Systematic review

Functional complaints and quality of life after transanal total mesorectal excision: a meta-analysis

J. A. G. van der Heijden1, T. Koëter1, L. J. H. Smits3, C. Sietses2, J. B. Tuynman3, A. J. G. Maaskant-Braat4, B. R. Klarenbeek1 and J. H. W. de Wilt1

Departments of Surgery, 1Radboud University Medical Centre, Nijmegen, 2Gelderse Vallei Hospital, Ede, 3Amsterdam UMC, Location VUMc, Amsterdam, and 4Maxima Medical Centre, Veldhoven, the Netherlands

Correspondence to: Dr J. A. G. van der Heijden, Department of Surgery, Radboud University Medical Centre, Nijmegen, Geert Grooteplein Zuid 10, 6525 GA, Nijmegen, the Netherlands (e-mail: joost.vanderheijden@radboudumc.nl)

Background: Total mesorectal excision (TME) gives excellent oncological results in rectal cancer treatment, but patients may experience functional problems. A novel approach to performing TME is by single-port transanal minimally invasive surgery. This systematic review evaluated the functional outcomes and quality of life after transanal and laparoscopic TME.

Methods: A comprehensive search in PubMed, the Cochrane Library, Embase and the trial registers was conducted in May 2019. PRISMA guidelines were used. Data for meta-analysis were pooled using a random-effects model.

Results: A total of 11,660 studies were identified, from which 14 studies and six conference abstracts involving 846 patients (599 transanal TME, 247 laparoscopic TME) were included. A substantial number of patients experienced functional problems consistent with low anterior resection syndrome (LARS). Meta-analysis found no significant difference in major LARS between the two approaches (risk ratio 1.13, 95% c.i. 0.94 to 1.35; $P = 0.18$). However, major heterogeneity was present in the studies together with poor reporting of functional baseline assessment.

Conclusion: No differences in function were observed between transanal and laparoscopic TME.

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Introduction

Total mesorectal excision (TME) is the standard surgical treatment for rectal cancer, with excellent long-term local recurrence-free and overall survival rates. Over time, advances in technology led to a shift from open to laparoscopic surgery owing to favourable short-term outcomes such as less pain, reduced blood loss and improved recovery time. However, quality of life (QoL) and functional outcomes were not significantly improved by the laparoscopic approach. The latest developments are the robotic and the transanal approach. The latter, called transanal TME (TaTME) has been developed to overcome surgical difficulties experienced during distal pelvic dissection, especially in men with a narrow pelvis, a low tumour and a high BMI. Long-term results of randomized studies are awaited, especially since the Norwegian moratorium on TaTME owing to an unexpectedly high local recurrence rate.

Although many studies have investigated functional bowel dysfunction after laparoscopic low anterior resection, little is known about these functional sequelae after TaTME and their impact on QoL. The most common postoperative complaints, such as incontinence, urgency and frequent bowel movement, are described as low anterior resection syndrome (LARS). This syndrome has a severe adverse effect on QoL. Known risk factors for the development of LARS are a low level of anastomosis, poor preoperative function and neoadjuvant chemoradiotherapy. With the TaTME technique, surgeons might choose a lower anastomosis for technical rather than oncological reasons, and urethral injuries are more likely. Concerns regarding functional outcomes after TaTME have been expressed. This meta-analysis was conducted to compare functional outcomes and QoL after TaTME and laparoscopic TME (LapTME).

Methods

This review was conducted in accordance with PRISMA guidelines, with an a priori developed review protocol (PROSPERO; CRD42019126975). A comprehensive search in PubMed, the Cochrane Library, Embase and the trial registers was conducted in May 2019. PRISMA guidelines were used. Data for meta-analysis were pooled using a random-effects model.

