Transanal total mesorectal excision for rectal cancer: hype or new hope?

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Abstract: Rectal cancer has always posed surgical challenges to the colorectal surgeon. The quality of the total mesorectal excision (TME) performed is key in determining local disease control. Unlike the great success in adoption of laparoscopic surgery in colon cancer treatment, studies comparing laparoscopy to open rectal surgery all revealed noninferiority was not achieved. Transanal TME (taTME) is the latest advanced technique pioneered to tackle difficult pelvic dissections. The evolution of taTME surgery in recent years was explored in this review. The outcomes to date on the latest literatures are reviewed, included complications, functional outcomes, oncological results and future clinical researches. taTME, while definitely still in its early stages of development, has steadily accumulated safety and feasibility data. It not only provides a better solution to an old problem that colorectal surgeons have been attempting to tackle for quite some time, but also appears to be quite promising in terms of outcomes on numerous fronts. With structured training models, and proctored clinical application, alongside design and implementation of international-scale large multicenter randomized clinical trials, one can only hope that taTME and its innovations will not only open a new era for colorectal surgery, but also for even more surgical disease pathologies.

Keywords: Transanal total mesorectal excision (taTME); total mesorectal excision (TME); laparoscopic surgery; rectal cancer; laparoscopic rectal surgery; minimally invasive surgery

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Background

Rectal cancer has always posed surgical challenges to the colorectal surgeon—confinement of the lesion of interest within the pelvis poses spatial limitations and hinders ideal tumor resection, leading to the possibility of local recurrence and subsequent poor oncological and survival outcomes.

In 1982, Dr. Heald et al. proposed total mesorectal excision (TME), a surgical advancement technique emphasizing sharp, nerve-sparing circumferential dissection along the congenital avascular plane between the mesorectum and surrounding tissue (1). By not disrupting the mesorectal fascia, TME dramatically decreased local recurrence of rectal cancer and has since then become the surgical gold standard for curative resection. Furthermore,
the aid of neoadjuvant/adjuvant chemotherapy and radiotherapy has even further decreased local recurrence rates.

It comes, as no surprise then, that the quality of the TME performed is key in determining local disease control. Studies have demonstrated that poor surgical TME quality is directly linked to local malignancy recurrence that unfortunately cannot be rectified by chemoradiotherapy. Recurrence is notoriously difficult to treat and not only immensely impacts quality of life, but also imbues a worse prognosis going forward (2).

The 1990s saw the introduction of laparoscopic surgery and its eventual role in colorectal surgery. While there were initial concerns regarding laparoscopy’s oncological safety, clinical trials including outcomes of surgical therapy like COST (3) and COLOR (4) subsequently demonstrated the safety and clinical benefit noninferiority of laparoscopy to traditional open colon surgery. Unfortunately, studies comparing laparoscopy to open rectal surgery including COLOR II (5), ALAcaRT (6), and ACOSOG Z6051 (7,8), all revealed noninferiority was not achieved. The investigators of these rectal surgery studies pointed towards numerous factors—the complexity of traction and countertraction while utilizing a straight rigid instrument, limited visualization offered via laparoscopy in a restricted operative space, and imperfections of linear stapling in transecting the rectum—as reasons why laparoscopy, unless in the most experienced of surgical hands, most likely still yielded similar outcomes to open surgery. With such a subjective variability involved, it thus became difficult to generalize laparoscopy’s use in treating rectal cancer.

Robotic surgery then arose in response to the aforementioned limitations by attempting to offer better visualization and increased instrument articulation. While there were anecdotal reports that robotics did indeed lead to better TME quality, lower circumferential resection margin (CRM) positivity, and lower conversion rate, the recently published ROLLAR trial did not support these proposed advances over traditional laparoscopy (9). In fact, only one sub-group analysis of higher body mass index (BMI) male patients supported the superiority of robotics. In addition, one must not forget the issue of cost-effectiveness of robotic surgery.

As a result, in the current state of affairs where the advancement and cost of robotics will determine robotic surgery’s fate, alongside evidence demonstrating that open surgery still reigns supreme as the gold standard in surgical treatment of rectal cancer, colorectal surgeons are left searching for the next breakthrough in surgical treatment of rectal cancer.

The evolution of transanal TME (taTME)

The year 1983 saw the development of transanal endoscopic microsurgery (TEM) by Buess et al. by facilitating magnified visualization during transanal resection (10), TEM not only allowed greater precision in rectal lesion excision when compared to during traditional open surgical approaches, but also yielded lower morbidity, lower local recurrence rates, and higher rates of negative resection margins. However, TEM never truly became a standard, owing to the cost of the specialized surgical instrument needed, as well as the procedure’s limited indications and steep learning curve. Nevertheless, it still firmly rooted the concept of integrating laparoscopy via natural orifices into the general approach of minimally invasive surgery.

