ORIGINAL STUDY

ANNALS OF SURGERY OPEN

OPEN

Completion Total Mesorectal Excision: A Case-Matched Comparison With Primary Resection

Thijs A. Burghgraef, MD,*† Marieke L. Rutgers, MD,‡ Jeroen W. A. Leijtens, PhD,§ Jurriaan B. Tuyman, PhD,‖ Esther C. J. Consten, PhD,*† and Roel Hompes, PhD,‡ on behalf of the MIRECA working group.

Objectives: The aim of this study was to compare the perioperative and oncological results of completion total mesorectal excision (cTME) *versus* primary total mesorectal excision (pTME).

Background: Early-stage rectal cancer can be treated by local excision alone, which is associated with less surgical morbidity and improved functional outcomes compared with radical surgery. When high-risk histological features are present, cTME is indicated, with possible worse clinical and oncological outcomes compared to pTME.

Methods: This retrospective cohort study included all patients that underwent TME surgery for rectal cancer performed in 11 centers in the Netherlands between 2015 and 2017. After case-matching, we compared cTME with pTME. The primary outcome was major postoperative morbidity. Secondary outcomes included the rate of restorative procedures and 3-year oncological outcomes.

Results: In total 1069 patients were included, of which 35 underwent cTME. After matching (1:2 ratio), 29 cTME and 58 pTME were analyzed. No differences were found for major morbidity (27.6% *vs* 19.0%; $P = 0.28$) and abdominoperineal excision rate (31.0% *vs* 32.8%; $P = 0.85$) between cTME and pTME, respectively. Local recurrence (3.4% *vs* 8.6%; $P = 0.43$), systemic recurrence (3.4% *vs* 12.1%; $P = 0.25$), overall survival (93.1% *vs* 94.8%; $P = 0.71$), and disease-free survival (89.7% *vs* 81.0%; $P = 0.43$) were comparable between cTME and pTME.

Conclusions: cTME is not associated with higher major morbidity, whereas the abdominoperineal excision rate and 3-year oncological outcomes are similar compared to pTME. Local excision as a diagnostic tool followed by completion surgery for early rectal cancer does not compromise outcomes and should still be considered as the treatment of early-stage rectal cancer.

Keywords: rectal cancer, surgery, total mesorectal excision

INTRODUCTION

The total mesorectal excision (TME), as propagated by Bill Heald in the eighties, is still the current gold standard in the surgical treatment of rectal cancer.[1] TME surgery in combination with (chemo)radiation has optimized oncological outcomes; however, TME is also associated with significant morbidity, long-term functional impairment, and a negative impact on quality of life.[2,3] Screening programs for bowel cancer have resulted in a substantial shift toward earlier-stage detection of colorectal cancer.[4–6] Early-stage, low-risk T1 cancers can be treated by local excision alone because the risk of lymph node involvement and subsequent local recurrence (LR) is low.[7–9] Local excision of early rectal carcinoma results in organ preservation with reduced morbidity and better functional outcome than radical TME surgery.[10–13] However, when any unfavorable histopathological features are present after local excision, completion TME (cTME) is indicated.[8,14–16]

Current literature reporting on oncological outcomes after cTME is scarce, but outcomes appear to be comparable when compared with pTME.[8,17–20] However, due to an inflammatory response at the local excision site and potential distortion of the embryological TME plane, cTME seems to be linked with higher perioperative morbidity and higher permanent stoma rates.[18,21,22]

The primary aim of this study was to assess the morbidity rate after minimal invasive cTME when matched to a pTME cohort. Secondary aims were to evaluate the restorative procedure rate, histopathological outcomes, functional anastomosis rate after 1 year, and oncological outcomes after 3 years.

MATERIALS AND METHODS

A retrospective multicenter cohort study was performed in 11 high-volume centers in the Netherlands with a large experience in 1 of the 3 minimal invasive expert techniques; 3 Transanal TME (TaTME), 3 Robot-assisted TME (R-TME) and 5 Laparoscopic TME (L-TME) centers, respectively. Patients that underwent a pTME were compared with patients that underwent a cTME,

*From the *Department of Surgery, Meander Medical Centre, Amersfoort, the Netherlands; †Department of Surgery, University Medical Centre, Groningen, the Netherlands; ‡Department of Surgery, Amsterdam University Medical Centre, location AMC, Amsterdam, the Netherlands; §Department of Surgery, Laurentius Hospital, Roermond, the Netherlands; and ‖Department of Surgery, Amsterdam University Medical Centre, location VUmc, Amsterdam, the Netherlands.*

Thijs A. Burghgraef and Marieke L. Rutgers contributed equally to this work.

SDC *Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.annalsofsurgery.com).*

E.C.J.C. received fees from Intuitive Surgical. R.H. is a consultant for Applied Medical and received lecturing fees from Medtronic and Stryker. The other author declares that there is nothing to disclose.

Reprints: Roel Hompes, PhD, Department of Surgery, Amsterdam UMC, Meibergdreef 9, 1105 AZ Amsterdam, the Netherlands. Email: r.hompes@amsterdumumc.nl.

Annals of Surgery Open (2023) 3:e327

Received: 19 July 2023; Accepted 24 July 2023

Published online 23 August 2023

DOI: 10.1097/AS9.0000000000000327

using case-matching. The study protocol was approved by the Medical Research Ethics Committees United (MEC-U, AW 19.023/W18.100) and the local ethical boards of all participating centers. This study was reported in accordance with the strengthening the reporting of observational studies in epidemiology guidelines.

Patient Selection

Patients were eligible for inclusion if they were 18 years of age and older, diagnosed with rectal cancer according to the sigmoid take-off, and underwent an elective TME with curative intent between January 2015 and December 2017 in 1 of the 11 participating hospitals. Only cases that were performed after completing the surgeons' learning curve for L-TME, R-TME, or TaTME were included, as previously described.[23,24] Patients were excluded from the analysis if they had a double tumor, underwent hyperthermal intraperitoneal chemotherapy, had synchronous metastasis, or underwent salvage procedures for LR after local excision or regrowth within a watch-and-wait program.

Data Extraction

Data were initially derived from the Dutch ColoRectal Audit (DCRA), which is a mandatory, independently validated, nationwide registry that collects information on all surgically resected primary colorectal cancer patients. Missing data and additional information not present in the DCRA data set were added by local investigators with the use of the local electronic medical record. All pseudonymized data were collected between January and April 2020 in the data management system Castor, Amsterdam, the Netherlands.[25] Each patient was discussed in a local multidisciplinary team, and indications for neoadjuvant treatment were given according to the current Dutch National guidelines for colorectal cancer.

