Evolution of surgery for rectal cancer: Transanal total mesorectal excision—new standard or fad?

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Abstract:
Transanal Total Mesorectal Excision (TaTME) has recently been developed to overcome the difficulties associated with conventional laparoscopic or robotic TME. TaTME has gained popularity and becomes the center of attention among colorectal surgeons globally. The present review aims to update the literature, clarify the current status and perspectives of TaTME. Complete TaTME specimens were obtained in 85-97.1\% of the case; the reported circumferential resection margin (CRM) ranged from 1.5\% to 8.1\%, whereas and distal resection margin (DRM) positive rates ranged from 0\% to 3.2\%. The conversion rate of TaTME occurred from 0 to 15\%, and there was no difference between TaTME and laparoscopic or robotic TME. Intraoperative complications occurred in 5-6\% of the case, which compared favorably to laparoscopic TME. The most serious intraoperative complication with this approach was urethral injury, although only small numbers were reported, which was possibly due to under-reporting. Clavien-Dindo I or II postoperative complications occurred in 22-24\% of the case, and III or IV in 10-11\% of the case, which did not differ between TaTME and laparoscopic or robotic TME. TaTME may be technically easier and more beneficial than laparoscopic, robotic or open TME in male patients with a narrow pelvis; in obese patients with a bulky tumor. At present two randomized controlled trials, COLOR III and GRECCAR, and comparing TaTME with laparoscopic TME are being conducted and their outcomes are awaited. TaTME is a complex procedure, but proved to be feasible, oncologically safe, and effective in difficult cases. Before this new technique is adopted, proper training with Proctor/mentorship is strongly advised. Careful case selection and audit of data are mandatory.

Keywords:
transanal total mesorectal excision, rectal cancer

Introduction
Surgery for rectal cancer has progressed greatly in the last few decades. Total mesorectal excision (TME), introduced by Bill Heald in 1982, was the gold standard in rectal cancer surgery, which removed the embryological plane as a package\textsuperscript{1}. Bill reported that the local recurrence rate was 4\% at 5 years after TME\textsuperscript{2}.

Laparoscopic surgery offers a magnified view, which enables meticulous and sharp dissection. For colon cancer, some large randomized controlled trials demonstrated equivalent long-term oncological outcomes of laparoscopic surgery, and the clinical benefits of short-term outcomes over open colectomy\textsuperscript{3,4}. As for rectal cancer, the safety of laparoscopic surgery has not been clearly defined. The results of randomized controlled trials are inconsistent. The early
UK CLASICCC trial showed a higher rate of circumferential resection margin (CRM) involvement in patients undergoing laparoscopic surgery, but there was no difference in the overall or disease-free survival between the laparoscopic and open groups\(^\text{15}\). The COLOR II and COREAN trials also showed no differences in the loco-regional recurrence or disease-free survival\(^\text{15}\). However, two recent trials failed to show the non-inferiority of laparoscopic surgery\(^\text{16,19}\). Both trials were well designed and conducted by experienced surgeons who used similar outcome measures defined by the completeness of TME, CRM positivity, and clear distal margin. In these trials, the CRM positivity was greater in the laparoscopic group than in the open group. The authors commented that the current platform of laparoscopic surgery might be less successful than open surgery in patients who have received neoadjuvant treatment, who have larger T3 tumors, or have a higher body mass index\(^\text{4}\).

It is well known that laparoscopic rectal cancer surgery is technically demanding, especially during the division of the rectum, due to poor visualization and limited working space in the narrow pelvis. These limitations have led to the need for other platforms of laparoscopy (minimally invasive surgery) in rectal cancer surgery. Robotic surgery was introduced to overcome these limitations. The advantages of robotics include improved ergonomics, reduced tremor, three-dimensional camera view, flexible wristed articulation, and enhanced dexterity. Nevertheless, the clear benefits of robotic rectal cancer surgery have not yet been defined. Although some studies addressed the efficacy and feasibility of robotic rectal cancer surgery, the randomized controlled trial, ROLARR trial, failed to demonstrate any significant advantages of robotic TME over laparoscopic TME\(^\text{14}\).