Albert et al. subsequently proposed Transanal Minimally Invasive Surgery (TAMIS) using an advanced transanal platform developed by GelPOINT Path® (Applied Medical, USA) (11). This platform quickly propelled TAMIS to much greater heights than TEM, given that TAMIS offered the familiarity of standard laparoscopic instrumentation combined with a superior visualization field that did not require purchase of additional specialized devices.

The latest advancement in this rapidly progressing field has emerged to be NOTES—Natural Orifice Transluminal Endoscopic Surgery. After procedures including cholecystectomy, appendectomy, and even rectosigmoid resection were completed via NOTES in both animal models and clinical patients, 2010 saw the first series of 20 patients who underwent taTME by de Lacy et al. This team was able to successfully perform the most difficult portion of rectal surgery—TME—via a novel “bottom up” approach (12). Many subsequent studies have demonstrated similar successes, proving the safety and feasibility of this innovative method (13). Heald et al. had hailed taTME as “a new solution to some old problems” and predicted 2013 to be the year of taTME (14).

As a result, taTME is not a novel concept. Rather, it is a culmination of inspiration and innovation founded in the advancements offered by TEM, TAMIS, and NOTES.

The evolution of surgical technique

The development of taTME was motivated by difficulties surrounding lower rectal dissection. The transanal approach
offered a shorter distance to approach most difficult location from below, and the in-line positioning was ideal in providing optimal visualization of the operative field to determine adequate distal resection margin and thereby increase the chances of preserving the sphincter. Early taTME studies dwelled on debates regarding transanal platform choice, surgical approach and technique, and final anastomosis creation method (13). Most innovative is the fact that taTME allows for two surgical teams to simultaneously operate on one case—Ceceil approach. This approach decreases operative difficulty, as well as operative time by approximately sixty minutes (15).

At its current stage of development, taTME has become standardized in its surgical techniques and identification of anatomical landmarks via the transanal view, thereby facilitating its reproducibility in ongoing cases. However, final anastomosis creation method remains a somewhat work in progress. In a preliminary series, over 60% of anastomoses were hand-sewn (12), but more recent series have yielded results as far off 40% hand-sewn versus 60% circular stapler performed (16). These latest statistics mirror those of traditional laparoscopic and robotic surgery and indirectly support the notion that distance of the tumor from the sphincter, rather than surgical technique, should determine method of anastomosis.

Complete taTME without transabdominal assistance—otherwise known as NOTES (Natural Orifice Tele-Endoscopic Surgery)—was once hypothesized to be the ultimate evolution of taTME. Case reports elicited difficulties arising from severely limited patient eligibility criteria and lack of appropriate surgical instrumentation (17,18). As a result, taTME has not yet progressed towards NOTES at this time.

**taTME indications**

The St. Gallen Consensus concluded that taTME may be technically easier than traditional abdominal TME in patients with narrow pelvic anatomy, obesity, and bulky mid-to-distal rectal tumors (19). However, if one considers usual markers for a so-called “difficult” pelvis—BMI and hip-waist ratio—there are no pre-determined cutoffs to help surgeons in deciding traditional TME versus taTME (19).

As touched upon earlier in this review, taTME’s innovative “bottom up” approach lessens the technical limitations present in laparoscopic TME and facilitates increased operative completeness and sufficiency. Congruently, a meta-analysis completed by Ma et al. demonstrated that laparoscopic TME carries a 4-time higher likelihood of conversion when compared to taTME (20). In addition, taTME also facilitates higher rates of complete TME quality, lower rates of CRM positivity, and increased CRM length (21). This superiority of pathological results may become the strongest motivator for performing taTME; however, further investigations are definitely necessary before this conclusion can be definitively drawn. Furthermore, the two-team simultaneous surgical approach can effectively shorten operative time by up to 60 minutes, indirectly suggesting that postoperative recovery can also be expedited. However, the resources involved in such an endeavor, both personnel and equipment wise, is not generalizable to all medical facilities.

Lastly, taTME has been extended to treatment of other disease pathologies as well. These include Crohn’s disease, ulcerative colitis, revision of anastomosis strictures, and reversal of Hartmann’s procedure.

**Complications**

With any new and technically challenging surgical approach, safety remains paramount over efficacy. Reported 30-day taTME-associated morbidity varies widely from 8.7% to 52%, while short-term taTME morbidity averages 31.5% in comparison to 39.6% for laparoscopic TME (21).