Outcomes and Definitions

The primary outcome was a major morbidity rate. Secondary outcomes included intraoperative outcomes, postoperative outcomes, restorative rate, histopathological outcomes, and functional anastomosis rate after 1-year and 3-year oncological outcomes.

Baseline characteristics of interest were age, body mass index, American Society of Anesthesiologists classification, history of abdominal surgery, tumor distance from the anorectal junction (ARJ) on magnetic resonance imaging (MRI), low rectal tumor (LOREC), threatened mesorectal fascia, anterior tumor location, clinical tumor nodal metastasis (TNM) stage, and neoadjuvant (chemo)radiation. Furthermore, histopathological data of the local excision was extracted, including pT stage, resection margin, differentiation grade, lymfangio-invasion, and time of cTME since local excision. A rectal tumor was defined as a tumor with its lower border below the sigmoid take-off as seen on cross-sectional imaging, according to D'Souza et al.[26] A LOREC tumor was defined as a tumor with the distal border located distal to the point where the levator ani muscles insert on the pelvic bone on a sagittal MRI.[27,28]

Intraoperative outcomes included type of surgery (low anterior resection [LAR] + anastomosis, LAR + colostomy or abdomino perineal excision [APE]), approach (Open, L-TME, R-TME, and TaTME), operating time; defined as incision until closure, conversion rate, and intraoperative complication rate. Type of procedure was categorized as either; LAR with anastomosis, being all sphincter-saving procedures with primary anastomosis with or without a temporary stoma. Nonrestorative procedures were classified as either LAR with end-colostomy or APE, which includes any procedure with perineal dissection with complete, intersphincteric or extrasphincteric proctectomy and definitive end-colostomy. A cTME was defined as a TME after initial local excision. Local excision was defined as either transanal endoscopic microsurgery (TEM) or transanal minimally invasive surgery (TAMIS). Not considered to be cTME were patients with only an endoscopic polypectomy or endoscopic mucosal resection before TME.

Postoperative outcomes included 30-day mortality rate, 30-day morbidity rate, 30-day surgical morbidity rate (abscess, ileus, wound infection, and anastomotic leakage), length of stay, reintervention rate, and readmission rate. Thirty-day morbidity was categorized according to the Clavien-Dindo classification.[29] Anastomotic leakages were registered during the whole follow-up and graded according to the International Study Group of Rectal Cancer classification for anastomotic leakage after anterior resection.[30] Histopathological and 3-year oncological outcomes included: pathological TNM stage, resection margin and quality of the TME specimen,[31] tumor differentiation, follow-up duration in months, functional anastomosis rate at 1 and 3 years postoperative, permanent stoma rate at the end of follow-up, and 3-year oncological outcomes: local recurrence, systemic recurrence, disease-free survival, and overall survival.

Statistical Analysis

To adequately compare groups, case-matching was performed in a 2 (pTME) to 1 (cTME) ratio, taking into account the following variables: age, body mass index, sex, American Society of Anesthesiologists score, tumor distance, anterior tumor location, cTNM staging, and the use of neoadjuvant (chemo) radiotherapy.

Descriptive statistics were used to describe baseline characteristics. Data were presented as numbers and percentages for categorical variables. Continuous variables were presented as mean (standard deviation) or median (interquartile range) depending on the type of distribution. Univariate analysis was performed using the χ^2 test for categorical data. The independent sample *T* test or the Wilcoxon-rank sum test was used for continuous data. Categorical and binary outcomes of matched patients were compared using the McNemar test, and continuous outcomes of matched patients were compared using the paired *T* test or the Wilcoxon signed rank test for non-normally distributed numeric data. Baseline characteristics of matched patients were compared using the standardized mean difference (SMD). An SMD lower than 0.10 was deemed negligible. A *P* value of <0.05 was considered significant. All statistical analysis was performed using R, version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

In total, 1834 patients were identified as eligible between January 1, 2015 and December 31, 2017. Of these, 765 patients were excluded. This resulted in 1069 patients, of which 35 were classified as cTME (Fig. 1).

Baseline characteristics for the cTME patients are displayed in Table 1. The majority of cases, before local excision, were clinically classified as cT1 (25.7%), cT2 (60.0%), and cN0 (94.3%). All local excisions in this series were carried out via TEM or TAMIS. The median time between local excision and cTME was 44 days (interquartile range [IQR]: 28–71). Most of the cases did not receive any type of (chemo)radiation after the local excision (85.7%).

Table 2 displays the baseline characteristics before and after case-matching. Before matching, more females were present in the cTME group with a shorter distance to the anal verge (3.8 *vs* 5.0 cm) with no threatened margins, fewer cT3 and cT4 tumors, and less neoadjuvant treatment. After matching 29 cTME patients and 58 pTME patients remained, eliminating all significant differences between the unmatched cohorts. Furthermore,

