Three-Year Nationwide Experience with Transanal Total Mesorectal Excision for Rectal Cancer in the Netherlands: A Propensity Score-Matched Comparison with Conventional Laparoscopic Total Mesorectal Excision

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BACKGROUND: Transanal total mesorectal excision (TaTME) is a relatively new and demanding technique for rectal cancer treatment. Results from national datasets are absent and comparative data with laparoscopic TME (lapTME) are scarce. Therefore, this study aimed to evaluate the initial TaTME experience in the Netherlands, by comparing outcomes with conventional lapTME.

STUDY DESIGN: Patients with rectal cancer who underwent curative TaTME or lapTME were selected from the nationwide and mandatory Dutch ColoRectal Audit (DCRA), between January 2015 and December 2017. Primary outcome was circumferential resection margin (CRM) involvement. Secondary outcomes included operative details and short-term (<30 days) clinical course. Propensity score matching was performed for 7 factors.

RESULTS: There were 3,777 patients included for analysis (TaTME, n = 416, lapTME, n = 3361). Transanal TME was performed in 38 hospitals and lapTME in 90 hospitals. Before matching, the patient category within the TaTME group was technically more challenging in terms of tumor height and preoperative threatened margins. After 1:1 matching, 396 patients were included in each group, with comparable baseline characteristics. Circumferential resection margin involvement was 4.3% after TaTME and 4.0% after lapTME ($p = 1.000$). Conversion rate was significantly lower in TaTME (1.5% vs 8.6%, $p < 0.001$). Anastomotic leak rate was not significantly different (16.5% vs 12.2%, $p = 0.116$). Other postoperative outcomes were also comparable between the groups. Significant independent risk factors for CRM involvement in TaTME were preoperative threatened margin on MRI (odds ratio [OR] 5.48, 95% CI 1.33 to 22.54) and conversion (OR 30.12, 95% CI 3.70 to 245.20).

CONCLUSIONS: This first nationwide study shows early experience with adoption of TaTME in the Netherlands. Considering that current data represent initial TaTME experience, acceptable short-term outcomes were demonstrated when compared with the well-established lapTME. (J Am Coll Surg 2019;228:235−244. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Drs Detering and Roodbeen contributed equally to this work.

Members of the Dutch ColoRectal Cancer Audit Group who co-authored this article are listed in the Appendix.

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Data-availability: the data, analytic methods, and study materials of this study are accessible from the Dutch ColoRectal Audit (DCRA) but are not publicly available. The data are made accessible to other authors upon reasonable request and with permission of the Dutch ColoRectal Audit.

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Abbreviations and Acronyms

APR	= abdominoperineal resection
ARJ	= anorectal junction
CRM	= circumferential resection margin
DCRA	= Dutch Colorectal Audit
lapTME	= laparoscopic total mesorectal excision
OR	= odds ratio
TaTME	= transanal total mesorectal excision
TME	= total mesorectal excision

Since its introduction in the late 1980s, total mesorectal excision (TME) has remained the key principle in the treatment of patients with rectal cancer.[1] The quality of the TME specimen is an important prognostic factor for oncologic outcome.[2] Achieving a high quality TME dissection might be technically demanding, especially for low, bulky tumors in a narrow, irradiated pelvis with limited view. This is true for both open and conventional laparoscopic resection, due to fixed trocar positions and restricted range of motion within the bony pelvis.[3] Transanal total mesorectal excision (TaTME) is perceived as a new technique that has the potential to overcome the difficulties faced in conventional laparoscopic total mesorectal excision (lapTME).[4] The "bottom-up" approach increases visibility and access to the dissection planes deep down in the pelvis. This approach may improve quality of the resected specimen and decrease positive resection margins, potentially resulting in better oncologic outcomes.

Laparoscopic TME is the gold standard in the Netherlands to treat patients with rectal cancer. However, after early introduction of TaTME in the Netherlands in 2012,[5] the procedure was gradually adopted by a few high-volume expert centers. Over the last 2 years, there has been a steady increase in hospitals performing the procedure. Of the 44 Dutch hospitals that have adopted TaTME into their practice, only 15 hospitals completed a structured training program with courses and additional proctoring.[6] Since 2015, this combined transabdominal transanal approach is registered on the mandatory Dutch Colorectal Audit (DCRA). The first published international cohort studies[7,8] and small matched comparative studies[9-14] reported promising results for TaTME in rectal cancer, including decreased involved resection margins, lower conversion rates, and morbidity comparable to that with lapTME. It has also been shown that TaTME has a substantial learning curve.[8]

However, results from national datasets and large comparative studies with lapTME are absent. The aim of this nationwide study was to evaluate the initial experience of TaTME in the Netherlands, by comparing differences in short-term oncologic and surgical outcomes with the well-established lapTME in patients with rectal cancer, by analyzing DCRA-data from 2015 to 2017.

