Editorial Commentary

Is the learning curve the Achilles heel of surgical innovation? —arguments against TaTME

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Introduction

Total mesorectal excision (TME) is the standard surgical care for rectal cancer (1-3). Local recurrence rates have decreased from 45% using traditional techniques to less than 10% after TME alone, and to less than 6% after neoadjuvant chemoradiotherapy and TME (3-7). A core quality indicator of the surgical resection is the circumferential resection margin (CRM) (8-10), which is a strong predictor of local recurrence, distal recurrence and survival (11). The management of rectal cancer has evolved substantially over recent decades (12-14).

Despite improvements in the rate of TME surgery for rectal cancer, decreased local recurrence rates and increased 5-year overall survival (15-18), there remains a large variation in the quality of treatment (19). The Consortium for Optimising the Treatment of Rectal Cancer (OSTRICH) demonstrated a 17.2% positive CRM rate (2,859/16,619 patients) (20). Several histological features, operative approach, type of surgery and facility location were all independent predictors of CRM positivity (20).

Furthermore, concerns arose regarding the oncological safety with the introduction of laparoscopic TME. The COLorectal cancer Laparoscopic or Open Resection (COLOR) II trial showed improved short-term and similar long-term outcomes following laparoscopic TME compared with open TME resections (21,22). Moreover, comparable disease-free and overall survival rates between laparoscopy and open surgery for rectal cancer were demonstrated in the long-term results from the MRC CLASICC and COREAN trials (23,24). However, mid and low rectal cancers are technically more demanding via the transabdominal approach, particularly in obese male patients with bulky or distally located tumours, factors that predispose to positive CRM, incomplete TME and conversion to open surgery, highlighted by the ACOSOG Z6051, ALaCaRT and COLOR II trials (21,25,26).

Transanal Total Mesorectal Excision (TaTME) was developed to overcome the limitations of the transabdominal approach and improve the oncological and functional outcomes of patients with mid and low rectal cancer. The COLOR III trial is a multi-centre superiority international trial comparing TaTME and conventional laparoscopic TME for mid and low rectal cancers, with the primary endpoint of positive CRM (27). Nevertheless, emerging evidence suggests that TaTME may not be superior to alternative methods.

Local recurrence concerns

Recently Norway introduced a moratorium on TaTME due to concerns regarding an unexpected pattern of recurrences occurring early after TaTME (28). Between January 2015 and December 2017, 110 TaTME procedures were performed at four hospitals in Norway, with specialist training in TaTME surgery. Following a snapshot analysis, at least 10 local recurrences (9.5%) were diagnosed, with a median time to recurrence of 11 months following surgery (28). The recurrence pattern observed after TaTME surgery was also different from conventional TME surgery, characterised by rapid, multifocal growth in the pelvic cavity and sidewalls (28), in an aerosolised pattern. According to the Norwegian Colorectal Cancer Registry, during the same time period, the local recurrence rate following conventional TME surgery

was only 3.4% (26).

To date, the majority of studies on TaTME have reported short-term outcomes or focused mainly on surrogate oncological endpoints observed at the time of surgery, such as, specimen quality, distal and circumferential resection margins (29). Long-term oncological endpoints, such as overall survival, disease-free survival and local recurrence have yet to be clarified (30). One systematic review estimated local recurrence rates after TaTME at 4%, ranging from 2.8% to 8.9% in high volume versus low volume centres (31), whilst another review estimated this to be 0% to 5.9% (32). Recently, two high-volume specialist centres from the Netherlands reported the combined long-term outcomes of TaTME surgery for 159 consecutive patients between 2012 and 2016. The 5-year local recurrence rate was 4.0% (33). However, with over 1,500 patients, the long-term follow-up data from the international TaTME registry (29) is awaited, particularly to address the concerns regarding local recurrence rates.