Results: A total of 11,660 studies were identified, from which 14 studies and six conference abstracts involving 846 patients (599 transanal TME, 247 laparoscopic TME) were included. A substantial number of patients experienced functional problems consistent with low anterior resection syndrome (LARS). Meta-analysis found no significant difference in major LARS between the two approaches (risk ratio 1.13, 95% c.i. 0.94 to 1.35; $P = 0.18$). However, major heterogeneity was present in the studies together with poor reporting of functional baseline assessment.

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search was undertaken in PubMed, Embase, the Cochrane database and the trial registers. The full search strategy is available in Appendix S1 (supporting information).

Two reviewers performed the selection process and reviewed all included studies. Discrepancies were resolved through discussion. The following inclusion criteria were applied: patients with rectal cancer who underwent TaTME and received any assessment of functional outcome or QoL. If a study also included patients who underwent LapTME, this group was used as a comparator for the TaTME group. All study designs with a population of ten or more patients were included. No filters for language or date were used. Studies were excluded if they evidently contained the same data, or were letters to the editor or expert opinions. If reported, the time from ileostomy closure to the evaluation of functional outcome was included. Quality assessment was performed by using the Newcastle–Ottawa Scale for observational studies24 and the Cochrane quality assessment tool for randomized trials25.

Analysis

Basic descriptive statistics were used to summarize patient characteristics and outcome data. A meta-analysis was performed if sufficient studies and adequate data were available. The Mantel–Haenszel method was used for dichotomous data. A random-effects model was used and checked using a fixed-effect model. If the requested data were not available, mean(s.d.) values were calculated for overall analysis, if possible26. A meta-analysis of P values was performed in comparative studies of QoL data evaluated by the European Organization for Research and Treatment of Cancer (EORTC) questionnaires27. The Cochrane handbook 6 was used as a guideline for this analysis28. No funnel plots were presented, owing to the limited number of studies available for meta-analysis28. Analyses were performed using Review Manager version 5.3.5 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark), and Microsoft Excel® (Microsoft, Redmond, Washington, USA) for the meta-analysis that combined P values.

Results

Study selection

The search was performed in May 2019 and returned 11 660 articles after removal of duplicates from which

TaTME, transanal total mesorectal excision; QoL, quality of life.
left 8572 studies. After exclusion of irrelevant articles, 90 potentially relevant studies and 39 potentially relevant trials were assessed further. Eventually 14 studies and six conference abstracts were included (Fig. 1)^9,29—47. Studies were excluded for the following reasons: did not investigate TaTME (11), did not provide functional/QoL data (34), included fewer than ten patients (2) or other reasons (62).

### Study characteristics and quality control

Six retrospective (3 cross-sectional, 2 cohort, 1 case–control) and 14 prospective (11 cohort, 2 cross-sectional, 1 RCT) studies were included (*Table S1, supporting information*). The studies included 599 patients who underwent TaTME. A total of 247 patients who underwent LapTME were identified as a control group to compare with patients who underwent TaTME. Duration of follow-up after surgery varied from 3 to 75 months. Seven studies included a baseline measurement in the study design. In the majority of studies, the tumour was located in the lower and middle rectum (tumour height 3.7–7.1 cm). Mean temporary ileostomy rates were 92.2 per cent in the TaTME group compared with 88.1 per cent in the LapTME group. Some 61.5 per cent of the

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**Table 1 Bowel dysfunction as measured by low anterior resection score**