**Transanal TME**

Before the introduction of transanal TME (TaTME), other minimally invasive approaches to rectal cancer surgery have been innovated. Gehard Buess developed the Transanal Endoscopic Microsurgery (TEM) procedure in 1983, offering a magnified view of the gas dilated rectum using a rigid scope\(^\text{23}\). This procedure enabled precise local excision of rectal lesions with a higher rate of negative surgical margins as compared with the conventional trans-anal local excision, and the defect closure of the bowel wall. However, this procedure did not become popular because of the cost of the specialized instrumentation and limited indications. Sam Atallah introduced Transanal Minimally Invasive Surgery (TAMIS), another platform of local excision, which was like TEM but used usual laparoscopic instruments and a single incision laparoscopic port\(^\text{10}\). Transanal Transabdominal (TATA) procto-sigmoidectomy with coloanal anastomosis, described by Gerald Marks in 1984, was a technique that preceded (or initiated) transanal rectal dissection, securing the distal and circumferential margins\(^\text{14}\). His son, John Marks, further integrated this technique with the aid of laparoscopy and robotics and reported favorable long-term outcomes\(^\text{15}\). Natural orifice transluminal endoscopic surgery (NOTES) is probably the most advanced platform for minimally invasive surgery via natural orifices, such as the transoral (gastrotomy), transvaginal, or transanal routes. Since the report of NOTES recto-sigmoid colectomy in cadavers, there have been several reports of NOTES in humans, however, NOTES is still at an experimental stage\(^\text{16-19}\).

TaTME is a combined approach of TATA’s concept that initiates the rectal dissection from the caudal side using the laparoscopic instruments in most cases. Since the first report of TaTME by Sylla, followed by small case series\(^\text{20,21}\), there have been numerous case reports and small case series suggesting that this approach is safe, feasible, and efficient in dissecting the rectum from below.

The aim of this manuscript is to review the up-to-date literature and clarify the status and perspectives of TaTME.

**Methods**

A comprehensive literature search was performed using PubMed and MEDLINE. The search period was from January 2015 to July 2018 using the term “transanal total mesorectal excision”. Only English articles were included, and case reports, or small case series (<20 cases) were excluded.

**Results**

A total of 43 manuscripts were selected and met the inclusion and exclusion criteria. There were 27 case series and 16 comparative studies. TaTME was performed with laparoscopic assistance (hybrid TaTME) in most reports. For hybrid TaTME, laparoscopic assistance was provided using multiport laparoscopy in most of the cases, however, robotic surgery or single port laparoscopic surgery were also utilized\(^\text{22-25}\).

For perineal phase, a rectal purse-string technique was adopted before full thickness rectotomy in the majority (57.6%) of the cases, but intersphincteric resection or mucosectomy was also performed in 26.1% and 7.2% of the cases\(^\text{22}\). Synchronous two-team TaTME was performed in 30% of the cases, potential to reduce the operation time, and to allow the teams to get the traction and counter-traction from above and below to facilitate the dissection\(^\text{25}\).

**Short term oncological outcome**

The potential oncological benefits of TaTME may include a higher quality TME specimen, lower CRM and the distal resection margin (DRM) positive rates. An international registry data, which is probably the largest data available at present, showed that a complete TME specimen was
achieved in 85% and the almost complete specimen in 11% of the case\textsuperscript{22,28}, which was comparable to data from other large series where complete TME specimens were obtained in 95.7-97.1%\textsuperscript{27,29-31}. It also demonstrated that CRM positive rates of 2.4% and DRM positive rates of 0.3% were recorded. These figures slightly increased in their most recent paper where the CRM positive rate rose to 3.9% and DRM positive rate to 0.6%, which were still consistent with other large series where the reported CRM rate ranged from 1.5% to 8.1%, and DRM positive rate ranged from 0% to 3.2%\textsuperscript{27,29-31}. Few comparative studies described that the CRM positive rate was lower after TaTME than laparoscopic TME\textsuperscript{32,33}, but many other studies found no difference in the TME specimen quality or pathological results\textsuperscript{34-38}. Studies comparing robotic TME with TaTME showed similar results concerning the TME specimen quality and CRM positive rate\textsuperscript{39,40}, but it should be noted that DRM involvement might be higher after TaTME than robotic TME\textsuperscript{41}.

\textbf{Operative outcome}

According to the International Registry, perineal conversion occurred in 2.8%, which was relatively low, considering that this registry comprised multiple, multinational institutions\textsuperscript{22,28,43-48}. The reported conversion TaTME rate ranges from 0 to 15.6\%\textsuperscript{26,28,44-47}, and there is no difference between TaTME and laparoscopic or robotic TME\textsuperscript{27,31}. Two papers claim that the conversion rate after TaTME is lower than laparoscopic TME, but their conversion rate of laparoscopic TME is 20-24%, which is extremely high\textsuperscript{36,40}.