METHODS

Data were derived from the Dutch ColoRectal Audit (DCRA), an obligatory nationwide registry in which information on patient, tumor, intraoperative details, and short-term outcomes (<30 days) of all patients with primary colorectal cancer undergoing resection is collected. Data from centers are regularly audited by an independent monitoring group. On a yearly basis, the number of patients surgically treated for colorectal cancer are cross-checked with the Dutch National Cancer Database (NCR) rates, showing that the DCRA has a close to 100% inclusion rate. Detailed information of this colorectal cancer-specific audit regarding the methodology and quality of data has been published previously.[15]

Patient selection

All patients who underwent TaTME or lapTME for primary rectal cancer and were registered in the DCRA between January 1, 2015 and December 31, 2017 were selected for analysis. Start date of inclusion was chosen based on the time when the TaTME approach was added to the DCRA dataset. If a combined endoscopic transanal and laparoscopic approach was registered, this was considered TaTME. Laparoscopic TME included procedures performed by only a transabdominal laparoscopic approach. A patient was eligible for analysis when information on the location of the tumor, date of surgery, and status of the patient was known (30-day/in-hospital mortality). Exclusion criteria were tumors >10 cm from the anorectal junction (ARJ), previous local excision, and an emergency setting. Abdominoperineal resections (APRs) were excluded because these procedures form another entity of rectal cancer surgery. No ethical approval or informed consent was required under the Dutch Law for this study.

Data extraction and outcome parameters

Patient and tumor characteristics, treatment characteristics, and short-term outcomes within 30 days after resection or in-hospital events were extracted from the DCRA. The primary outcome was circumferential resection margin (CRM) involvement, defined as the presence of tumor or malignant lymph node ≤1 mm from the CRM. Secondary endpoints included proportion of primary anastomosis, diverting stoma, laparoscopic conversion, intraoperative complications, and short-term (<30 days) postoperative outcomes (overall complications, anastomotic leakages, length of postoperative hospital stay, complicated course, readmission, and mortality). Anastomotic leakage was defined as anastomotic dehiscence or intra-abdominal abscess adjacent to the anastomotic site, requiring radiologic or surgical reintervention. Complicated course was defined as a postoperative complication resulting in a hospital stay >14 days and/or reintervention and/or postoperative mortality. Preoperative threatened margin on MRI was defined as the presence of tumor or malignant lymph nodes ≤1 mm from the mesorectal fascia. Missing data did not exceed 15% for the variables presented.

Statistical analysis

Categorical variables were defined as absolute numbers of cases and percentages, excluding missing values, and continuous data were shown as medians with interquartile range (IQR). For intergroup variation, the chi-square test was used; the Mann-Whitney U test was used for continuous variables. By uni- and multivariable logistic regression analysis, independent risk factors for CRM involvement were identified. Factors with a value of $p < 0.10$ in univariable analysis were entered in multivariable logistic regression analysis. Factors showing a value of $p < 0.05$ were considered significant, and therefore predisposing for CRM involvement. Odds ratios (OR) and 95% confidence intervals (CI) were used to present the results in uni- and multivariable logistic regression analysis. In an attempt to reduce bias of confounding factors in this observational study, the 2 groups were matched for 7 relevant and available variables using propensity scores with a tolerance of 0.01, on a 1-to-1 basis. Independent variables included in the model were sex, BMI (<30 or >30 kg/m^2), tumor height from ARJ (0 to 3 cm, 3 to 6 cm, or 6 to 10 cm), clinical TNM stage (1 to 2 or 3 to 4), preoperative threatened margin on MRI, neoadjuvant therapy, and year of operation. The matching was performed using propensity scores derived from a logistic regression model; the dependent variable was the operative approach (TaTME or lapTME). For categorical variables, the McNemar test was used; for continuous variables, the paired *t*-test. Statistical analyses were performed in SPSS version 24.0 Statistics for Windows (IBM Corp).

RESULTS

Between 2015 and 2017, 562 TaTME (44 hospitals) and 12,152 lapTME procedures were performed and registered in the DCRA in the Netherlands (eFig. 1). After exclusion of tumors more than 10 cm from the ARJ, previous local excision, emergency procedures, and APR procedures, 416 TaTME and 3,361 lapTME procedures were eligible for analysis. Figure 1 shows the hospital distribution of TaTME and lapTME procedures for patients with rectal cancer operated on between 2015 and 2017. Transanal TME was done in 38 hospitals, of which 18 (47.4%) hospitals performed 0 to 5 TaTME cases, 8 (21.1%) hospitals performed 6 to 10 cases, 6 (15.8%) hospitals performed 11 to 20 cases, and another 6 (15.8%) hospitals performed >20 cases. Laparoscopic TME was performed in 90 hospitals, 64 (71.1%) of which performed >20 cases.