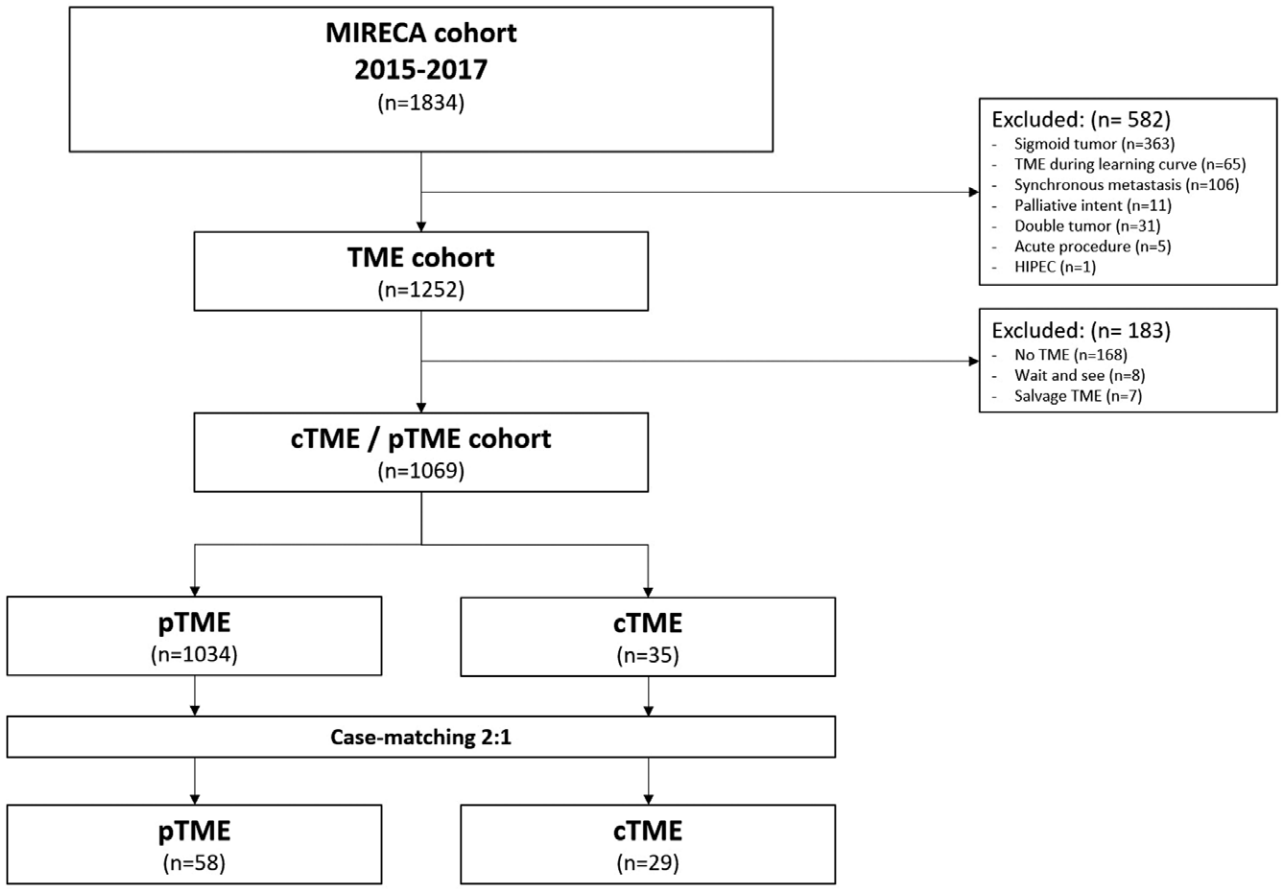

FIGURE 1. Patient flow of included patients. cTME indicates completion total mesorectal excision, HIPEC, hyperthermal intraperitoneal chemotherapy; MIRECA, Minimally Invasive REctal CAncer working group; pTME, primary total mesorectal excision; TME, total mesorectal excision.

SMDs were less than 0.10 for all variables used for matching, except for history of abdominal surgery (SMD: 0.106).

Table 3 displays the perioperative and postoperative outcomes between the 2 matched cohorts. Less unrestorative LARs were performed in the cTME group compared with the pTME group (3.4% *vs* 19%; $P = 0.01$) with equal APE rates. More restorative procedures were performed in the cTME group, although this did not reach statistical significance (65.5% *vs* 48.3%; $P = 0.08$). The overall postoperative morbidity rate was comparable (41.4% *vs* 48.3%; $P = 0.47$). However, the major morbidity rate was higher in the cTME group (27.6% *vs* 19.0%; $P = 0.28$), although this did not reach statistical significance. Likewise, anastomotic leakage was observed more often in the cTME group (26.3%; n = 5 *vs* 10.7%; n = 3; $P = 0.32$), whereas the difference was not statistically significant. The majority of the leakages were classified as type III anastomotic leakage requiring surgery and the construction of an ostomy. In the cTME group, all patients had a tumor ≤5 cm in the ARJ, whereas only 1 pTME patient had a tumor ≤5 cm in the ARJ. Furthermore, one of the cTME patients received radiotherapy and developed a fistula after 8 months, recognized as a late anastomotic leakage. After 1 year of follow-up functional anastomosis rate was comparable between the cTME and pTME groups (51.7% *vs* 46.6%; $P = 0.60$), whereas the functional anastomosis rate was higher after 3 years of follow-up (55.2% *vs* 44.8%; $P = 0.32$), without reaching statistical significance. In the cTME group, 2 patients with an initial restorative procedure had a nonfunctional anastomosis after 3 years as reversal was not performed due to comorbidity, whereas 1 patient received an ostomy after anastomotic leakage. In the pTME group, 1 patient received an ostomy after anastomotic leakage, and 1 patient had to undergo an APE due to local recurrence. Length of stay was 5.0 days for cTME *versus* 7.0 days for pTME ($P = 0.59$) with comparable readmission and 30-day mortality rates between the 2 groups.

The histopathological outcomes and oncological follow-up are displayed in Table 4. circumferential resection margin (CRM) positivity was comparable in the cTME group (0.0% *vs* 5.2%). However, as 1 patient had a positive distal resection margin in the cTME group, the positive resection margin (R1) rate was higher in the cTME group compared with the pTME group; 1 out 7 patients with a residual tumor (14.2%) *versus* 3 out of 58 patients with a residual tumor (5.2%), respectively ($P = 0.65$). Despite the clinical difference, this was not statistically significant ($P = 0.65$). The completeness of the TME specimens was also comparable between the 2 groups, and no incomplete specimens were found in patients with a residual tumor. After a median follow-up of 30 and 36 months for cTME and pTME, respectively, LR was 3.4% (n = 1) in the cTME group *versus* 8.6% (n = 5) in the pTME group ($P = 0.43$) (Fig. 2A). The characteristics of the 6 local recurrences are described in Supplemental Table 1, http://links.lww.com/AOSO/A245. After 3 years of follow-up systemic recurrence (3.4% *vs* 12.1%; $P = 0.25$), disease-free survival (89.7% *vs* 81.0%; $P = 0.43$), and overall survival (93.1% *vs* 94.8%; $P = 0.71$) were comparable between the cTME group and the pTME group (Figs. 2B–D), respectively.

DISCUSSION

This observational cohort study compared cTME after local excision with pTME for early rectal cancer management in 11 minimally invasive expert centers in the Netherlands between 2015 and 2017. First, this study shows higher postoperative major morbidity rates while obtaining a higher rate of restorative surgery, although both did not reach statistical significance.

TABLE 1.