The operative time depends on the surgeon’s experience, the learning curve, the patient’s body habitus, and tumor-related factors. The operative time from the International Registry improved from 277 to 252 minutes\textsuperscript{22,28,43}, and the reported operative time ranged from 158 to 358 minutes\textsuperscript{23,43-45,47,50-51}. Some papers addressed that TaTME resulted in shorter operative time and less blood loss was recorded as compared with laparoscopic TME\textsuperscript{25,37,41,52,53}, but other papers reported that the operative time and blood loss were similar between the TaTME and laparoscopic TME except for one paper where the blood loss was greater in TaTME\textsuperscript{33,34,38,40}.

\textbf{Perioperative complications}

Intraoperative complications occurred in 5-6\%\textsuperscript{22,26,28,44-47,51,56,57}, which was favorably to laparoscopic TME\textsuperscript{34,52,54}. The most serious and devastating intraoperative complication in this approach is urethral injury, which is rare in conventional open, laparoscopic or robotic TME. Small numbers of urethral injuries were reported in the literature and International Registry, and the incidence was 0.7\%. These figures may possibly be underreported\textsuperscript{22,44,55}. Similarly, rectal tube perforation was reported in 0.3\% intraoperatively, but the histopathological analysis did it occur in 2\%, suggesting that this might occur more frequently during TaTME\textsuperscript{22}.

Postoperative complications were reported in 24-40\%\textsuperscript{22,26,28,44-47,51,56,57}. Clavien-Dindo classification I or II complications occurred in 22-24\%, and III or IV did in 10-11\%\textsuperscript{22,26,41}. There is one audit in 186 patients reporting that major postoperative complications and anastomotic leak decreased from 47\% to 17.5\% and from 28\% to 5\%, respectively after the first 40 cases\textsuperscript{48}. None of the comparative studies reported that postoperative complications differed between TaTME and laparoscopic or robotic TME\textsuperscript{23,35,41,44-47,52-54}. The International Registry reported that anastomotic leak developed in 6.7\%, of which 5.4\% were early, but the recent data showed that the early anastomotic leak rate rose slightly to 7.8\% and anastomotic failure occurred in 15.7\% possibly due to an increase in the number of complex cases performed by TaTME; wider adoption of TaTME by surgeons during their learning curve, or reporting improved adverse events\textsuperscript{22,29}.

\textbf{Long-term outcome}

Since TaTME has recently evolved, no studies have mentioned the long-term outcome. Some studies report the medium-term outcome as summarized in Table 1. Inadvertent rectal perforation might be more frequent in TaTME, which might lead to higher rates of local recurrence. Local recurrence was reported in 0\%—4\% at median follow-up of 10 to 15 months, and the reported disease-free survival rate was 80\% to 94.2\% at 29 months follow-up\textsuperscript{28,31,44-47,56,57}.  

\begin{table}[h]
\centering
\begin{tabular}{llllll}
\hline
reference & Author & year published & # patients & follow-up period (months) & mid-term outcome \\
\hline
57 & Muratore A & 2015 & 26 & 23 & no local recurrence \\
56 & Tuch JJ & 2015 & 56 & 29 & 5-year OS: 96.4\%, DFS: 94.2\% \\
28 & Lacy AM & 2015 & 140 & 15 & local recurrence 2.3\%, distant metastasis 7.6\% \\
31 & Veltcamp Helbach M & 2016 & 80 & 30* & 2 local recurrence \\
46 & Buchs NC & 2016 & 40 & 10 & no local recurrence, 6 distant metastasis \\
44 & Burke JP & 2016 & 50 & 15 & 2 local recurrence \\
47 & Meillat H & 2017 & 41 & 29 & DFS: 80\% \\
\hline
\end{tabular}
\end{table}  

OS: overall survival, DFS: disease-free survival, *: study period
As to the functional outcome, a recent study which evaluated the functional outcome and quality of life of 30 patients, undergoing TaTME at one and six months postoperatively, showed an acceptable functional and quality of life at 6 months comparable in published results after conventional laparoscopic low anterior resection, except that social function and anal pain remained significantly worse\(^\text{60}\). Another subsequent comparative study also demonstrated that patients undergoing TaTME or laparoscopic TME showed comparable functional and quality of life outcomes\(^\text{60}\).