Baseline patient and tumor characteristics of the cohort before and after matching are demonstrated in Table 1. Relatively more males and younger patients were represented in the TaTME group. Less preoperative therapy was given in patients who underwent TaTME (36.3% vs 41.8%, $p < 0.001$). Preoperative threatened margin on MRI was higher in the TaTME group (31.8% vs 23.9%, $p = 0.004$), and the proportion of low tumors (0 to 3 cm from ARJ) was significantly higher in the TaTME group (26.2% vs 9.5%, $p < 0.001$).

After propensity matching for 7 factors (sex, BMI, tumor height, cTNM-stage, preoperative threatened margin on MRI, neoadjuvant therapy, and operation year) 396 patients in each group were analyzed. No statistically significant differences were observed with regard to baseline characteristics between both groups.

Circumferential resection margin involvement

In the unmatched cohorts, CRM involvement was 4.4% and 3.0% after TaTME and lapTME, respectively ($p = 0.132$). After matching, CRM involvement rate was similar: 4.3% after TaTME and 4.0% after lapTME ($p = 1.000$) (Table 2).

Table 3 shows a multivariable analysis to identify independent risk factors for CRM involvement in the unmatched groups, separately for TaTME and lapTME. For TaTME, preoperative threatened margin on MRI and conversion were identified as independent risk factors for CRM involvement (OR 5.48 [95% CI1.33 to 22.54] and OR 30.12 [95% CI 3.70 to 245.20], respectively). For lapTME, 4 independent factors predisposing for CRM involvement were found: preoperative threatened margin on MRI (OR 1.99 [95% CI 1.18 to 3]), multivisceral resection (OR 4.11 [95% CI 1.77 to 9.55]), (y) pT-stage (OR 4.47 [95% CI 1.95 to 10.24]), and (y) pN-stage (OR 4.84 [95% CI 3.03 to 7.75]).

Secondary endpoints

Table 2 shows the short-term outcomes of the unmatched and matched groups. Before matching, a primary anastomosis was more often created in the TaTME group (80.8% vs 76.7%), and significantly less often diverted (51.1% vs 42.5%; $p = 0.035$). Conversion rate of TaTME was 1.4%, which was significantly lower than

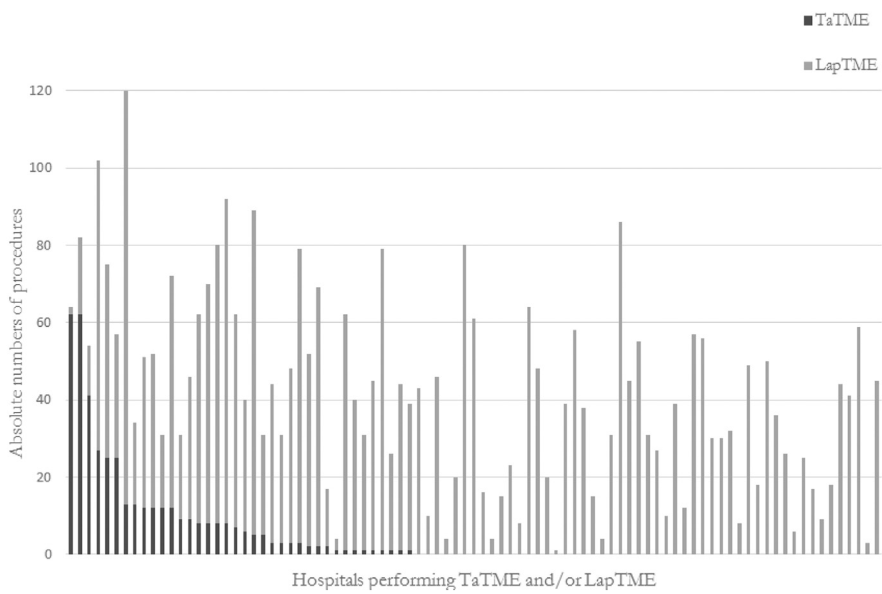

Figure 1. Transanal total mesorectal excision (TaTME) and laparoscopic total mesorectal excision (LapTME) performing hospitals in the Netherlands, 2015 to 2017.

8.7% of lapTME ($p < 0.001$). Other intraoperative complications were rare, and only 1 patient in each group had a ureter or urethral injury. Anastomotic leakage occurred more often in TaTME; 16.0% vs 11.4% ($p = 0.013$). The postoperative complication rate was higher (42.3% vs 36.1%; $p = 0.042$) and postoperative hospital stay was 1 day longer in the TaTME group (median 7 vs 6 days, $p < 0.001$).