Baseline Characteristics cTME Patients

Baseline Characteristics		cTME (n = 35)
Clinical TNM	cT1	9 (25.7%)
	cT2	21 (60.0%)
	cT3	5 (14.3%)
	cT4	0
	cN0	33 (94.3%)
	cN1	1 (2.9%)
	cN2	1 (2.9%)
	cM0	35 (100%)
Type of local excision	TEM/TAMIS	35 (100%)
Histopathology after local excision		
Pathological tumor stage	pT0	0
	pT1	9 (25.7%)
	pT2	21 (60.0%)
	pT3	4 (11.4%)
	pT4	0
	Unknown	1 (2.9%)
Resection margin	>1 mm	19 (54.3%)
	≤1 mm	14 (40.0%)
	Inconclusive	1 (2.9%)
	Unknown	1 (2.9%)
Differentiation grade	Well/moderate	28 (80.0%)
	Poor	4 (11.4%)
	Unknown	3 (8.6%)
Lymfangio-invasion	None	23 (65.7%)
	EMVI	5 (14.3%)
	Lymfangio-invasion	3 (8.6%)
	Intramural invasion	2 (5.7%)
	Unknown	2 (5.7%)
(Chemo)radiotherapy	Yes	5 (14.3%)
	RT	3 (8.6%)
	CRT	2 (5.7%)
	Before local excision	2 (40%)
	After local excision	3 (60%)
Time local excision—cTME	Days (median, [IQR])	44 (28–71)

Baseline characteristics cTME patients.

CRT indicates chemoradiotherapy; cTME, completion total mesorectal excision; EMVI, extramural venous invasion; IQR, interquartile range; RT, radiotherapy; TAMIS, transanal minimally invasive surgery; TEM, transanal endoscopic microsurgery; TME, total mesorectal excision; TNM, tumor nodal metastasis.

Histopathological outcomes and 3-year oncological outcomes were comparable between cTME and pTME.

cTME after local excision is claimed to be a procedure that can lead to inferior outcomes with higher rates of perioperative morbidity, and less restorative surgery, leading to more permanent stomas.[18,21,22,32] Furthermore, poor specimen outcomes, and even worsened oncological outcomes have been reported.[20,33,34] It is thought that the previous local excision causes scarring and fibrosis in the mesorectal plane, resulting in a more challenging oncological dissection.

In this study, intraoperative complication rate and conversion were comparable between groups. Furthermore, overall postoperative morbidity was comparable between both groups, whereas major morbidity was higher after cTME (27.6% *vs* 19.0%; $P = 0.28$), although the difference was not statistically significant. This is in line with a recent systematic review and meta-analysis by Wyatt et al,[35] showing that conversion to open surgery is equal, whereas postoperative complication rate and rate of major morbidity (Clavien-Dindo ≥III) is higher in the cTME group without reaching statistical significance. The difference in major morbidity in this study may be due to the statistically nonsignificant difference in anastomotic leakage rate (26.3%, n = 5 *vs* 10.7% n = 3; $P = 0.32$), as major morbidity was due to anastomotic leakage in 3/8 cTME patients and 3/11 pTME patients. The higher rate of anastomotic leakage was likely related to more anastomosis being performed in patients with a local excision in the lower part of the rectum, as all tumors in cTME patients with an anastomotic leakage were within 5 cm of the anal verge.[36,37]

In this study, the APE rate was comparable (31.0% *vs* 32.8%; $P = 0.85$) between the 2 groups, whereas a higher primary anastomosis rate with a trend towards significance was observed in the cTME group (65.5% *vs* 48.3%; $P = 0.08$). A significantly lower rate of LAR + colostomy was observed in the cTME group (3.4% *vs* 19.0%; $P = 0.01$). Several studies suggested that a cTME could lead to higher APE rates. Although we saw comparable APE rates between the 2 groups, still an APE rate of around 30% is higher compared with the data of the DCRA among all rectal cancer patients between 2015 and 2017,[35,38] and in line with studies showing higher APE rates, ranging from 28% to 41%.[18,19,21,22] A reason for the

TABLE 2.

Baseline Characteristics Before and After Case-Matching

		Unmatched				Matched			
Baseline Characteristics		**cTME n = 35**	**pTME n = 1034**	***P***	**SMD**	**cTME n=29**	**pTME n=58**	***P***	**SMD**
Age	Year (mean, [SD])	69.5 (7.2)	67.1 (10.4)	0.17	0.275	69.4 (7.5)	69.7 (7.7)	0.87	0.036
BMI	(Mean, [SD])	25.3 (2.5)	26.1 (4.3)	0.24	0.244	25.2 (2.5)	25.3 (3.0)	0.88	0.037
Sex	Male	16 (45.7)	667 (64.5)	0.04	0.385	13 (44.8)	26 (44.8)	1.00	<0.001
	Female	19 (54.3)	367 (35.5)			16 (55.2)	32 (55.2)		
ASA	1	9 (25.7)	206 (19.9)	0.35	0.269	7 (24.1)	14 (24.1)	1.00	<0.001
	2	22 (62.9)	613 (59.3)			19 (65.5)	38 (65.5)		
	3 + 4	4 (11.4)	215 (20.8)			3 (10.3)	6 (10.3)		
History of abdominal surgery	Yes	13 (37.1)	296 (28.6)	0.37	0.182	12 (41.4)	21 (36.2)	0.82	0.106
Tumor distance to ARJ on MRI	cm (median [IQR])	3.8 [0.3–5.0]	5.0 [2.0–8.0]	0.02	0.378	4.0 [0.8–5.1]	4.0 [2.0–6.0]	0.64	0.040
LOREC	Yes	22 (62.9)	602 (59.1)	0.79	0.076	17 (58.6)	41 (71.9)	0.32	0.282
Threatened MRF	Yes	0	319 (31.3)	<0.001	0.955	0	2 (3.4)	0.82	0.267
Tumor location	Anterior	5 (14.7)	175 (17.4)	0.02	0.626	3 (10.7)	6 (10.5)	1.00	0.006
Clinical TNM	cT1-cT2	29 (85.3)	316 (30.7)	<0.001	1.348	25 (86.2)	50 (86.2)	1.00	0.014
	cT3	5 (14.7)	620 (60.2)			4 (13.8)	8 (13.8)		
	cT4	0	94 (9.1)			0	0		
	cN0	33 (94.3)	463 (44.9)	<0.001	1.273	27 (93.1)	54 (93.1)	1.00	0.010
	cN1-2	2 (5.7)	569 (55.1)			2 (6.9)	4 (6.9)		
	cM0	36 (100)	1031 (100)	1.00	<0.001	28 (100)	58 (100)	1.00	<0.001
n(C)RT	Yes	5 (14.3)	629 (61.8)	<0.001	1.122	2 (6.9)	4 (6.9)	1.00	<0.001

ARJ indicates anorectal junction; ASA, American Association of Anesthesia Classification; BMI, body mass index; cTME, completion total mesorectal excision; IQR, interquartile range; LOREC, LOw REctal Cancer; MRF, mesorectal fascia; MRI, magnetic resonance imaging; n(C)RT, neoadjuvant chemoradiation; pTME, primary total mesorectal excision; SD, standard deviation; SMD, standardized mean difference; TNM, tumor nodal metastasis.

TABLE 3.