The higher local recurrence rates and patterns of recurrence observed at certain centres, may be related to the significant learning curve that exists with TaTME (33). These elements cannot be evaluated by examining the specimen, instead could be related to the rectal transection and air flow during dissection from the perineum and therefore assessed by scrutinising the technical aspects, such as, the tightness of the purse-string (28). Despite the intention of the purse-string to isolate the tumour area, during TaTME, the rectal lumen immediately distal to the tumour is exposed to the plane of dissection, potentially allowing for the spread of cancer cells (34). Furthermore, insufficient closure of the rectum before dissection, interruption of the purse-string, perforation and/or inadequate dissection, all increase the risk of tumour spillage (33,35), and potential aerosolising of tumour cells into the pelvic cavity from the airflow (36). Due to the recent concerns expressed regarding the oncological safety of TaTME surgery, Hompes *et al.* recently proposed a modification to the current technique, a reinforcement of the purse-string. After completion of the circumferential rectotomy following the TaTME principles, a further running suture over the initial purse-string to invert the rectal mucosa and repeating a thorough second washout with a tumouricidal solution is suggested, to ensure complete occlusion of the rectal lumen and reduce the risk of tumour cell aerolisation (36).

Following the introduction of the moratorium on TaTME in Norway, a national audit was conducted focusing on the local recurrence rate as the primary outcome compared to conventional TME surgery. This study recently published showing that despite more favourable cancer stages in the TaTME group in comparison to the national cohort, the oncological outcomes were inferior, with a greater than 6-fold higher (HR 6.71) estimated local recurrence rate compared with the national conventional TME group (37). The positive CRM rate was also 12.7% (37).

The introduction of TaTME highlights some of the fundamental challenges associated with implementing new surgical techniques. There is strict regulation regarding the introduction of new pharmaceutical agents and the requirement for robust phase I to III clinical trials to document effectiveness and safety (26). However, in contrast, there is no such regulations for new surgical techniques. The Idea, Development, Exploration, Assessment and Long-term follow-up (IDEAL) framework aims to prevent surgical innovation from being implemented too early (38). Currently, no standardisation or global consensus has been reached for TaTME, and it remains in the developmental stage, thus this technique may have been adopted too early by the surgical community. Therefore, does the early adoption of TaTME expose patients to potential intra-operative complications and morbidity, whilst the long-term oncological safety of the technique has yet to be established (26)?

Learning curve

Proponents of the TaTME technique have emphasised the potential benefits, especially in the obese, those with a narrow pelvis and male patients, due to the visualisation of the distal rectum and benefits of nerve identification, but stress that the new bottom-up approach to TME dissection is associated with a significant learning curve (39). A recent systematic review demonstrated that studies assessing TaTME for rectal cancer were commonly associated with spin, with the majority of studies concluding that this technique was safe despite a lack of support from the study results (39).

Evaluation of major postoperative complications (Clavien-Dindo ≥3) demonstrated a clear learning curve for TaTME with a cut-off point of 40 patients (40). The major postoperative morbidity was 47.5% for the first 40 patients, which decreased to 17.5% for the following 40 patients operated on by the primary surgeon (40). The learning curve is clearly significant and potentially exposes patients to serious harm. The associated high rate of intra-operative complications

(21%) also during the TaTME learning curve and the lack of reported significant benefit of this technique (41), means it is difficult to justify adoption of this surgical technique currently. Proponents of TaTME for rectal cancer surgery, state that there are clear advantages to beginning the dissection at the distal side of the rectum, including a more precise assessment of the distal margin (33). Conversely, the anatomical approach is different and requires experience to identify the correct dissection planes, which the TaTME registry has highlighted the risks of bleeding and new patterns of complications including urethral injuries that lead to increased morbidity and poor functional outcomes (29,33). The registry also reported technical issues in 39.3% of the operations, highlighting the vital importance of safe implementation of the technique (42). A consensus statement was subsequently issued regarding a detailed structured training curriculum for TaTME to provide quality control whilst implementing this new surgical technique (43).