| Reference                  | No. of patients | Duration of follow-up (months) | Total LARS score | No LARS | Minor LARS | Major LARS |
|----------------------------|-----------------|--------------------------------|------------------|---------|------------|------------|
| Bjoern et al.^29           | 49 TaTME        | 22–7 (10–3)^†                  | 26–2 (10–3)^†    | 17 (33) | 15 (31)    | 17 (35)    |
| 36 LapTME                  | 75–1 (17)^†     | 20–6 (14–5)^†                  | 16 (44)          |         | 6 (22)     | 12 (33)    |
| Veitcamp-Heibach et al.^30 | 27 TaTME        | 20–0 (6–6–44–4)^†              | 27–7 (13–3)^†    | 7 (26)  | 4 (15)     | 16 (59)    |
| 27 LapTME                  | 59–5 (39–7–82)^†| 24–0 (10–5)^†                  | 11 (41)          |         | 8 (30)     | 8 (33)     |
| Turrado-Rodriguez et al.^31| 80 TaTME        | 37–6; n.r.                     | 31 (39)          |         | 49 (61)    |           |
| Rubinkiewicz et al. ^32    | 25 TaTME        | Baseline                       | 6 (0–12)^‡       | 4 (16)  | 21 (84)    | n.r.       |
| Reali et al.^33            | 29 TaTME        | Baseline                       | 11 (38)          |         | 5 (17)     |           |
| Mora et al.^34             | 16 TaTME        | 6 (0–12)^‡                     | 3 (19)           |         | 10 (63)    |           |
| Koedam et al.^37           | 30 TaTME        | Baseline                       | 16 (53)          |         | 10 (33)    | 13 (41)    |
| Hanke et al. ^38           | 31 TaTME        | 3 (0–12)^‡                     | 0 (0)            |         | 9 (30)     | n.r.       |
| Pontallier et al. ^40      | 38 TaTME        | >12                            | 36 (12–42)^†     | n.r.    | 31 (82)    | n.r.       |
| 34 LapTME                  | 37 (12–42)^†    | n.r.                           | 26 (76)          |         |           | n.r.       |
| Kneist et al. ^41          | 10 TaTME        | Baseline                       | 9 (90)           |         | 1 (10)     | 0 (0)      |
| Keller et al. ^44          | 61 TaTME        | 28 (9–38)^†                    | 3 (30)           |         | 4 (40)     | 1 (10)     |
| Leão et al. ^46            | 20 TaTME        | 23–0 (9–7)^†                   | 22 (40)          |         | 20 (36)    | 13 (24)    |
| Dou et al. ^47             | 54 TaTME        | 25–6 (8–0)^†                   | 25 (63)          |         | 26 (48)    | n.r.       |
| 53 LapTME                  | 17–2 (12–1–30–4)^†| n.r.                          | 22 (42)          |         |           | n.r.       |

Values in parentheses are percentages unless indicated otherwise; values are *mean(s.d.), †median (range), ‡median, §median (i.q.r.), ¶mean (95 per cent c.i.) and #mean. LARS, low anterior resection syndrome; TaTME, transanal total mesorectal excision; LapTME, laparoscopic total mesorectal excision; n.r., not reported. P values are shown for TaTME versus LapTME.

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A Mantel–Haenszel random-effects model was used for meta-analysis. Risk ratios are shown with 95 per cent confidence intervals. The longest follow-up data for each study were used. If a study favours laparoscopic total mesorectal excision (LapTME), fewer patients experienced major low anterior resection syndrome (LARS) in this group. TaTME, transanal total mesorectal excision.

**Table 2** Continence status as measured by Wexner score

| Reference          | No. of patients | Duration of follow-up (months) | Wexner score* | Wexner score > 10 (major incontinence) |
|--------------------|-----------------|-------------------------------|---------------|----------------------------------------|
| Turrado-Rodriguez et al. | 80 TaTME | 37-6 (17-7) | 10 (5) | n.r. |
| Rubinkiewicz et al.  | 25 TaTME | Baseline | 0 (0-2) | n.r. |
| Hanke et al. | 31 TaTME | 3 | 9 | n.r. |
|                   | 17 | 6 | 6 | n.r. |
|                   | 13 | 9 | 4 | n.r. |
|                   | 10 | 12 | 2 | n.r. |
|                   | 7 | 18 | 4 | n.r. |
|                   | 4 | 24 | 0 | n.r. |
| Elmore et al.     | 12 TaTME | Baseline | 3 (1-8) | n.r. |
| Pontallier et al. | 38 TaTME | > 12 | 9 (2-20) | 16 (42) |
|                   | 34 LapTME | 10 (3-20) | (P = 0.932) | 14 (41) |
| (P = 0.936)       |                 |                 |               |               |
| Kneist et al.     | 10 TaTME | Baseline | 1 (0-7) | 0 (0) |
|                   | 3 | 9 (1-20) | 4 (40) | 3 (50) |
|                   | 6 | 7 (0-15) | 7 (13) | > 7 points |
| Tuech et al.      | 52 TEAP | > 12 | 4 (3-12) | 7 (13) |
| De’Angelis et al. | 32 TaTME | 3 | 9 (3-15) | 10 (32) |
|                   | 32 LapTME | 3 | 10-5 (4-19) | 16 (50) |
| Rouanet et al.    | 30 TEAP | 12 | 11 | n.r. |
| Keller et al.     | 61 TaTME | Baseline | 10-3 | n.r. |
|                   | 12 | n.r. | n.r. | n.r. |
| Leão et al.       | 20 TaTME | 1 | 10-3 | n.r. |
|                   | 20 | 3 | 7-9 | n.r. |
|                   | 20 | 6 | 4-6 | n.r. |
|                   | 8 | 12 | 2-8 | n.r. |