Perioperative and postoperative outcomes after matching

Perioperative Outcomes		cTME n = 29	pTME n = 58	*P*	Posthoc Analysis
Surgery	LAR + anastomosis	19 (65.5)	28 (48.3)	0.08	0.08
	LAR + colostomy	1 (3.4)	11 (19.0)		0.01
	APE	9 (31.0)	19 (32.8)		0.85
Approach	Open	1 (3.4)	1 (1.7)	0.19	
	L-TME	9 (31.0)	32 (55.2)		
	TaTME	11 (37.9)	13 (22.4)		
	R-TME	8 (27.6)	12 (20.7)		
Skin-to-Skin time	Minutes (mean, [SD])	193.5 (63.1)	174.9 (51.7)	0.15	
Conversion	Yes	1 (3.4)	3 (5.2)	0.65	
Stoma	No stoma	8 (27.6)	13 (22.4)	0.24	0.55
	Ileostomy	9 (31.0)	13 (22.4)		0.28
	Colostomy (temporary)	3 (10.3)	2 (3.4)		0.16
	Colostomy (permanent)	9 (31.0)	30 (51.7)		0.03
Intraoperative complication	Yes	1 (3.4)	2 (3.4)	1.00	
Postoperative outcomes					
Complications	<30 days	12 (41.4)	28 (48.3)	0.47	
Clavien-Dindo	CD 1 + 2 (minor)	5 (17.2)	17 (29.3)	0.28	
Classification	CD 3 + 4 (major)	8 (27.6)	11 (19.0)		
Surgical complications	Yes	8 (27.6)	16 (27.6)	1.00	
	Abscess	1 (3.4)	4 (6.9)	0.41	
	Ileus	2 (6.9)	10 (17.2)	0.11	
	Wound infection	0	4 (6.9)	0.05	
	Anastomotic leakage*	5 (26.3)	3 (10.7)	0.32	
Anastomotic leakage, ISREC	Type A	0	0	NA	
	Type B	2 (40.0)	1 (33.3)		
	Type C	3 (60.0)	2 (66.7)		
Length of stay	Days (median, [IQR])	5.0 [4.0–7.5]	7.0 [5.0–9.8]	0.59	
Reintervention	Yes	6 (20.7)	6 (10.3)	0.13	
Readmission	Yes	3 (10.3)	3 (5.2)	0.26	
Mortality	<30 days	1 (3.4)	0	0.16	

APE indicates abdomino perineal excision; CD, clavien-dindo; cTME, completion total mesorectal excision; IQR, interquartile range; ISREC, International study group of rectal cancer, LAR, low anterior resection; L-TME, laparoscopic total mesorectal excision; pTME, primary total mesorectal excision; R-TME, robot-assisted total mesorectal excision; SD, standard deviation, TaTME, transanal total mesorectal excision.

TABLE 4.

Histopathological outcomes of TME surgery and oncological follow-up after matching

Histopathological Outcomes		cTME n = 29	pTME n = 58	*P*	Posthoc Analysis
Pathological TNM	pT0	4 (13.8)	0	0.01	NA
	pT1	4 (13.8)	9 (15.5)		0.78
	pT2	16 (55.2)	21 (36.2)		0.06
	pT3	5 (17.2)	27 (46.6)		<0.001
	pT4	0	1 (1.7)		NA
	pN0	24 (82.8)	41 (70.7)	0.22	
	pN1	5 (17.2)	12 (20.7)		
	pN2	0	5 (8.6)		
Residual tumor	Residual tumor, N0	5 (17.2)	NA		
	Residual tumor, N+	2 (6.9)			
	No residual tumor, N0	19 (65.5)			
	No residual tumor, N+	3 (10.3)			
Resection margin	CRM ≤1 mm	0 (0.0)	3 (5.2)	NA	
	R1 (CRM+DRM)	1 (14.2)	3 (5.2)	0.65	
TME specimen	Complete	20 (69.0)	45 (77.6)	0.30	
	Nearly complete	6 (20.7)	6 (10.3)		
	Incomplete	1 (3.4)	5 (10.0)		
	Missing	2 (6.9)	2 (3.2)		
Tumor differentiation	Well/moderate	24 (82.8)	54 (93.1)	0.62	
	Poor	1 (3.4)	1 (1.7)		
	Unknown	4 (13.8)	3 (5.2)		
Long term outcomes					
Follow-up	Months (median, [IQR])	30.3 (23.6–41.3)	36.1 (23.6–47.5)	0.32	
Functional anastomosis rate	1 year postoperative	15 (51.7)	27 (46.6)	0.60	
	3 years postoperative	16 (55.2)	26 (44.8)	0.32	
Permanent stoma rate	Yes	13 (44.8)	32 (55.2)	0.32	
3-year survival	Local recurrence	1 (3.4)	5 (8.6)	0.43	
	Systemic recurrence	1 (3.4)	7 (12.1)	0.25	
	Disease-free survival	26 (89.7)	47 (81.0)	0.43	
	Overall survival	27 (93.1)	55 (94.8)	0.71	

CRM indicates circumferential resection margin; cTME, completion total mesorectal excision; DRM, distal resection margin; IQR, interquartile range; NA, not applicable; pTME, primary total mesorectal excision; R1, positive resection margin; TME, total mesorectal excision; TNM, tumor nodal metastasis.