After matching, proportions of primary anastomosis (80.1% in TaTME vs 74.1% in lapTME) and proportions of defunctioning in case of an anastomosis (50.4% vs 45.2%) were no longer significantly different ($p = 0.351$). Conversion rate remained significantly lower in TaTME; 1.5% vs 8.6% ($p < 0.001$). Intraoperative complications (excluding conversion) occurred in similar percentages of 3.8% and 2.3% ($p = 0.307$), respectively. Postoperative endpoints within 30 days did not significantly differ between the matched cohorts. If comparing TaTME with lapTME, anastomotic leak rates were 16.5% and 12.2% ($p = 0.116$), overall complication rates were 42.4% and 36.9% ($p = 0.135$), median length of stays were 6.5 and 6 days ($p = 0.280$), and readmission rates were 17.2% and 18.7% ($p = 0.640$), respectively. One patient in the TaTME group and 3 patients in the lapTME group died within 30 days, of unknown causes.

DISCUSSION

This nationwide study shows the short-term oncologic and clinical outcomes of the initial experience with TaTME in the Netherlands. It is unique in describing outcomes of TaTME on a national level from an obligatory audit with high quality data. To our knowledge, this study is the largest comparative cohort study on TaTME vs lapTME published to date. Comparability of surgical techniques was increased by propensity matching for 7 available and relevant factors. Matched comparison revealed no difference in CRM involvement between TaTME and lapTME. Conversion rate was significantly lower in TaTME. No significant differences in postoperative outcomes were observed between the matched groups. The results found in this study demonstrate the outcome of rapid and effective implementation of TaTME in the Netherlands.

The TaTME group consisted of significantly more males, more threatened resection margins on baseline MRI, and a larger proportion of lower tumors (26.2% vs 9.5%). This indicates a patient selection for TaTME with more difficult cases, and the results before matching must be interpreted in this view. Although potential risk factors for poor oncologic outcomes such as extramural vascular invasion (EMVI) and anterior location[16] were not available in the DCRA dataset, 7 other potential confounding factors for CRM positivity were used for propensity score matching to increase comparability. After matching, a similar proportion of CRM involvement was found. This is remarkable, considering that TaTME was only introduced recently and surgeons are likely to be still in their learning curve, while lapTME has been a well-established procedure for more than a decade. The positive

Table 1. Patient- and Tumor Characteristics for Transanal Total Mesorectal Excision and Laparoscopic Total Mesorectal Excision, Before and After Matching

Characteristic	Before matching TaTME	Before matching lapTME	p Value	After matching TaTME	After matching lapTME	p Value
Patients, n*	416	3361		396	396	
Sex						
Male, n (%)	301 (72.4)	2,143 (63.8)	0.001	288 (72.7)	281 (71.0)	0.349
Female, n (%)	115 (27.6)	1,216 (36.2)		108 (27.3)	115 (29.0)	
Missing, n		2				
Age						
<75 y, n (%)	343 (82.5)	2,547 (75.8)	0.003	324 (81.8)	304 (76.8)	0.090
≥75 y, n (%)	73 (17.5)	811 (24.2)		72 (18.2)	92 (23.2)	
Missing, n		3				
ASA, n (%)						
I–II	347 (83.4)	2,837 (84.4)	0.598	330 (83.8)	331 (83.6)	1.000
>III	69 (16.6)	524 (15.6)		66 (16.7)	65 (16.4)	
Charlson Score, n (%)						
0	233 (56.0)	1,933 (57.5)	0.125	219 (55.3)	227 (57.3)	0.275
1	76 (18.3)	701 (20.9)		75 (18.9)	85 (21.5)	
2+	107 (25.7)	727 (21.6)		102 (25.8)	84 (21.2)	
BMI						
≤30 kg/m^2, n (%)	337 (81.4)	2,727 (82.8)	0.475	324 (81.8)	327 (82.6)	0.780
>30 kg/m^2, n (%)	77 (18.6)	566 (17.2)		72 (18.2)	69 (17.4)	
Missing, n	2	68				
History of abdominal surgery, n (%)	118 (28.4)	873 (26.0)	0.301	112 (28.4)	102 (25.8)	
Missing, n		3		1	1	0.468
Tumor						
Preoperative pelvic imaging, n (%)						
MRI	409 (98.3)	3,277 (97.5)	0.571	391 (98.7)	391 (98.7)	0.657
CT	4 (1.0)	53 (1.6)		3 (0.8)	3 (0.8)	
Preoperative MDT-meeting, n (%)	414 (99.8)	3,348 (99.7)	0.657	395 (99.7)	395 (99.7)	1.000
Missing, n	1	3				
Threatened margin on MRI						
Yes	117 (31.8)	718 (23.9)	0.004†	112 (31.4)	116 (32.2)	0.053
No	251 (68.2)	2,285 (76.1)		245 (68.6)	244 (67.8)	
Missing	48	358		39	36	
Distance from ARJ, n (%)						
0–3cm	109 (26.2)	320 (9.5)	<0.001	100 (25.3)	105 (26.5)	0.056
3–6	163 (39.2)	946 (28.1)		157 (39.6)	152 (38.4)	
6–10 cm	144 (34.6)	2,095 (62.3)		139 (35.1)	139 (35.1)	
cT-stage, n (%)						
cT1	16 (3.8)	96 (2.9)	0.541	11 (2.8)	12 (3.0)	0.636
cT2	105 (25.2)	938 (27.9)		99 (25.0)	106 (26.8)	
cT3	266 (63.9)	2,133 (63.5)		260 (65.7)	250 (63.1)	
cT4	21 (5.0)	139 (4.1)		20 (5.1)	25 (6.3)	
cTX	8 (1.9)	55 (1.6)		6 (1.5)	3 (0.8)	
cN-stage, n (%)						
cN0	185 (44.5)	1,505 (44.8)	0.953	175 (44.2)	176 (44.4)	0.991
cN1	133 (32.0)	1,093 (32.5)		129 (32.6)	125 (31.6)	
cN2	93 (22.4)	716 (21.3)		92 (23.2)	94 (23.7)	
cNX	5 (1.2)	47 (1.4)		0 (0.0)	1 (0.3)	

