BJS Open, 2024, zrae103
https://doi.org/10.1093/bjsopen/zrae103
Original Article

Short-term outcomes after primary total mesorectal excision (TME) versus local excision followed by completion TME for early rectal cancer: population-based propensity-matched study

Annabel S. van Lieshout[1,2,*], Lisanne J. H. Smits[1,2], Julie M. L. Sijmons[2,3,4], Susan van Dieren[2,4], Stefan E. van Oostendorp[5], Pieter J. Tanis[4,6] and Jurriaan B. Tuynman[1]

[1]Department of Surgery, Amsterdam UMC location Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
[2]Treatment and Quality of Life, Cancer Center Amsterdam, Amsterdam, The Netherlands
[3]Dutch Institute for Clinical Auditing, Leiden, The Netherlands
[4]Department of Surgery, Amsterdam UMC location University of Amsterdam, Amsterdam, The Netherlands
[5]Department of Surgery, Rode Kruis Ziekenhuis, Beverwijk, The Netherlands
[6]Department of Surgical Oncology and Gastrointestinal Surgery, Erasmus MC, Rotterdam, The Netherlands

Correspondence to: Annabel S. van Lieshout, Department of Surgery, Amsterdam UMC location Vrije Universiteit Amsterdam, De Boelelaan 1117, Amsterdam, 1081 HV, The Netherlands (e-mail: a.vanlieshout@amsterdamumc.nl)

Abstract

Background: Colorectal cancer screening programmes have led to a shift towards early-stage colorectal cancer, which, in selected cases, can be treated using local excision. However, local excision followed by completion total mesorectal excision (two-stage approach) may be associated with less favourable outcomes than primary total mesorectal excision (one-stage approach). The aim of this population study was to determine the distribution of treatment strategies for early rectal cancer in the Netherlands and to compare the short-term outcomes of primary total mesorectal excision with those of local excision followed by completion total mesorectal excision.

Methods: Short-term data for patients with cT1–2 N0xM0 rectal cancer who underwent local excision only, primary total mesorectal excision, or local excision followed by completion total mesorectal excision between 2012 and 2020 in the Netherlands were collected from the Dutch Colorectal Audit. Patients were categorized according to treatment groups and logistic regressions were performed after multiple imputation and propensity score matching. The primary outcome was the end-ostomy rate.

Results: From 2015 to 2020, the proportion for the two-stage approach increased from 22.3% to 43.9%. After matching, 1062 patients were included. The end-ostomy rate was 16.8% for the primary total mesorectal excision group *versus* 29.6% for the local excision followed by completion total mesorectal excision group ($P < 0.001$). The primary total mesorectal excision group had a higher re-intervention rate than the local excision followed by completion total mesorectal excision group (16.7% *versus* 11.8%; $P = 0.048$). No differences were observed with regard to complications, conversion, diverting ostomies, radical resections, readmissions, and death.

Conclusion: This study shows that, over time, cT1–2 rectal cancer has increasingly been treated using the two-stage approach. However, local excision followed by completion total mesorectal excision seems to be associated with an elevated end-ostomy rate. It is important that clinicians and patients are aware of this risk during shared decision-making.

Introduction

Since the implementation of the colorectal cancer screening programme in the Netherlands in 2014, an incidence shift towards early-stage cancer has been observed[1]. This shift has led to more interest in local therapy preserving the organ, avoiding radical surgery. For rectal cancer, the impact of radical surgery in the form of total mesorectal excision (TME) is relatively high, with associated morbidity, poor functional outcomes, and high ostomy rates that contribute to a decrease in quality of life[2–4]. Therefore, less invasive treatment strategies for early rectal cancer, such as endoscopic or surgical local excision (LE), have gained popularity over the last decade. For pT1 rectal tumours without histopathological risk factors, treatment with LE only is considered sufficient. Risk factors such as poor differentiation, a positive resection margin (R1), lymphovascular invasion, and tumour budding have been shown to be associated with an increased risk of recurrence[5–8]. Therefore, when these risk factors are documented for the resected specimen, early completion TME (cTME) is recommended by guidelines[7,9].