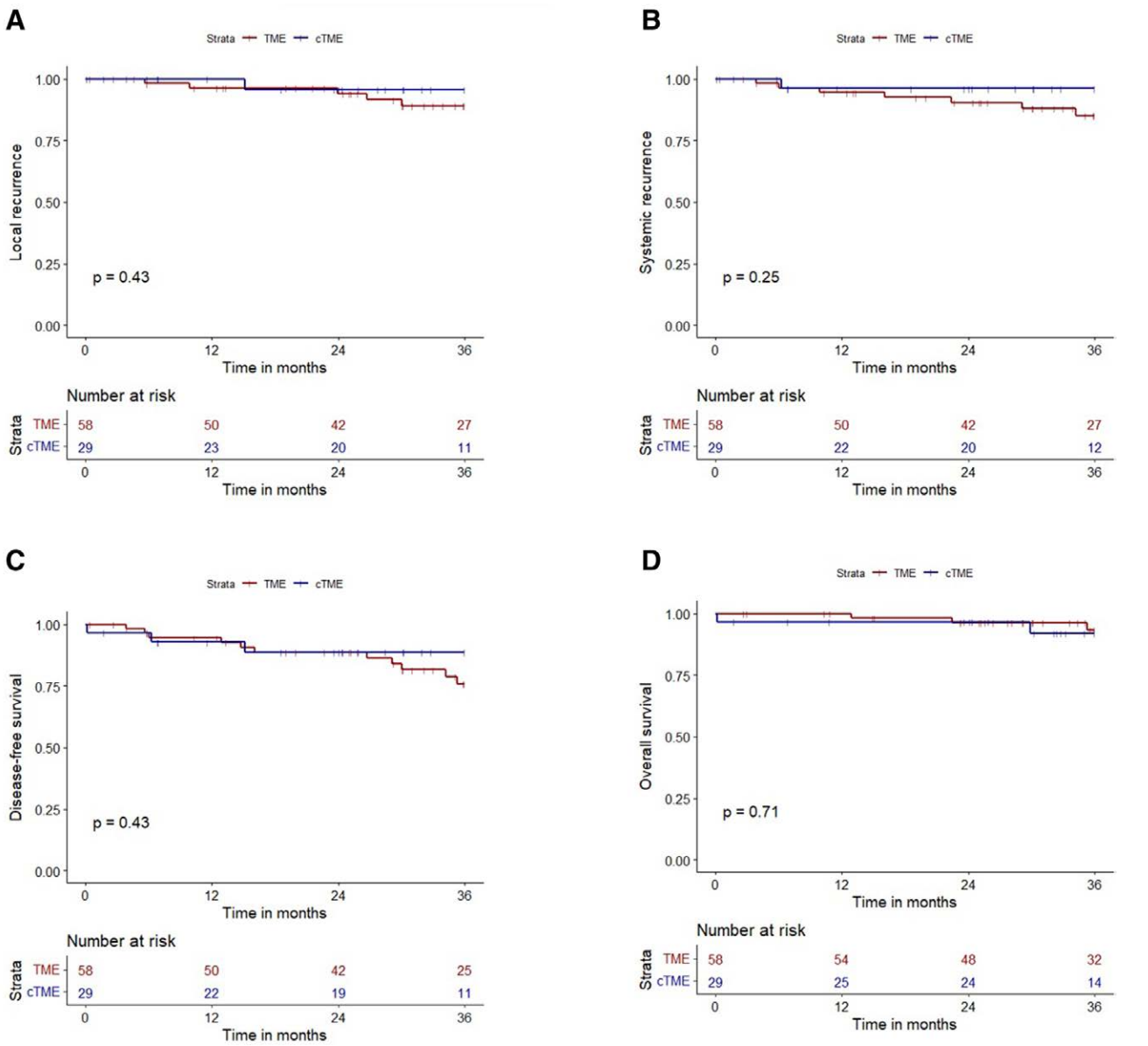

FIGURE 2. Kaplan Meier Curves after 3-year follow-up. A, Local recurrence Kaplan–Meier, (B) systemic recurrence Kaplan–Meier, (C) disease-free survival Kaplan–Meier, (D) overall survival Kaplan–Meier. cTME indicates completion total mesorectal excision; pTME: primary total mesorectal excision.

comparable but high APE rates might be the fact that we only included patients with an MRI-defined rectal tumor, leading to a higher proportion of patients with a low rectal tumor.[26,39] Additionally, local excision is often offered to patients with a deemed early rectal cancer, who—without local excision—would have undergone an APE, because of the tumor location. In the long term, the statistically nonsignificant difference in restorative rate resulted in a nonsignificant lower permanent stoma rate and a nonsignificant higher functional anastomosis rate in the cTME group. Despite the higher rate of anastomotic leakage in the cTME group, in both groups, only 1 patient had a permanent stoma after an initial anastomotic leakage. Although some studies show a higher permanent stoma rate after cTME,[20,21] more recent studies are in line with our study and do not report this.[19,22] Most likely, the absence of statistical significance for permanent stoma rate, anastomotic leakage, major morbidity, and functional anastomosis rate at 3 years is due to a type II error; lack of power caused by the small sample size of the current study.

Short-term oncological results for cTME revealed comparable and low rates of positive CRM (0.0% *vs* 5.2%); however, as 1 patient with a residual tumor in the cTME group had a positive distal resection margin, the R1 rate within patients with a residual tumor in the TME specimen was higher in the cTME group (14.2% *vs* 5.2%; $P = 0.65$), although this did not reach statistical significance. Furthermore, a low rate of incomplete specimens was found in the cTME group (3.4% *vs* 10.0%; $P = 0.30$), which is better than the significantly higher incidence of incomplete specimens found in the systematic reviews by Wyatt et al[35] and Zinicola et al.[40] This is an important finding, as it has been shown that a poor cTME specimen quality may lead to worsened oncological outcomes, specifically with higher LR rates as a result.[33,34] The 3-year oncological outcomes were comparable between cTME and pTME patients, with absolute numbers showing a lower LR rate (3.4% *vs* 8.6%; $P = 0.43$) and a lower systemic recurrence rate (3.4% *vs* 12.1%; $P = 0.25$) in the cTME group, although this was not statistically significant. This is in line with recent literature reporting comparable long-term results.[35,40]

Furthermore, the LR rate reported in this study is in line with a recent systematic review and meta-analysis. This study showed LR rates in high-risk pT1 tumors with a weighted average of

13.6% *versus* 4.1% *versus* 3.9%, for, respectively, local excision alone, local excision with cTME, and local excision with adjuvant chemoradiotherapy.[8] In pT2 tumors, a weighted average of 28.9% *versus* 4% *versus* 14.7% was found.[8] Hence, in high-risk pT1 tumors and especially pT2 tumors, cTME could be of added value. Unfortunately, preoperative tumor staging using MRI, endoscopic ultrasound, and endoscopy is known to have a low accuracy for identifying low-risk T1 from high-risk T1 or T2 tumors.[41,42] Therefore, local excision should be considered as a diagnostic procedure with the possibility of being therapeutic in selected cases, as Oostendorp et al[8] suggested.

