EDITORIAL

**taTME: boom or bust?**

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Since Sylla et al. [1] introduced transanal total mesorectal excision (taTME) in 2010, there has been rapid global uptake of this approach, predicated upon the postulated advantage of improved visualization of and access to the deep pelvic anatomy. This approach has been proposed for locally adipec cancers and has demonstrated the procedural safety and short- and long-term oncologic adequacy of taTME in carefully selected patients, when performed by experienced high-volume taTME surgeons [1–7].

Larsen et al. [8] initially reported a 9.5% rate of local recurrence among 110 Norwegian patients who underwent taTME across four hospitals, which is significantly higher than the 3.4% total mesorectal excision (TME) local-recurrence rate from the Norwegian Colorectal Cancer Registry (NCCR). The detailed report of all 157 taTME cases performed in Norway during 4 years reported a 7.6% local-recurrence rate at a median follow-up of 19.5 months [9]. All 12 local recurrences occurred early, at a median of 9.5 months following taTME; 8 recurrences were in patients with R0 resection and 6 were multifocal, demonstrating a worrisome pattern of multifocal growth along the pelvic cavity and sidewall, very unlike typical locoregional recurrences following conventional TME [8]. Interestingly, only 1 patient had received neoadjuvant treatment despite 8 with stage III disease and 4 patients with stage II disease among the 12 patients with recurrences. Overall, the estimated local-recurrence rate after taTME was 11.6% at 2.4 years compared to 2.4% after TME from the NCCR [9]. The authors hypothesized that this higher rate of local recurrences is likely due to the long learning curve associated with the introduction of a new complex procedure. In the Norwegian audit, three centers abandoned taTME after just five cases and the other four averaged <10 taTME cases per year. Even if only one surgeon performed taTME in each hospital, the number of taTMEs performed by each surgeon would be <1 per month [8, 9]. taTME experts have proposed that a minimum of 20 cases per year are needed as a prerequisite for the safe implementation of this complex procedure [10].

It is important to note that, relative to laparoscopic TME (laTME), taTME requires several additional technical steps, each with incremental levels of complexity. Surgeons must master endoluminal suturing skills to complete adequate purse-string closure of the rectum, and gain an in-depth understanding of the perineal and pelvic anatomy via the perineal view. The recent international report on urethral injury during taTME highlights the technical errors that can occur during the early phase of the learning curve, with 51% of 34 ureteral injuries occurring during the first eight taTME cases [11]. The Norwegian report stated that all taTME surgeons had to complete
structured training before implementing taTME, but it is not clear what the training consisted of and whether surgeons met all the prerequisites for implementing taTME safely, namely case volume, prerequisite skills, and proctoring. Proctoring is a critical element of conquering the learning curve while minimizing potential adverse patient outcomes. However, in Norway, proctoring was only utilized in one center. No mechanism for the assessment of technical competency was included. The relatively high rate of intraoperative complications reported in the Norwegian series, including seven rectal perforations, two urethral injuries, and one bladder injury, reflects the technical errors made during the earliest phase of the taTME learning curve. One would expect a similar learning curve with respect to oncologic outcomes, and it would be of great interest to know the case number along the surgeons’ learning curve who developed local recurrences.

A number of studies have shown a relationship between the taTME case volume and clinical outcomes. In an analysis of their institutional learning curve with taTME, Koedam et al. [12] determined that case volume associated with a significant reduction in the major post-operative complications from 47.5% to 17.5% and leak rate from 27.5% to 5% occurred in 40 cases. It is important to note that Koedam et al. [12] performed two or more taTME cases per month, which would be considered high-volume and likely represents the case volume most likely required in order to achieve expertise, reduce intraoperative and post-operative complications, and achieve adequate oncologic outcomes. A 2016 systematic review by Deijen et al. [13] comparing low-volume (<30 total cases) vs high-volume taTME centers (~30 total cases) demonstrated higher conversion rates (4.3% vs 2.7%), lower rates of complete TME (80.5% vs 89.7%), and higher rates of local recurrence (8.9% vs 2.8%) at low-volume centers.

Overall, achieving and maintaining a high case volume in a complex procedure such as taTME is essential to establish competency and minimize learning-curve-related adverse events. Institutions with surgeons who are still along their early learning curve should institute safeguards to mitigate potential negative outcomes such as an ongoing proctoring program with feedback on technique, more stringent patient selection excluding bulky T3b and T4 tumors with threatened circumferential resection margin (CRM), and referring cases to the highest-volume taTME surgeons at the institution and/or regional center. One of the limitations of the Norwegian study is the lack of stipulated proctoring.