Staging of early rectal cancer using endoscopy, ultrasonography, or MRI is not accurate enough to distinguish low-risk T1 tumours from high-risk T1 and early T2 tumours[10–12]. A possible approach could be performing an LE to obtain a pathological assessment. Subsequently, for those patients with high-risk lesions, a cTME is performed, the so-called two-stage approach. However, a national study showed that 71% of locally

Received: March 14, 2024. **Revised:** June 27, 2024. **Accepted:** July 25, 2024

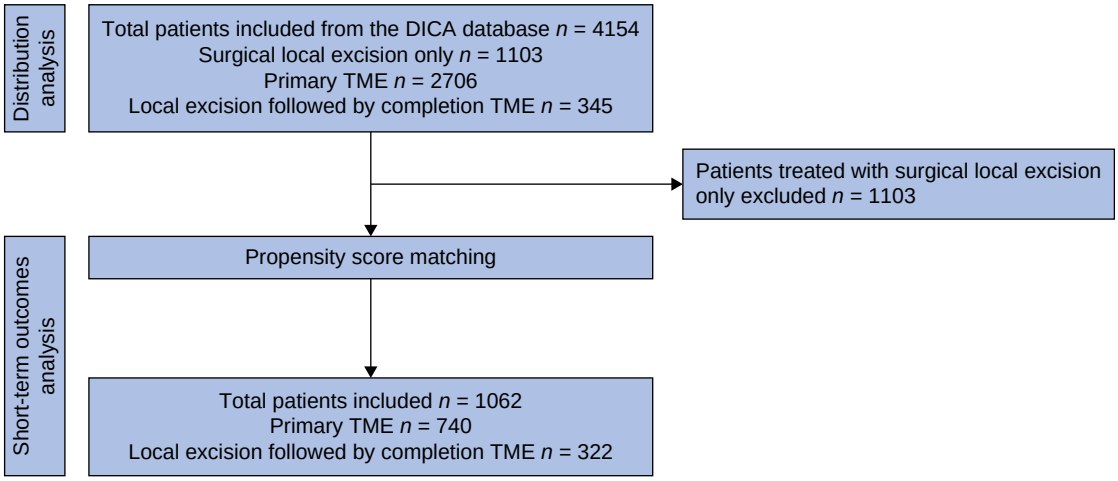

Fig. 1 Flow chart of patient selection

DICA, Dutch Institute for Clinical Auditing; TME, total mesorectal excision.

resected high-risk lesions did not undergo further radical treatment, probably due to the presumed complexity of cTME, as well as patient wishes[13]. Although limited literature is available and small studies have reported conflicting results, cTME may be associated with worse outcomes, including high end-colostomy rates, poor specimen quality, higher risks of rectal perforation, and increased re-intervention rates[14–21]. These outcomes could potentially cause surgeons to opt for a primary TME (that is the one-stage approach) instead of performing an LE first. Therefore, it is important to investigate whether a rectal-sparing LE is a safe first step in treatment for early rectal cancer, avoiding unnecessary undertreatment and overtreatment[2–4]. The aim of this population-based study was to determine the distribution of the chosen treatment strategies (one-stage *versus* two-stage approach) for cT1–2 N0xM0 rectal cancer in the Netherlands between 2012 and 2020 and to compare the short-term outcomes of primary TME with those of LE followed by cTME.

Methods

This study was not pre-registered in an independent, institutional registry.