Complications and technical challenges

The implementation of the TaTME surgical technique has resulted in a new profile of surgical complications reported. These include carbon dioxide embolisms causing haemodynamic instability, which are associated with venous bleeding resulting from wrong plane surgery, high insufflation pressures and steep patient positioning, that may result in the loss of cardiac output (44). Other uncommon complications in conventional TME surgery, but have been reported more frequently in TaTME include urethral injuries. A recent study concluded that the incidence of urethral injuries during TaTME were higher than previously reported and that the morbidity associated with injuries can be severe, including permanent urinary diversion (45). The most common elicited factor for urethral injury was failure to identify the correct anterior TME plane due to tissue distortion, especially in low bulky tumours with post-radiation fibrosis compounded by a lack of familiarity with perineal anatomy (45). If difficulties are encountered identifying the correct plane, the authors advocate an open perineal approach until the correct landmarks and plane are identified and if this cannot be achieved, to convert to the conventional TME surgery (45).

Proponents of TaTME suggest this technique is superior to conventional TME surgical techniques for mid to low rectal cancers, providing a better view of the distal margin and better mobilisation in the narrow pelvis (27). It is also suggested that for mid to low rectal cancers, TaTME has other potential benefits including less morbidity as a result of better anastomotic techniques, more sphincter-preserving rectal resections, less conversions, without compromising oncological outcomes and better specimen quality (27). However, the TaTME registry most recently reported intraoperative adverse events in 30.6%, postoperative morbidity of 35.4% and an anastomotic failure rate of 15.7% (29). Due to the technical challenges and accompanying learning curve associated with TaTME, structured training pathways exist to improve the short and long-term outcomes. In the Netherlands, following completion of the training program, 12 hospitals submitted the first 10 cases for evaluation. Despite participating in a structured training program, designed to ensure adequate skills to participate in COLOR III, this study also demonstrated substantial overall postoperative morbidity of 45%, with an anastomotic leak rate of 17.3% (46).

The era of robotics

Recent technological advancements in robotic surgery overcome some of the limitations of conventional laparoscopy, providing a platform to facilitate precise dissection in confined spaces (47). Sammour *et al.* demonstrated that robotic proctectomy for rectal cancer can be performed with good oncological outcomes, including a positive CRM rate of 2.5% and local recurrence rate of 2.4% (48). A study comparing robotic versus laparoscopic TME surgery demonstrated a lower proportion of patients required conversion to a transanal approach (1.7% versus 16.7%; P=0.004) (49). The robotic surgery platform enabled complete rectal dissection in the difficult TME cases, overcoming the limitations of laparoscopic surgery that required alternative approaches to be utilised (49). Furthermore, another study compared outcomes of robotic TME for varying difficulties of pelvic anatomy based on MRI pelvimetry, which showed no difference in operative or pathological outcomes between anatomical groups, suggesting the robotic system compensates for the difficulties posed by challenging pelvic anatomy (50). Meta-analyses also confirm the benefits of robotic surgery in achieving complete TME (51), CRM negativity and lower conversion rates (52).

Despite the ROLARR trial not showing a reduction in the risk of conversion with robotic surgery, partly due to the overestimation of conversion rates in laparoscopy during sample size calculation and a potential learning curve effect among participating surgeons, subgroup analysis

demonstrated an apparent benefit of robotics in technically challenging rectal surgery, such as the obese male (53). A recent propensity score matched study between robotic and laparoscopic rectal cancer resections in obese patients showed that robotic surgery was associated with shorter length of hospital stay and reduced morbidity profile in this challenging subgroup of patients (54).

Conclusions

Despite the early promises of TaTME that was conceived to overcome the challenges in the era of conventional laparoscopy, evidence to date has not shown that TaTME has delivered on its promise and therefore, alternative approaches such as the robotic platform need further evaluation.

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