actual technique utilized during taTME. However, some technical considerations should be emphasized. The authors find it crucial to utilize an AirSeal® (Conmed; Utica, NY) insufflator for the perineal dissection to maintain a stable pneumo-pelvis and increase smoke evacuation. Seven different transanal platforms have been described in the literature: the GelPOINT Path Transanal Access Platform (Applied Medical, Inc., Rancho Santa Margarita, CA, United States), SILS Port (Covidien, Mansfield, MA, United States), TriPort (Olympus Medical Europe Holding GmbH, Germany), TEO proctoscope (Karl Storz, Tuttlingen, Germany), TEM proctoscope (Richard-Wolf, Knittlingen, Germany), Endorec Trocar (Aspide Medical, La Talaudiere, France), PAT transanal access port (DevelopiahumV, Santander, Spain) and the D-Port (Karl Storz-Endoskope, Tuttlingen, Germany). Regardless of the platform used, the surgeon should have adequate experience and feel comfortable with his/her choice of instruments. The operation should always start with a laparoscopic exploration to rule out any intra-abdominal carcinomatosis. Thereafter, the procedure may be initiated simultaneously from both the abdominal and perineal approach, in case of a two-team approach. This saves operative time as shown in the systematic review by Deijen *et al.* comparing the two-team procedure to the single team procedure times (209.8 *vs.* 264.5 minutes, respectively) (14). If only one team is available, the procedure may be initiated from the perineal or abdominal phase, according to the surgeon's preference, after ruling out intra-abdominal carcinomatosis. We advocate beginning with the transanal dissection for two major reasons. Firstly, if the surgeon finds it impossible to obtain a clear distal margin, then the plan for the abdominal portion changes and full splenic flexure mobilization is no longer needed and an end colostomy is constructed. Secondly, placement of the purse-string suture and initiation of the transanal dissection are easier with the patient in the Trendelenburg position, which may interfere with the simultaneous abdominal portion.

The distance of the tumor from the dentate line dictates the type of dissection and anastomosis. For low-lying tumors, an inter-sphincteric dissection is required using an open approach. A Lone Star Retractor (Lone Star Medical Products Inc., Houston, TX, United States) is positioned and then under direct vision a circumferential incision is performed at the dentate line. The rectum is then closed using a purse-string suture and the perineal dissection begins, first in an open fashion and, once ample space is created, the transanal platform is positioned and the dissection resumes under camera-guidance. A hand-sewn colo-anal anastomosis is obviously created after such dissection. For tumors located more proximally, the purse-string suture can first be applied either using an open or laparoscopic approach approximately 1 cm distal to the tumor, after which a rectotomy is performed and the dissection commences. A hand-sewn or single stapled anastomosis can be performed based on the distance of the rectotomy from the dentate line. If the surgeon chooses to perform a stapled anastomosis, adequate cut edge of the distal rectum must be mobilized for the purse-string to be applied. It is of paramount importance, particularly in such low anastomoses, to fully mobilize the splenic flexure and perform a high ligation of the inferior mesenteric artery and inferior mesenteric vein at its border with the duodenum to facilitate ample reach for a tension-free anastomosis. Either an end-to-end colo-anal anastomosis or colonic J-pouch anal anastomosis can be constructed based on the reach of the proximal bowel.

The specimen can be extracted transanally or trans-abdominally. Before delivering the specimen, a wound protector should be placed regardless of the extraction site and attention should be given to gentle extraction maintaining the integrity of the mesorectum. The transanal extraction avoids an abdominal incision and perhaps helps lower post-operative pain and analgesic use as well as the risk of future incisional hernia and intra-abdominal adhesions. In patients with a bulky tumor or in those with a very narrow pelvis, a trans-abdominal extraction may help avoid harming the integrity of the TME specimen.