**Urethral injury**

Injury to the membranous portion of the urethra during taTME often arises secondary to unfamiliarity of the dissection plane anterior to the rectum in male patients. The international taTME registry currently documents a 0.8% risk of urethral injury amongst a database of 720 patients (22). Consequences of this complication are particularly difficult to address, especially in those who have already received neoadjuvant radiotherapy and are left with impaired tissue healing abilities. This specific complication can be mitigated via structured taTME training followed by mentored operative supervision.

**Pelvic abscess**

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have suggested that anastomotic complication, rather than the taTME procedure itself, is the root cause (15,25).

**Pelvic wall bleeding**

Excessive lateral pelvic wall dissection can lead to bleeding, most often arising from lateral pelvic side-wall vessels surrounding the mid-rectum. The aforementioned taTME registry currently documents an incidence rate of 6.9% (22). Insufflating the pelvis, particularly with use of advanced insufflators such as AirSeal® (ConMed Corporation, Milford, CT, USA), may mitigate some of the risk, but can also create false areolar planes and mislead the surgeon. Massive intraoperative bleeding will most definitely call for open surgical conversion.

**Anastomotic leak**

Anastomotic leak is considered the major complication in lower rectal surgery. The double stapling technique remains the primary anastomosis method in both laparoscopic and robotic transabdominal approaches, and the difficulties associated with applying a linear stapler in the pelvis’ narrow operative field and having to fire multiple times in order to transect the rectum greatly raise the chance of resultant anastomotic leak (26).

Given that taTME utilizes a single circular stapler in 70–75% of cases, proponents of taTME strongly believe that the single stapler method leads to decreased likelihood of anastomotic leak. Unfortunately, data thus far paints a mixed picture. The aforementioned taTME registry documents an anastomotic leak rate of 15.7% with 79% of those cases requiring repeat intervention (16), while the also aforementioned analysis by Ma et al. documents a leak rate of 10% (20). Another recently published multicenter case-matched study documents a rate of 11.1% as compared to a rate of 9.5% in robotic cases, but failed to reach statistical significance upon analysis (27). In a multicenter prospective audit of elective rectal cancer surgeries from the European Society of Coloproctology (ESCP) collaborating group, laparoscopic taTME [odds ratio (OR) 1.61, P=0.04] and robotic taTME (OR 3.05, P=0.02) were both associated with higher risks of anastomotic leak when compared to non-transanal laparoscopic or robotic TME. However, this association was subsequently lost when a mixed effect model controlling for patient and disease factors was applied (28).

Thus, literature has failed to support the initial notion that single stapling would decrease rates of anastomotic leak. However, one must keep in mind that taTME, particularly robotic-assisted taTME, has come a long way since the initial times these data arise from, and one wonders whether technique maturation will lead to fruition of the initial notion. Nevertheless, taTME remains technically challenging and requires intensive multimodal training—lectures, hands-on cadaver training, proctored clinical application—in order to protect patients from reckless employment of the technique and subsequent devastating complications. Most importantly, one must refer to the St. Gallen consensus for safe implementation of the technique (19).

**Functional results**

Bowel, bladder, and sexual dysfunction rank amongst the most common and devastating postoperative functional impairments arising secondary to rectal cancer surgery. While taTME may increase the chances of performing sphincter-preserving surgery, the lower anatomical anastomosis poses a counterpoint and may in fact cause greater impairments in anal function. This risk is further increased by the transanal platform intraoperatively stretching the anal sphincter. As for urinary and sexual function, the taTME approach provides better visualization of the operative field, facilitating neurovascular bundle preservation and thus increasing the chances and degree of preserving urinary and sexual function.

A recent series report encompassing 30 patients’ status post taTME at 6 months revealed noninferior quality of life and functional outcomes when compared to those who underwent conventional laparoscopic low anterior resection (29). However, it must be noted that at the one-month postoperative point, all evaluated markers actually demonstrated a decline with the majority improving back to comparable baseline at the six-month mark—except for anal pain and social functioning. In another study comparing 27 patients undergoing laparoscopic TME to another 27 undergoing taTME, low anterior resection syndrome (LARS) at 6 months post stoma reversal was higher in the taTME group (16/27 versus 8/27), but failed to elicit statistical significance. As a result, the authors concluded that functional outcomes and quality of life outcomes were similar between the two groups (30).