(Continued)

Table 1. Continued

Characteristic	Before matching			After matching		
	TaTME	lapTME	p Value	TaTME	lapTME	p Value
Neoadjuvant therapy						
No, n (%)	151 (36.3)	1,406 (41.8)	<0.001[†]	140 (35.4)	143 (36.2)	0.103
SCRT-IS, n (%)	72 (17.3)	722 (21.4)		70 (17.7)	62 (15.7)	
SCRT-DS, n (%)	51 (12.3)	234 (7.0)		50 (12.7)	34 (8.6)	
(L)CRT, n (%)	141 (33.9)	971 (28.9)		135 (34.2)	156 (39.5)	
Missing, n				1	1	

Percentages for the variables are calculated from the total number of actual results available, excluding the missing values.
*Note: exclusion of abdominoperineal resection, watchful waiting, distance from anorectal junction > 10 cm, year of operation < 2015, missing date of surgery/status/tumor location.
[†]Statistically significant.
ARJ, anorectal junction; ASA, American Society of Anesthesiologists-Classification; cN-stage, clinical nodal stage; cT-stage, clinical tumor stage; lapTME, laparoscopic transanal total mesorectal excision; (L)CRT, long course radiotherapy/chemoradiotherapy; MDT, multidisciplinary team; junction; SCRT-DS, short course radiotherapy-delayed surgery; SCRT-IS, short course radiotherapy-immediate surgery; TaTME, transanal total mesorectal excision.

CRM rate of 4.3% found in our matched TaTME group, is comparable to the 3.9% in the latest international TaTME registry paper.[17] It must be taken into account that the international TaTME registry[18] is voluntary, and surgeons with good results are more likely to enter cases to this database; our data originate from a mandatory national database.

Circumferential resection margin involvement in lapTME varied between 6% and 10% in the 4 most recent randomized controlled trials comparing open or robotic TME with lapTME,[19-22] implying the CRM involvement rates in both TaTME and lapTME found in this study are more than acceptable. Moreover, in the ALaCaRT trial,[21] one of the recent randomized controlled trials, resection margin involvement on preoperative MRI and clinical T4 tumors were exclusion criteria, possibly resulting in lower involved CRM rates; while this study reflects real life practice.

The low conversion rate after TaTME (1.5%) correlates with findings in systematic reviews and data from the TaTME registry.[7,8,17] Again, in the 4 most recent randomized controlled trials on conventional lapTME, conversion rates of 9% to 16% were found. This adds more evidence to the thought that by approaching from below in TaTME, the problem with decreased visualization and limited space deep down in the pelvis, as experienced with a pure abdominal approach, is no longer an issue, and conversion rate decreases. This is of paramount importance because conversions are not only associated with higher intraoperative morbidity, but, more importantly, with poorer oncologic outcomes and higher rates of local recurrence.[23,24]