An explanation for the observed differences in restorative rate, and functional anastomosis rate might be the increased use of the newer TaTME and R-TME techniques for cTME, as both techniques might be better equipped for this type of difficult surgery through enhanced visualization of the surgical field and correct planes, which is partially supported by studies showing improved resection quality after completion of TaTME.[43,44] Another explanation might be the fact that the median duration of local excision until cTME was 44 days (IQR: 28–71), as time from local excision until cTME <5 weeks has been found to be independently associated with a higher risk of APR.[18] On the other hand the cTME should not be performed after a too lengthy time period, as this might increase the risk of inferior quality specimen.[33]

Although this study shows comparable outcomes between cTME and pTME and is unique as it offers a side-by-side comparison by means of case-matching within a relatively short time period in a homogeneous population of patients who underwent minimally invasive TME, certain limitations should be taken into account when interpreting the results. First, this is a retrospective series, introducing the risk of selection bias and confounding by indication. As this is a cohort of consecutive patients operated in 11 centers, and referral for rectal cancer is uncommon, the risk of selection bias is suggested to be small, but not diminishable. Furthermore, confounding by indication might be present. Ideally, randomized controlled trials should be performed. However, most trials are feasibility trials investigating different (neo) adjuvant treatment schemes in combination with local excision. Therefore, we performed case-matching, resulting in comparable groups. Nevertheless, residual confounding might still be present. Second, this series represents a rather small cohort of 35 cTME patients, which might have introduced a type II error for major morbidity, anastomotic leakage, restorative rate, permanent stoma rate, and functional anastomosis rate. However, only 4 other comparative studies reported on a larger cTME group of between 41 and 60 patients.[18,20,22,45] Additionally, the data were collected within a rather short time period in a homogenous cohort of 11 expert centers for minimally invasive rectal cancer surgery. This makes the data less prone to changes in clinical practice over time or institutional differences. Third, we did not collect quality of life data or functional data, which should ideally be incorporated in every rectum cancer surgery result. Nevertheless, the rate of restorative procedures and morbidity gives an indication of these numbers. Finally, as we only included patients in this cohort who underwent a TME, we were unable to register patients in this database who only underwent a local excision or a local excision with adjuvant therapy. Nevertheless, as the aim of this study is to compare cTME with pTME, this does not cause selection bias.

CONCLUSIONS

This retrospective cohort study comparing cTME with pTME shows comparable perioperative (major) morbidity rates and restorative rates while achieving equally well histopathologic outcomes with low CRM positivity rates and low rates of incomplete specimens, resulting in comparable 3-year oncological outcomes. A step-up approach for early rectal cancer using local excision does not compromise perioperative outcomes or oncological outcomes and should therefore still be considered in the treatment of early-stage rectal cancer.

Acknowledgments

On behalf of the Minimal Invasive RECtal Cancer surgery study group (MIRECA): R.M.P.H. Crolla; A.A.W. van Geloven, MD, PhD; F. Polat, MD, PhD; A. Pronk, MD, PhD; A.B. Smits, MD, PhD; E.G.G. Verdaasdonk, MD, PhD; C. Sietses, MD, PhD P.M. Verheijen, MD, PhD; R.T.J. Geitenbeek, MD; J.C. Hol, MD, PhD.

T.A.B. contributed to the acquisition of data, interpretation and analysis of data, and drafting the article. M.L.R. contributed to the acquisition of data, interpretation of data, and drafting the article. J.W.A.L., J.B.T., and R.H. contributed to the conception and design, interpretation of data, drafting of the article, and revising the article critically for important intellectual content. E.C.J.C contributed to the conception and design, interpretation of data and revising the article critically for important intellectual content. All authors gave final approval of the version to be published.

REFERENCES

1. Heald RJ, Ryall RDH. Recurrence and survival after total mesorectal excision for rectal cancer. *Lancet*. 1986;327:1479–1482.
2. Bennis M, Parc Y, Lefevre JH, et al. Morbidity risk factors after low anterior resection with total mesorectal excision and coloanal anastomosis: a retrospective series of 483 patients. *Ann Surg*. 2012;255:504–510.
3. Lezoche E, Paganini AM, Fabiani B, et al. Quality-of-life impairment after endoluminal locoregional resection and laparoscopic total mesorectal excision. *Surg Endosc*. 2014;28:227–234.
4. Steele RJC, McClements P, Watling C, et al. Interval cancers in a FOBT-based colorectal cancer population screening programme: implications for stage, gender and tumour site. *Gut*. 2012;61:576–581.
5. Breekveldt ECH, Lansdorp-Vogelaar I, Toes-Zoutendijk E, et al; Dutch National Colorectal Cancer Screening Working Group. Colorectal cancer incidence, mortality, tumour characteristics, and treatment before and after introduction of the faecal immunochemical testing-based screening programme in the Netherlands: a population-based study. *Lancet Gastroenterol Hepatol*. 2022;7:60–68.
6. Morris EJA, Whitehouse LE, Farrell T, et al. A retrospective observational study examining the characteristics and outcomes of tumours diagnosed within and without of the English NHS bowel cancer screening programme. *Br J Cancer*. 2012;107:757–764.
7. Borstlap WAA, van Oostendorp SE, Klaver CEL, et al. Organ preservation in rectal cancer: a synopsis of current guidelines. *Color Dis*. 2018;20:201–210.
8. van Oostendorp SE, Smits LJH, Vroom Y, et al. Local recurrence after local excision of early rectal cancer: a meta-analysis of completion TME, adjuvant (chemo)radiation, or no additional treatment. *Br J Surg*. 2020;107:1719–1730.
9. Zwager LW, Bastiaansen BAJ, Montazeri NSM, et al. Deep submucosal invasion is not an independent risk factor for lymph node metastasis in T1 colorectal cancer: a meta-analysis. *Gastroenterology*. 2022;163:174–189.
10. Clermonts SHEM, van Loon YT, Wasowicz DK, et al. Comparative quality of life in patients following transanal minimally invasive surgery and healthy control subjects. *J Gastrointest Surg*. 2018;22:1089–1097.
11. Hompes R, Ashraf SQ, Gosselink MP, et al. Evaluation of quality of life and function at 1 year after transanal endoscopic microsurgery. *Color Dis*. 2015;17:O54–O61.
12. Rullier E, Vendrely V, Asselineau J, et al. Organ preservation with chemoradiotherapy plus local excision for rectal cancer: 5-year results of the GRECCAR 2 randomised trial. *Lancet Gastroenterol Hepatol*. 2020;5:465–474.
13. Restivo A, Zorcolo L, D'Alia G, et al. Risk of complications and long-term functional alterations after local excision of rectal tumors with transanal endoscopic microsurgery (TEM). *Int J Colorectal Dis*. 2016;31:257–266.