Selection criteria

Although taTME was initially developed to facilitate resection of low rectal tumors, the procedure may also be considered for benign procedures. In fact, 86 of 720 patients (11.9%) reported in the International taTME Registry underwent this procedure for benign disease (18). Potential benign indications may include reversal of Hartmann's procedure, restorative proctocolectomy or completion proctectomy and ileal-pouch anal anastomosis (IPAA), and abdomino-perineal resection. The authors personally avoid a taTME in patients with an IPAA due to risk for impaired functional outcome after lengthy dilation and stretching of the anal sphincter complex, especially when a pouch anal anastomosis is performed. Furthermore, and for the same reasoning, the authors avoid taTME in elderly females if decreased anal tone is documented pre-operatively by physical exam or anal manometry. It seems that the perfect candidate to benefit from taTME is an obese male with an anteriorly located, advanced, mid-low rectal tumor. Nevertheless, it is reasonable to select easier cases at the beginning of the learning curve including females and normal weight patients, and those with early stage tumors located higher and posterior.

Training and education

As for any new surgical technique and especially for those considered technically advanced, the danger of widespread and unmonitored implementation exists. A controlled introduction of the technique is crucial for both patient safety and surgeon performance. McLemore *et al.* acknowledged six key elements that may facilitate introduction of taTME into practice (29). The surgeon should have expertise in TME for rectal cancer, minimally invasive (laparoscopic and/or robotic) TME, transanal endoscopic surgery, inter-sphincteric dissection for very low rectal tumors, and practice in taTME techniques in human cadaver labs. Institutional review board (IRB)-approved data collection with publication of outcomes and/or participation in a clinical registry is also recommended.

There are currently two major online resources for taTME education. The iLapp smart phone application is an outstanding tool offering three major themes: video-based educational modules with high-quality 3D animations, medical illustrations and teaching videos that clarify the anatomic planes and structures for an enriched understanding of taTME; a publication and video library, which highlights selected publications of relevance to taTME; and, lastly, educational events information, currently only European taTME conferences and workshops (30) (http://www.ilappsurgery.com/). Another excellent online resource is the archived Advances in Surgery (AIS) channel (https://aischannel.com/).

The taTME consensus group has stated that at least 14 procedures should be performed annually to ensure optimal quality of the procedure (31). This hypothetical learning curve is supported by a systematic review by Deijen *et al.* who performed a subgroup analysis of low (<30 patients per year) *vs.* high volume centers (14). The results show that high volume centers enjoyed a shorter operative time (222 *vs.* 282 minutes), more two-team approach (51% *vs.* 13%), lower conversion rate (2.7% *vs.* 4.3%), more "complete" TME (89.7% *vs.* 80.5%), a lower major complication rate (12.2% *vs.* 10.5%), and lower rates of local recurrence (2.8% *vs.* 8.9%). Furthermore, low volume centers had a higher rate of colostomy.

Future perspectives

Several future concerns and perspectives related to taTME should be highlighted. These can be roughly categorized into education, clinical practice, and clinical research. Education and training should focus on how to shorten the learning curve, what prerequisite skills are required, and working towards standardizing the technique. Future clinical practice should aim to explore new boundaries of taTME such as for redo pelvic surgery and in the form of totally taTME without a transabdominal approach. Clinicians should also work closely with the industry to develop new platforms and instruments to overcome the technical difficulties of this procedure.

One major limitation of the available current data is the lack of randomized controlled trials. The available studies are case series at best, which are heterogenous in terms of surgeon experience, technique, platforms used, indication, and patient selection. Moreover, some of the studies include the same patients in different reports (14). The results of the COLOR III Trial, a multi-center randomized clinical trial comparing transanal and traditional laparoscopic TME for rectal cancer are eagerly awaited. Of note, the study's protocol excludes T3 tumors with margins <1 mm to the endopelvic fascia, tumors with ingrowth into the internal sphincter or levator ani muscle, and all T4 tumors staged prior to neoadjuvant therapy (32). The COLOR III trial may shed light on the functional and oncological results following surgery.

The aims of future clinical research include the long-term follow up of oncologic outcomes, functional outcomes, and quality of life. Future research should also examine the cost effectiveness of the procedure.

Conclusions

Although there is currently limited data, taTME appears to be safe and feasible with an acceptable and comparable complication rate when performed by properly trained surgeons at high volume centers. Pathologic results are excellent and short-term oncologic results are promising.

Future randomized controlled trails are needed to evaluate long-term oncologic and functional outcomes. Surgeons seeking to perform this procedure should participate in an official course and pursue proctorship.

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Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ales.2017.08.07). The authors have no conflicts of interest to declare.

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