A specific concern for TaTME are urethral injuries, something rarely seen when approaching from above. These data did not show an increased risk of ureter- or urethral injuries in TaTME intraoperatively. Postoperative morbidity was comparable in TaTME and lapTME after matching. Anastomotic leakage rate was higher in the unmatched TaTME cohort, but this difference lost statistical significance after propensity score matching for confounding factors. The leak rate of 16.5% after TaTME and 12.2% after lap TME might be interpreted as relatively high. But there is a wide range in reported leak rates in the literature, depending on definition, clinical setting, and length of follow-up. The observed leak rate is comparable to the 13.4% leak rate from a large Dutch cross-sectional study by Borstlap and colleagues,[25] including all TME procedures in 2011, which increased to 20% beyond 30 days. A prospective study from a French expert center[26] showed a 26% leak rate if asymptomatic and late leakages were also included. Current literature still under-reports anastomotic leak incidence, yet the aforementioned studies highlight that leaks might occur more often than what is actually believed. Founders of the technique hypothesized that TaTME may decrease anastomotic leakage, due to excellent exposure, the purse string anastomosis at the start of the procedure, and the ability to perform a single stapled anastomosis for bowel continuity. Using a laparoscopic transabdominal approach for cross stapling of the rectum, often multiple staple firings are needed due to limited angulation of the instruments, which is associated with an increased risk of anastomotic leakage.[27] However, in this study, this hypothesis could not be confirmed. This could be explained by the learning curve of TaTME, which includes a new way of constructing the anastomosis. This part of the procedure should receive more attention during training courses because the learning curve for TaTME is particularly long and demanding.

Transanal TME is a novel minimally invasive technique that has the potential to tackle difficult pelvic dissections, and it has captured the attention of the surgical community worldwide. Laparoscopic surgery

Table 2. Outcome Characteristics for TaTME and lapTME, Before and After Matching

	Before matching			After matching		
Outcome*	TaTME (n = 416)	lapTME (n = 3,361)	p Value	TaTME (n = 396)	lapTME (n = 396)	p Value
Operative outcome						
Anastomosis and stoma						
Anastomosis +stoma, n (%)	122 (29.7)	1,130 (34.2)	0.035	116 (29.7)	112 (28.9)	0.351
Anastomosis-stoma, n (%)	210 (51.1)	1405 (42.5)		199 (50.4)	175 (45.2)	
Hartmann's, n (%)	79 (19.2)	772 (23.3)		76 (19.4)	100 (25.8)	
Missing, n	5	54		5	9	
Conversion, n (%)	6 (1.4)	292 (8.7)	<0.001	6 (1.5)	34 (8.6)	<0.001
Intraoperative complication†						
No, n (%)	401 (96.4)	3,254 (96.8)	0.507	381 (96.2)	387 (97.7)	0.307
Ureter/urethra injury, n (%)	1 (0.2)	6 (0.2)		1 (0.3)	1 (0.3)	
Other organ injury, n (%)	14 (3.4)	82 (2.4)		14 (3.5)	8 (2.0)	
Bleeding needing transfusion, n (%)	0 (0.0)	14 (0.4)		0 (0.0)	0 (0.0)	
Missing, n		5				
Multivisceral resection	9 (2.2)	61 (1.8)	0.620	9 (2.3)	5 (1.3)	0.388
Missing		1				
Pathologic outcome						
pT-stage						
(y)pT0, n (%)	34 (8.2)	226 (6.7)	0.421	33 (8.3)	39 (9.8)	0.295
(y)pT1, n (%)	45 (10.8)	435 (13.0)		40 (10.1)	46 (11.6)	
(y)pT2, n (%)	152 (36.5)	1,121 (33.5)		144 (36.4)	148 (37.4)	
(y)pT3, n (%)	180 (43.3)	1,490 (44.5)		174 (43.9)	156 (39.4)	
(y)pT4, n (%)	4 (1.0)	67 (2.0)		4 (1.0)	4 (1.0)	
(y)pTX, n (%)	1 (0.2)	10 (0.3)		1 (0.3)	3 (0.8)	
Missing, n		10				
pN-stage						
(y)pN0, n (%)	271 (65.1)	2,236 (66.7)	0.073	258 (65.3)	291 (73.7)	0.012
(y)pN1, n (%)	89 (21.4)	805 (24.0)		84 (21.3)	78 (19.7)	
(y)pN2, n (%)	56 (13.5)	308 (9.2)		53 (13.4)	26 (6.6)	
(y)pNX, n (%)	0 (0.0)	2 (0.1)		0 (0.0)	0 (0.0)	
Missing, n		9		1	1	
CRM, n (%)‡						
Positive	18 (4.4)	98 (3.0)	0.132	17 (4.3)	16 (4.0)	1.000
Negative	390 (95.6)	3,142 (97.0)		379 (95.7)	380 (96.0)	
Lymph nodes retrieved, n (%)						
>10	345 (82.9)	2,763 (82.2)	0.587	334 (84.3)	320 (80.8)	0.227
Postoperative outcome§						
Overall complication, n (%)	176 (42.3)	1,213 (36.1)	0.042	168 (42.4)	146 (36.9)	0.135
Anastomotic leakage, n (%)‖	53/332 (16.0)	289/2,535 (11.4)	0.013	52/315 (16.5)	35/287 (12.2)	0.116
Length of stay, d, (median, IQR)	7 (5–13)	6 (4–10)	<0.001	6.5 (5–13)	6 (4–9)	0.280
Complicated course, n (%)	109 (26.2)	703 (20.9)	0.013	107 (27.0)	86 (21.7)	0.099
Readmission, n (%)	71 (17.1)	517 (15.4)	0.371	68 (17.2)	74 (18.7)	0.640
Mortality, n (%)	1 (0.2)	41 (1.2)	0.072	1 (0.3)	3 (0.8)	0.625

Percentages for the variables are calculated out of the total number of actual results available, excluding the missing values. Complicated course indicates complications resulting in hospital stay >14 days, reintervention, or mortality.