**Training**

TaTME is a complex procedure and requires special knowledge of pelvic anatomy, which is unfamiliar to most surgeons. To safely implement TaTME, surgeons who wish to adopt this technique should undergo proper systematic and structured training. A training course using cadavers is useful, but the urethral injury is reported even after the course. A total of 25% of the training course participants who responded to the feedback, suggested that a training course using cadavers alone was insufficient\(^\text{61,62}\). A structured training curriculum using fresh-frozen cadavers and including didactic sessions, dry-lab purse-string suture practice and post-course mentorship has been proven to provide surgeons with a complete training package and support for TaTME safely\(^\text{61}\). This opinion reached a consensus among the expert colorectal surgeons throughout the world\(^\text{63,64}\). Nonetheless, few institutions can still provide cadaveric training courses with post-course mentorship in Japan.

**Indications**

One of the most important questions regarding TaTME that needs to be addressed is its indications: what sort of rectal cancer patients will be most likely to benefit from this procedure? Experts agree that TaTME should be offered to both female and male patients with mid and low rectal cancers\(^\text{61,64}\). Female patients are relatively easy and straightforward cases can ascend the learning curve\(^\text{65}\). Obesity, particularly visceral obesity is another limitation. Bulky tumors in the mid or low rectum are also more difficult\(^\text{66}\). Hence, a TaTME may be technically easier and more beneficial than laparoscopic, robotic or open TME in male patients with a narrow pelvis, and obese patients with a bulky tumor\(^\text{67}\).

TaTME can also be performed safely in benign diseases. Of the 1594 patients registered in the International TaTME registry, 97% were cancer and 3% were a benign disease, most of which were proctectomy with ileal pouch-anal anastomosis\(^\text{68}\). Indeed, there are some reports showing that restorative proctocolectomy with ileal pouch-anal anastomosis using TaTME technique in patients with ulcerative colitis or familial adenomatous polyposis is feasible and cosmetically excellent\(^\text{68-70}\). These patients may also be a good indication to start embarking on bulky cancers.

**Limitations and future perspectives**

As mentioned in the previous section, TaTME may be best suited to male, obese patients with bulky tumors in the mid or low rectum. Female patients with small cancer in the mid rectum are more straightforward and suitable for laparoscopic TME. There is a dilemma at the very beginning of the introduction of TaTME as to whether this technique should be performed in these patients.

It should be noted that most experts agreed that TaTME should not be offered by every colorectal unit, but rather should be centralized to high volume centers with a minimum volume of 20 cases per year\(^\text{63}\). It is also suggested that at least 20 cases per year may be required to maintain competency\(^\text{63}\). To ascend the learning curve, and reach an acceptable incidence of high-quality TME specimen and lower operative time, 45-51 cases were required\(^\text{68}\).

Recent data of the International TaTME Registry indicated that 66% of the cases were stapled anastomoses, which was quite different from Japan. Itoh, who had 135 TaTME cancer cases, the largest cases in Japan reported that almost all his cases were intersphincteric resections with hand-sewn anastomoses, suggesting that TaTME might not be needed in non-obese Asian patients with mid rectal tumors\(^\text{60}\). Given the body habitus of Japanese patients, the indications for TaTME may be limited.

The International TaTME Registry is the largest database available and may represent the real world data; however, the limitations of this registry are that the data may be underreported, particularly the adverse events data in the registry after the operation is voluntary.

Combining the robotic TME and TaTME, robotic TaTME with single site plus one port has been reported\(^\text{71}\). It has been suggested that robotic TaTME has advantages of fully wristed instruments, preventing interference from the instruments in a confined pelvic space, and the three-dimensional view, but even so, abdominal assistance is essential. Transanal NOTES using robotic TaTME has recently been reported in cadaver, which may be the ultimate endpoint of minimally invasive rectal surgery\(^\text{72}\). At present, two randomized controlled trials, COLOR III and GRECCAR, comparing TaTME with laparoscopic TME are being conducted\(^\text{73,74}\) and their outcomes are awaited.

**Conclusions**

TaTME has rapidly been evolving and has become a popular subject for colorectal surgeons. TaTME is a complex procedure, but has proved to be feasible, oncologically safe, and effective in difficult cases. Before this new technique is adopted, a proper training with Proctor/mentorship is strongly advised. Careful case selection and audit of data are mandatory.
Conflicts of Interest
There are no conflicts of interest.

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