Values in parentheses are percentages unless indicated otherwise; *values are median (range), except †mean(s.d.). TaTME, transanal total mesorectal excision; n.r., not reported; LapTME, laparoscopic total mesorectal excision; TEAP, transanal endoscopic proctectomy. P values are shown for TaTME versus LapTME.
patients received neoadjuvant treatment before TaTME compared with 70.8% per cent before LapTME. The height of anastomosis was not reported systematically, but was significantly lower after TaTME in the study of Mosquera and colleagues\(^45\). Other comparative studies showed no relevant differences in tumour height or site (mid, low, high).

Four of the included studies were of high quality based on the Newcastle–Ottawa Scale, scoring at least 7 points (Table S2, supporting information). Overall quality was acceptable, except that baseline measurements were not frequently reported and relatively few studies presented a comparator LapTME group. The only RCT was of good quality, except for an unclear risk of selective reporting.

**Bowel dysfunction**

Thirteen studies assessed bowel dysfunction by measuring the LARS score (Table 1), and five compared LARS scores after TaTME versus LapTME. Meta-analysis showed no significant differences in the incidence of major LARS between the procedures (Fig. 2). Sensitivity analyses excluding studies with follow-up of less than 12 months (risk ratio (RR) 1.15, 95 per cent c.i. 0.93 to 1.43) and studies with significant differences in baseline characteristics between TaTME and LapTME groups (RR 1.08, 0.89 to 1.32) showed no differences in bowel dysfunction outcomes between procedures.

Bjoern and colleagues\(^29\) reported no significant difference in LARS scores after TaTME compared with LapTME (P = 0.054) (Table 1). For the subcategories clustering of stools (P = 0.017) and faecal urgency (P = 0.032), a significant disadvantage for TaTME was found. Koedam and co-workers\(^37\) reported significantly worse LARS scores 1 month after TaTME surgery, but did not note a significant difference at 6 months compared with baseline scores. A significant increase in LARS scores was demonstrated after surgery in all studies\(^33\). However, these scores returned to baseline values in the majority of studies\(^33,44,46\).

**Urogenital dysfunction**

The International Index of Erectile Function (IIEF/ IIEF-5), International Prostate Symptom Score (IPPS) and Female Sexual Function Index (FSFI) were used to evaluate urogenital dysfunction after TaTME (Table 3).

**Urogenital function in men**

Foo and colleagues\(^35\) noted that erectile function in 23 men worsened significantly after surgery (P = 0.002) but returned to baseline after 6 months (P = 0.142). Pontallier and co-workers\(^40\) did not find any significant differences in IIEF scores (P = 0.119) or category of erectile dysfunction (IIEF 21 or less; P = 0.108). Regarding urological function, Foo et al.\(^35\) showed no significant differences in scores measured at baseline, and 3 and 6 months after surgery. In studies that compared TaTME with LapTME\(^29,30,40\), there were no significant difference in IPPS scores between procedures (Table 3). Bjoern and co-workers\(^29\) reported a significant effect on the IPPS QoL score in favour of TaTME (P = 0.01).