*Note: exclusion of abdominoperineal resection, watchful waitings, distance from anorectal junction > 10 cm, year of operation < 2015, missing date of surgery/status/tumor location.

†Note: Intraoperative complications, excluding conversion.

‡Note: CRM+ rates (<1 mm) were calculated after exclusion of (y)pT0N0 stage.

§Note: All postoperative outcomes describe outcomes within 30 days after index surgery.

‖Note: Anastomotic leakage was calculated after exclusion of patients with a permanent stoma without anastomosis.

pT-stage, pathologic tumor stage; pN-stage, pathologic nodal stage; CRM, circumferential resection margin; IQR, interquartile range.

Table 3. Multivariable Analysis for Various Factors, Casemix Factors and Year of Operation for Transanal Total Mesorectal Excision and Laparoscopic Total Mesorectal Excision. Data Represent the Total (Unmatched) Cohort

	TaTME			LapTME		
Variable	CRM+ (%)	OR (95% CI)	p Value	CRM+ (%)	OR (95% CI)	p Value
Distance to mesorectal fascia on MRI						
≤1 mm	8.8	5.48 (1.33−22.54)	0.018	5.8	1.99 (1.18−3.35)	0.010
>1 mm	1.6			2.2		
Conversion	50.0	30.12 (3.70−245.20)	0.001	5.3		
Multiple visceral resection	11.1			20.7	4.11 (1.77−9.55)	0.001
pT stage						
(y)pT1−pT3	4.2			2.7		
(y)pT4	25.0			22.8	4.47 (1.95−10.24)	<0.001
pN stage						
(y)pN0	4.5			1.3		
(y)pN1−2	4.2			6.6	4.84 (3.03−7.75)	<0.001

Factors included in univariable analysis: sex, BMI, history of abdominal surgery, distance to mesorectal fascia, neoadjuvant therapy, tumor height, restorative procedure (Hartmann vs other), conversion, intraoperative complications, multiple visceral resection, (y)pT-score, (y)pN-score, year of operation.
CRM, circumferential resection margin; LapTME, laparoscopic total mesorectal excision; OR, odds ratio; TaTME, transanal total mesorectal excision.

has shown to improve outcomes for many surgical indications; however, for rectal cancer surgery, the benefit with regard to oncologic outcomes compared with those from open surgery is still debated.[20,21,28] The down-to-up approach in TaTME should improve visualization of the dissection plane and facilitate a meticulous TME procedure. Potentially, this leads to higher quality specimens with fewer involved margins and lower conversion rates.

Other minimally invasive techniques, such as robotic surgery, may also overcome the challenges of deep pelvic dissection that are faced with conventional laparoscopic TME. The DCRA data did not allow for a comparison of TaTME with robotic TME because there were very few robotic TME cases done in the Netherlands. The first randomized controlled trial comparing robotic with laparoscopic TME, however, did not show a significant reduction in conversion to open laparotomy and showed comparable positive CRM rates, when performed by surgeons of varying experience with robotic-assisted surgery.[19]

Currently, 44 centers in the Netherlands have performed 562 TaTME procedures for rectal cancer in total (eFig. 1). Figure 1 shows the distribution of TaTME and lapTME for patients with rectal cancer operated on between 2015 and 2017, indicating some centers switched almost entirely to TaTME to resect rectal cancers; the majority just started performing this procedure and are still in their learning curves. The increasing use of minimally invasive approaches adds complexity to the procedure and requires enhanced surgical skills.

Transanal TME is not an easy procedure to learn. An assessment of the outcomes after cadaveric training in North America[29] showed a high risk of iatrogenic injury after training, indicating that only cadaver workshops are not sufficient to implement this technique safely. This is why a structured training program that includes proctoring is needed, and hospitals need to have enough case-volume to get over their learning curve quickly. In this study, only 15 of the 44 centers were included in a structured Dutch training program,[5] although we do not know if other surgeons received training abroad. Unfortunately, we could not compare the outcomes of the 15 centers that were trained with the "untrained" centers because the available data from the DCRA are anonymized for patients and centers. Moreover, only 3 centers performed more than 40 cases. After exceeding a learning curve threshold of 40 procedures, Koedam and associates[30] found significantly lower surgical complications and leak rates for TaTME. Therefore, in the Netherlands, not all procedures were done in TaTME-trained centers, and almost all surgeons, except at the 3 high-volume centers, are likely to still be in their learning phase. This must be taken into account when interpreting our data. An improvement of outcomes after TaTME is to be expected, when more centers pass the volume threshold of 40 patients.