Larsen et al. [8] hypothesized that the multifocal pelvic sidewall recurrences might relate to the open rectal transection and the insufflated CO2 flow during taTME. It is not clear why this type of local recurrence has not been reported elsewhere by other investigators [3, 4]. In a recent editorial on this topic, Atallah et al. [14] hypothesized that an inadequately tightened purse-string suture may contribute to spillage of live tumor cells during transanal dissection, with increased risk of tumor implantation along the pelvic sidewalls, which may account for the multifocal local recurrences reported in the Norwegian report. Another possibility is that tumor cells may be shed during transanal specimen extraction, especially when performed without a wound protector [15]. Koch et al. [16] proposed reinforcing the purse-string closure of the rectum by placement of a second purse-string suture after full-thickness circumferential incision of the rectum, and repeated washing with a tumoricidal solution to ensure airtight closure of the rectal lumen and avoid the potential tumor and fecal spillage and implantation within the resection bed. We concur that placement of a double purse string will help re-airtight closure of the rectal stump and should be performed, in addition to strict adherence to the recommended taTME procedural steps.

Structured training programs tailored to local resources have become increasingly standard in North America, Europe, and China [17–19]. Thorough comprehensive didactics on peri-rectal anatomy; video-based review of the technical steps, errors, and pitfalls during taTME dissection; case observation with live or deferred taTME surgery; and trainees with prerequisite expertise in transanal surgery and minimally invasive TME are well positioned to undergo hands-on training on cadavers. Cadaver training is essential to master endoscopic purse-string closure of the rectum and identify anatomic landmarks and the correct TME planes during difficult taTME dissection in order to avoid organ injury or incomplete TME [20]. Moreover, structured training emphasizes the importance of multidisciplinary preoperative staging and careful case selection for taTME.

In this evolving debate regarding the long-term oncologic safety of taTME for rectal cancer, it is important to critically appraise the evidence published to date on this topic. In 2019, the most recent update from the International taTME Registry reported on 2,653 patients with rectal cancer with a CRM-positive rate of 4%, distal resection margin (DRM) positive rate of 1.0%, and 91.2% of TME specimens being graded as complete/near-complete [21]. Previous data from the international registry had reported that 96.6% of TME specimens are complete or near-complete [11]. In preliminary analysis of an ongoing randomized control trial (TaLaR, NCT02966483) comparing pathological outcomes after taTME (n = 128) vs laTME (n = 133), Zeng et al. [2] reported a 0 vs 1.5% DRM-positive rate in the taTME vs laTME group respectively and a 1.5% CRM rate in both groups. A systematic review evaluating outcomes of 573 patients who underwent transanal or laparoscopic TME found a higher rate of complete or near-complete TME (95.3% vs 88.2%) and a lower rate of positive CRM (4.5% vs 10.3%) in the taTME group [22]. Preliminary long-term oncological results of taTME have also been promising. A recently published study from the Netherlands on 159 patients who underwent taTME for rectal cancer reported local-recurrence rates of 2% and 4%, disease-free survival rates of 92% and 81%, and overall survival rates of 84% and 77% at 3 and 5 years, respectively [3]. These results compare favorably to historical long-term oncologic outcomes of laparoscopic TME [23–25]. Furthermore, a recent Chinese multicenter cohort study of 211 rectal-cancer patients undergoing taTME demonstrated a laudable 98.5% rate of complete or near-complete TME with a 2.3% rate of positive CRM, 3-year disease-free survival (DFS) of 80.2%, and 3-year overall survival (OS) of 92.9% [26]. The local-recurrence rate was 6.2%, which was similar to the historical local-recurrence rates after both taTME and TME [27].

It is unlikely that this debate on the oncologic safety of taTME will quickly be solved. The early introduction of laparoscopic TME was intensely scrutinized, especially in light of the incidence of port-site metastases. Unfortunately, the preliminary results from the Australian Laparoscopic Cancer of the Rectum Randomized Clinical Trial (ALaCaRT) and the American College of Surgeons Oncology Group (ACOSOG) did not help in the adoption of laparoscopic TME. Sadly, due to well-intentioned but poorly designed statistical models, both trials failed to support the non-inferiority of laparoscopic surgery compared with open surgery with respect to preliminary oncologic outcomes [28, 29]. Thankfully, long-term results from the two trials consequently demonstrated no statistical differences in local-recurrence rates and 2-year DFS or OS between laparoscopic and open TME [24, 25]. taTME adoption required careful prerequisite skill acquisition,
participation in formal training programs with ongoing proctoring, and oversight of clinical outcomes. In addition, careful case selection through a multidisciplinary rectal-cancer program and maintenance of high per-surgeon case volume are additional essential prerequisites to help mitigate against reproducing the very disturbing Norwegian data.

In conclusion, published data support the safety and efficacy of taTME for carefully selected mid- and low-rectal cancers. The recent data from Norway highlights the critical importance of adequate taTME training, proper case selection, and proctorship with maintenance of high procedural volumes in a multidisciplinary setting to help ensure optimal outcomes. Many unanswered questions remain regarding the exact mechanisms at the basis of multifocal local recurrences that warrant further investigation. Meanwhile, several multicenter randomized control trials such as COLOR III [30] and TaLaR (NCT02966483) are well underway to confirm the long-term oncological safety of taTME.

Authors’ contributions

L.K. and P.S. conceived this study and drafted the manuscript. S.A. and M.I. revised this manuscript. S.D.W. and J.P.W. reviewed, revised, and confirmed this paper. All authors read and approved the final manuscript.

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Conflicts of interest

The authors declare that they have no conflict of interest.

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