14. Labianca R, Nordlinger B, Beretta GD, et al; ESMO Guidelines Working Group. Early colon cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2013;24(SUPPL.6):vi64–vi72.
15. Watanabe T, Muro K, Ajioka Y, et al; Japanese Society for Cancer of the Colon and Rectum. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2016 for the treatment of colorectal cancer. *Int J Clin Oncol*. 2018;23:1–34.
16. Bach SP, Hill J, Monson JRT, et al; Association of Coloproctology of Great Britain and Ireland Transanal Endoscopic Microsurgery (TEM) Collaboration. A predictive model for local recurrence after transanal endoscopic microsurgery for rectal cancer. *Br J Surg*. 2009;96:280–290.
17. Levic K, Bulut O, Hesselfeldt P, et al. The outcome of rectal cancer after early salvage TME following TEM compared with primary TME: a case-matched study. *Tech Coloproctol*. 2013;17:397–403.
18. Levic Souzani K, Bulut O, Kuhlmann TP, et al. Completion total mesorectal excision following transanal endoscopic microsurgery does not compromise outcomes in patients with rectal cancer. *Surg Endosc*. 2022;36:1181–1190.
19. Clermonts SHEM, Köeter T, Pottel H, et al. Outcomes of completion total mesorectal excision are not compromised by prior transanal minimally invasive surgery. *Color Dis*. 2020;22:790–798.
20. Van Gijn W, Brehm V, De Graaf E, et al. Unexpected rectal cancer after TEM: outcome of completion surgery compared with primary TME. *Eur J Surg Oncol*. 2013;39:1225–1229.
21. Morino M, Allaix ME, Arolfo S, et al. Previous transanal endoscopic microsurgery for rectal cancer represents a risk factor for an increased abdominoperineal resection rate. *Surg Endosc*. 2013;27:3315–3321.
22. Lossius WJ, Stornes T, Myklebust TA, et al. Completion surgery vs. primary TME for early rectal cancer: a national study. *Int J Colorectal Dis*. 2022;37:429–435.
23. Hol JC, Burghgraef TA, Rutgers MLW, et al. Comparison of laparoscopic versus robot-assisted versus transanal total mesorectal excision surgery for rectal cancer: a retrospective propensity score-matched cohort study of short-term outcomes. *Br J Surg*. 2021;108:1380–1387.
24. Burghgraef TA, Hol JC, Rutgers ML, et al. Laparoscopic versus robot-assisted versus transanal low anterior resection: 3-year oncologic results for a population-based cohort in experienced centers. *Ann Surg Oncol*. 2022;29:1910–1920.
25. Castor electronic data capture system [Castor website]. Available at: https://www.castoredc.com/electronic-data-capture-system/. Accessed August 1, 2022.
26. D'Souza N, Lord A, Shaw A, et al. The sigmoid take-off: an anatomical imaging definition of the rectum validated on specimen analysis. *Eur J Surg Oncol*. 2020;46:1668–1672.
27. Kusters M, Slater A, Betts M, et al. The treatment of all MRI-defined low rectal cancers in a single expert centre over a 5-year period: is there room for improvement? *Color Dis*. 2016;18:O397–O404.
28. Roodbeen SX, Penna M, Mackenzie H, et al. Transanal total mesorectal excision (TaTME) versus laparoscopic TME for MRI-defined low rectal cancer: a propensity score-matched analysis of oncological outcomes. *Surg Endosc*. 2019;33:2459–2467.
29. Clavien PA, Strasberg SM. Severity grading of surgical complications. *Ann Surg*. 2009;250:197–198.
30. Rahbari NN, Weitz J, Hohenberger W, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the international study group of rectal cancer. *Surgery*. 2010;147:339–351.
31. Nagtegaal ID, Van de Velde CJH, Van Der Worp E, et al; Cooperative Clinical Investigators of the Dutch Colorectal Cancer Group. Macroscopic evaluation of rectal cancer resection specimen: clinical significance of the pathologist in quality control. *J Clin Oncol*. 2002;20:1729–1734.
32. Piessen G, Cabral C, Benoist S, et al. Previous transanal full-thickness excision increases the morbidity of radical resection for rectal cancer. *Color Dis*. 2012;14:445–452.
33. Hompes R, McDonald R, Buskens C, et al; Association of Coloproctology of Great Britain and Ireland Transanal Endoscopic Microsurgery Collaboration. Completion surgery following transanal endoscopic microsurgery: assessment of quality and short- and long-term outcome. *Colorectal Dis*. 2013;15:e576–e581.
34. Junginger T, Goenner U, Hitzler M, et al. Local excision followed by early radical surgery in rectal cancer: long-term outcome. *World J Surg Oncol*. 2019;17:168.
35. Wyatt JNR, Powell SG, Altaf K, et al. Completion total mesorectal excision after transanal local excision of early rectal cancer: a systematic review and meta-analysis. *Dis Colon Rectum*. 2022;65:628–640.
36. Qu H, Liu Y, Bi D-S. Clinical risk factors for anastomotic leakage after laparoscopic anterior resection for rectal cancer: a systematic review and meta-analysis. *Surg Endosc*. 2015;29:3608–3617.
37. Penna M, Hompes R, Arnold S, et al; International TaTME Registry Collaborative. Incidence and risk factors for anastomotic failure in 1594 patients treated by transanal total mesorectal excision results from the international TATME registry. *Ann Surg*. 2019;269:700–711.
38. DCRA. DCRA Jaarverslag 2018. Published 2018. Available at: https://dica.nl/jaarrapportage-2018/dcra. Accessed August 19, 2019
39. Burghgraef TA, Hol JC, Rutgers ML, et al; MIRECA Study Group. Implications of the new MRI-based rectum definition according to the sigmoid take-off: multicentre cohort study. *BJS open*. 2023;7:zrad018.
40. Zinicola R, Nascimbeni R, Cirocchi R, et al. The impact of transanal local excision of early rectal cancer on completion rectal resection without neoadjuvant chemoradiotherapy: a systematic review. *Tech Coloproctol*. 2021;25:997–1010.
41. O'Connell E, Galvin R, McNamara DA, et al. The utility of preoperative radiological evaluation of early rectal neoplasia: a systematic review and meta-analysis. *Color Dis*. 2020;22:1076–1084.
42. Detering R, van Oostendorp SE, Meyer VM, et al; Dutch ColoRectal Audit Group*. MRI cT1–2 rectal cancer staging accuracy: a population-based study. *Br J Surg*. 2020;107:1372–1382.
43. Koedam TWA, Veltcamp Helbach M, Penna M, et al. Short-term outcomes of transanal completion total mesorectal excision (cTaTME) for rectal cancer: a case-matched analysis. *Surg Endosc*. 2019;33:103–109.
44. Letarte F, Raval M, Karimuddin A, et al. Salvage TME following TEM: a possible indication for TaTME. *Tech Coloproctol*. 2018;22:355–361.
45. Coton C, Lefevre JH, Debove C, et al. Does transanal local resection increase morbidity for subsequent total mesorectal excision for early rectal cancer? *Colorectal Dis*. 2019;21:15–22.