**Urogenital function in women**

Pontallier and colleagues\(^40\) reported sexual dysfunction in two of five women after TaTME and in two of three in the LapTME group. Turrado-Rodriguez and co-workers\(^31\) reported sexual dysfunction in 17 of 26 women after TaTME and concluded that these outcomes were similar to those of LapTME.

**Quality-of-life assessment**

Four different QoL questionnaires were used, namely the EuroQol Five Dimensions (EQ-5D™; EuroQol Group, Rotterdam, the Netherlands), EORTC QLQ-C30, QLQ-CR29 and Faecal Incontinence Quality of Life scale (FIQL) questionnaire. The QLQ-CR38 is also frequently used for colorectal cancer, but not in the studies included in the present review. EQ-5D™ data are known to correlate weakly with changes in defaecation pattern\(^48\), and are shown in Table S3 (supporting information).

**Faecal Incontinence Quality of Life scale**

Only one study\(^46\) included the FIQL, and reported baseline scores of 4.0 (lifestyle, coping/behaviour, embarrassment) and 4.4 (depression/self-perception). A decrease in...
QoL scores was seen 1 and 3 months after surgery (lifestyle 2.1–2.4, coping 2.5–3.5, depression 2.2–2.5, embarrassment 2.0–3.2), but scores returned to baseline within 1 year after TaTME (lifestyle 3.8, other scores 3.9).

**EORTC QLQ-C30**

Two studies presented QoL scores over time (Table S4, supporting information). Keller and colleagues\(^\text{44}\) reported that emotional function increased significantly after 1 year compared with preoperative measurements (\(P \leq 0.01\)). Koedam and co-workers\(^\text{37}\) described a significant decrease in QoL (\(P = 0.012\), physical functioning (\(P = 0.001\), role functioning (\(P = 0.001\)), fatigue (\(P = 0.002\)) and general pain (\(P = 0.001\)). After 6 months, these effects disappeared, except for social functioning (\(P = 0.013\)) and anal pain (\(P = 0.013\)), which remained significantly worse than at baseline.

Three studies\(^\text{29,30,34}\) compared TaTME with LapTME. Veltcamp Helbach and colleagues\(^\text{10}\) reported scores for role functioning (89.5 \textit{versus} 80.2; \(P = 0.042\)), fatigue (12 \textit{versus} 26.5; \(P = 0.021\)) and faecal incontinence (2.4 \textit{versus} 14.8; \(P = 0.032\)) in favour of LapTME. A discrepancy between studies was found for the domain emotional functioning; scores favouring LapTME were reported by...
Bjoern et al.29 (83.51 versus 87.07; P = 0.041), whereas Mora and colleagues34 described better scores for TaTME (89.58 versus 77.38; P = 0.031). Functional scores for diarrhoea were in favour of LapTME in the study of Bjoern and co-workers29 (17.69 versus 4.62; P = 0.009). In a meta-analysis combining significance levels, no statistically significant differences were found between QoL subdomains for the comparative studies (Table S4, supporting information).

EORTC QLQ-CR29
Buttock pain (P = 0.01) and faecal incontinence (P = 0.03) were significantly worse in the TaTME group29,30. Scores on all other scales were comparable, including flatulence and sexual function. Mora et al.34 described more abdominal pain and a bloated feeling in the LapTME group. A meta-analysis combining significance levels showed no significant differences between the QoL subdomains for the comparative studies (Table S4, supporting information).

Discussion
The present review investigated the impact of TaTME on functional outcomes and QoL. A significant proportion of patients who underwent TaTME experienced impaired postoperative bowel function. These complaints appeared to be present equally in patients treated by transanal and laparoscopic approaches.