Therefore, at this point in time, it is simply too early to draw any preliminary conclusions regarding taTME functional results.
Oncologic results

TaTME was developed on the premise that it could achieve higher quality TME. The aforementioned international taTME registry currently demonstrates a near-complete to complete mesorectal excision rate of 96%, CRM positivity rate of 2.4%, and distal rectal margin (DRM) positivity rate of 0.3% (22). In our own case-matched study, taTME yielded statistically significant longer distal margin lengths in both middle and lower rectal cancer surgeries. Furthermore, taTME also yielded longer CRM distances and a less than 1mm incidence rate (4% versus 10%) (15). The previously reference meta-analysis from Ma et al. similarly concluded that taTME is able to obtain significantly higher rates of near-complete to complete mesorectal excision when compared to that of laparoscopic TME, and that taTME also yields longer CRM distances with a significantly lower risk of CRM positivity (20).

While these short-term pathological advantages have been re-created in numerous small preliminary taTME reports, whether or not these advantages in fact translate into the ultimate goals of lower local recurrence rate and prolonged long-term survival remains in question. Lelong et al. demonstrated a 5.3% versus 5.7% local recurrence rate in laparoscopic versus taTME groups, respectively, at 31.9-month follow-up (31). While this result seems somewhat disappointing, one must keep in mind that only 72 patients were included in this study, thereby highlighting the need for multicenter, long-term, and large randomized controlled trials for taTME to truly evaluate long-term oncologic outcomes.

Ongoing clinical investigations

A quick search on clinicaltrials.gov reveals over ten randomized clinical trials evaluating laparoscopic TME versus taTME. While the majority do not offer much public detail, Table 1 summarized two well-known and actively ongoing studies of interest.

Table 1 Clinical trials

<table>
<thead>
<tr>
<th>Item</th>
<th>ETAP-GRECCAR 11 TRIAL (32)</th>
<th>COLOR III (33)</th>
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<tbody>
<tr>
<td>Goal</td>
<td>To evaluate the efficacy, morbidity, and functional outcome of endoscopic transanal proctectomy versus laparoscopic proctectomy for low-lying rectal cancer</td>
<td>To compare transanal TME to laparoscopic TME for middle and lower rectal cancers</td>
</tr>
<tr>
<td>Inclusion criteria</td>
<td>Patients with T3 lower-third rectal adenocarcinomas planned to undergo conservative surgery with manual coloanal anastomosis</td>
<td>Patients with rectal adenocarcinoma in the low-mid rectum 0-10AV on MRI, cT1-3 N0-2 with or without neoadjuvant treatment, without threatening CRM in MRF (distance &gt;1 mm), with intent to undergo sphincter-saving procedure</td>
</tr>
<tr>
<td>Designation</td>
<td>Noninferiority</td>
<td>Noninferiority</td>
</tr>
<tr>
<td>Primary endpoint</td>
<td>R0/R1 resection</td>
<td>Three-year local recurrence rate</td>
</tr>
<tr>
<td>Secondary endpoints</td>
<td>Conversion rate; minimal invasiveness of abdominal approach; postoperative morbidity; hospital-stay length; mesorectal macroscopic assessment; urologic and sexual function outcomes; fecal incontinence; global quality of life; stoma-free survival; three-year disease-free survival</td>
<td>Pathological parameters; morbidity; quality of life; anal function; disease-free survival; overall survival</td>
</tr>
<tr>
<td>Anticipated recruitment</td>
<td>226 patients, in a 1:1 assignment ratio, over 3 years with a subsequent 3-year follow-up duration</td>
<td>1,104 patients in a 2:1 taTME:laparoscopic TME ratio</td>
</tr>
<tr>
<td>Notes</td>
<td>Inclusion criteria befits taTME indication consensus, but constitutes quite the minority of taTME eligible patients.</td>
<td>Has already attained surgical quality assurance, recruited fifteen centers, and enrolled over eighty patients.</td>
</tr>
</tbody>
</table>

TME, total mesorectal excision; taTME, transanal total mesorectal excision; CRM, circumferential resection margin; MRF, mesorectal fascia; MRI, magnetic resonance imaging.

Conclusions

TaTME, while definitely still in its early stages of development, has steadily accumulated safety and feasibility
data while simultaneously adapting to said data in order to grow and mature. It not only provides a better solution to an old problem that colorectal surgeons have been attempting to tackle for quite some time, but also appears to be quite promising in terms of outcomes on numerous fronts. As mentioned earlier, with intensive multimodal training that must include lectures, hands-on cadaver training, and proctored clinical application, alongside design and implementation of international-scale large multicenter randomized clinical trials, one can only hope that taTME and its innovations will not only open a new era for colorectal surgery, but also for even more surgical disease pathologies.

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Footnote
Conflicts of Interest: The authors have no conflicts of interest to declare.

References