Limitations of a nationwide registration study need to be discussed. The quality and completeness of the data improve over the years due to factors like training of registrars. However, missing data are inevitable because not all variables in the registry are mandatory and new variables are introduced, eg TME quality. Also, the registry does not offer long-term surgical and oncologic data that could be essential for the comparison of 2 surgical techniques. Potential concerns of TaTME, such as nerve and sphincter damage and functional outcomes, could not be explored in this study, again because of limited dataset recorded, and should be further explored in future studies. However, with the ongoing COLOR III-trial and RESET-trial, this information on long-term data is expected soon.[31] We acknowledge that this study design could not approach the quality of a well-run randomized controlled trial. Nevertheless, "real world" evidence that reflects daily practice is increasingly considered to be of additional value along with the trials with strict inclusion and exclusion criteria, and cohorts from expert centers.

CONCLUSIONS

This nationwide study demonstrated the rapid and effective implementation of TaTME in the Netherlands for patients with rectal cancer. Consequently, TaTME proves to be a good alternative for the surgical treatment of patients with low- and midrectal cancer. We believe that monitoring of outcomes is crucial when introducing a new technique, and we encourage registration of data in (inter-)national registry databases. Furthermore, future studies should focus on long-term oncologic and functional outcomes.

APPENDIX

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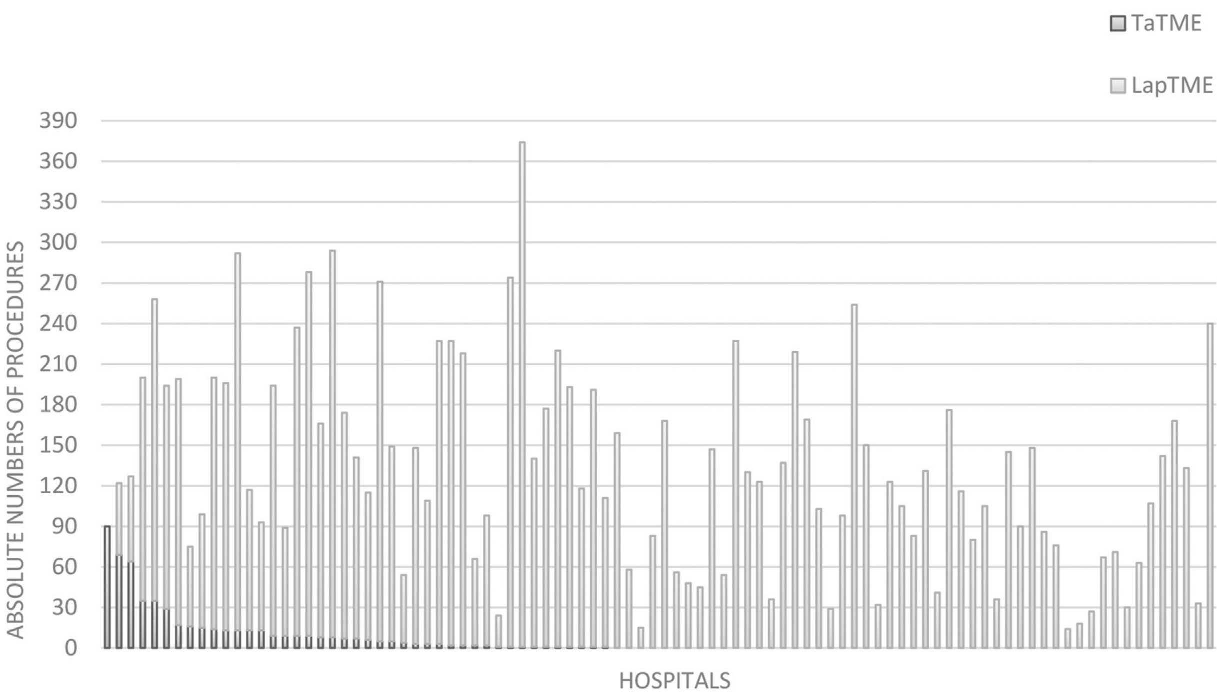

eFigure 1. Transanal total mesorectal excision (TaTME) and laparoscopic total mesorectal excision (LapTME) performing hospitals in the Netherlands, 2015 to 2017. (All procedures performed in the Netherlands, before exclusion of cases following our inclusion and exclusion criteria).