A potential advantage of TaTME is that it allows construction of a (low) anastomosis in patients in whom abdominoperineal resection would previously have been necessary32. However, since the introduction of TaTME, concerns have been raised about postoperative function and QoL owing to factors such as the low anastomosis, urethral injuries, insertion of the transanal platform and anal stretch21,49. Anal stretch and dilatation carries a potential risk of damaging the sphincter complex during transanal surgery. Previous studies of transanal endoscopic microsurgery (TEM) showed that controlled anal dilatation caused significant decreases in resting and voluntary contraction pressures, but had no influence on Wexner scores indicating clinical incontinence50, or long-term QoL after TEM51.

To the extent that the included studies allow, given their follow-up and quality, TaTME appears to be similar to LapTME in terms of functional outcomes. Potential risk factors for functional outcomes after TaTME were not investigated in this review. In a meta-analysis regarding major LARS, no significant differences were found between LapTME and TaTME (RR 1·13, 95 per cent c.i. 0·94 to 1·35). In several non-comparative studies that analysed TaTME only, variations in outcomes were found that could be explained by patient characteristics. In the study of Bjoern and colleagues29, scores for the subcategories clustering of stools and faecal urgency reached statistical significance not in favour of TaTME, but it is important to note that this study failed to report several important patient characteristics (such as preoperative function) and showed a significant difference in the timing of questionnaires. Although LARS scores were impaired after TaTME, only a few patients were reported who underwent complete disconnection of the anastomosis and construction of colostomy owing to faecal incontinence52.

Male erectile function worsened after surgery but returned to baseline within 6 months51. No differences in sexual function for women31 or urological function for men29,30,40 were described between the two approaches.

Discrepancies in results were found between studies that used the EORTC questionnaires to measure QoL. Emotional functioning scores favoured LapTME in the study by Bjoern and co-workers29 but were reported to favour TaTME by Mora et al.34. A difference in follow-up was suggested as an explanatory factor because median follow-up was 22·7 months for TaTME but 75·1 months for LapTME in the Bjoern study. The duration of follow-up was also suggested to explain the differences in individual domains described by Veltcamp Helbach et al.30 (role function, fatigue and faecal incontinence in favour of LapTME). Overall, QoL and global health status were comparable between the TaTME and LapTME groups. In terms of buttock pain29 and faecal incontinence10, QoL was worse after TaTME. It is remarkable that these QoL deteriorations were not detected by the functional assessment tools used in these studies.

Overall, reporting of the included studies was complete, except for the conference abstracts that were obviously restricted in reporting, and some did not report all QoL domains34. A wide variety of adequate and valid questionnaires were used to assess QoL and functional outcomes52,53. The overall quality of evidence was moderate, owing to considerable heterogeneity, lack of baseline measurements and relatively small sample sizes. The heterogeneity may have been the result of wide selection criteria, but these were specifically chosen to allow review of all available functional TaTME data. Additional treatment, preoperative function, height of the tumour and anastomosis, and differences in follow-up times were important factors contributing to heterogeneity and the interpretation of functional outcomes29. Height of anastomosis was not reported systematically, but was significantly lower among patients who underwent TaTME in the study of Mosquera and colleagues35. In other

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comparative studies, no relevant differences in tumour height (in centimetres) and site (mid, low, high) were found. Six of eight studies properly described the rate of neoadjuvant therapy, and generally patients in the TaTME group underwent neoadjuvant therapy less frequently, yet this difference was not statistically significant.

The main limitation of this study is the lack of large RCTs. The majority of the studies were heterogeneous comparative studies and only seven of 20 reported preoperative baseline measurements. In addition, the surgeon’s learning curve was reported poorly. These limitations make it difficult to reach firm conclusions. However, it is important to draw attention to the oncological concerns surrounding TaTME: an unexpected pattern of recurrences early after TaTME resulted in a moratorium in Norway. Several studies are currently investigating different aspects of transanal methods of TME surgery. The COLOR III trial is comparing TaTME with LapTME in a large cohort that should provide decisive data about the safety of TaTME.

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Supporting information
Additional supporting information can be found online in the Supporting Information section at the end of the article.