Patients and outcomes

Patient data for this observational retrospective nationwide cohort study were collected from the national Dutch Colorectal Audit (DCRA), coordinated by the Dutch Institute for Clinical Auditing (DICA). This database contains short-term (less than 90 days) follow-up data for all colorectal cancer patients in the Netherlands who received a surgical intervention. The study included all patients aged greater than or equal to 18 years with cT1–2 N0xM0 rectal carcinoma who underwent a primary TME, a surgical LE, or an LE (endoscopic or surgical) followed by cTME (LE + cTME) between 2012 and 2020. The only exclusion criterion was neoadjuvant treatment. For the first part of the study, outcomes included the distribution of surgical treatment strategies for cT1 and cT2 tumours and the proportion of one-stage and two-stage procedures per year. The primary outcome of the comparison between primary TME and LE + cTME was the end-ostomy rate. Secondary outcomes included postoperative complications within 90 days, conversion rate, diverting ostomy rate, radical (R0) resections (tumour tissue less than or equal to 1 mm from the resection margin), re-interventions, readmissions, and postoperative deaths within 90 days. The postoperative complication pelvic sepsis was defined as anastomotic leakage and/or pelvic abscess formation.

Statistical analysis

Patient characteristics, tumour characteristics, perioperative data, and short-term outcomes are described using descriptive statistics. Categorical data are presented as *n* (%) and continuous variables are presented as mean (95% c.i.). Univariable analyses were performed using logistic regressions. The results are presented as OR (95% c.i.). To reduce potential confounding, multiple imputation by chained equations of missing variables was performed by making five imputation sets using predictive mean matching. Furthermore, propensity score matching was performed using the Matchthem package[22]. Propensity score matching was done based on age, distance to the anorectal junction in mm, ASA grade, and cT category using a variable matching ratio, with a maximum of 1 : 3[23]. $P < 0.050$ was considered statistically significant. All statistical analyses were performed using both SPSS® (IBM, Armonk, NY, USA; version 26) and R (version 4.2.1).

Results

Patient and tumour characteristics

Between 2012 and 2020, a total of 4154 patients received surgical treatment for cT1–2 N0xM0 rectal carcinoma in the Netherlands and were included in this study. Of these patients, 1103 underwent LE only, 2706 underwent primary TME, and 345 underwent LE + cTME. A flow chart of patient selection is presented in *Fig. 1*. Patient and tumour characteristics of these unmatched groups are presented in *Table S1*.

Distribution of chosen treatment per year

Figure 2 shows the number of surgical procedures for cT1–2 rectal cancer per year in the Netherlands. From 2012 until 2016, the total number of surgical procedures for early-stage rectal cancer increased from 193 to 663, with a steep incline in 2014. Subsequently, this number decreased from 663 in 2016 to 424 in 2020, which corresponds to the observed decline in the overall incidence of rectal carcinoma in the Netherlands during these years, shown in *Fig. 3*[1].

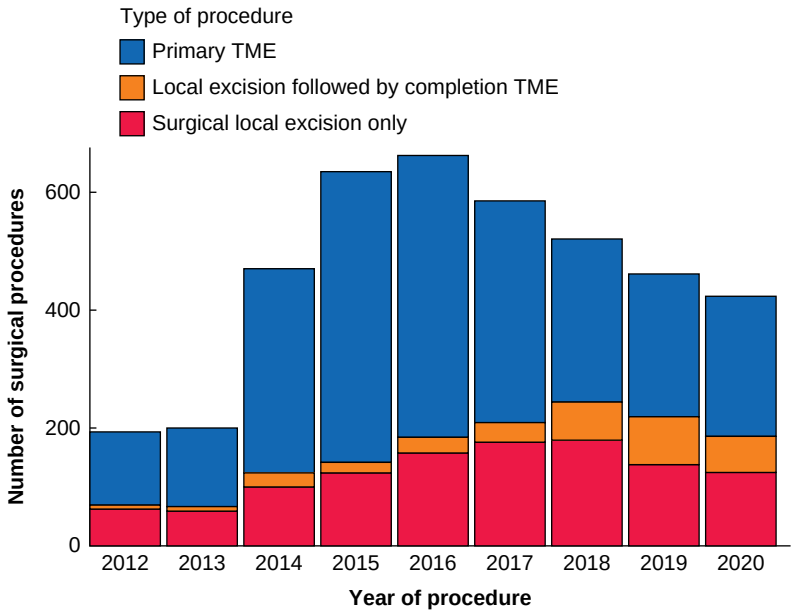

Fig. 2 Number of surgical procedures for cT1–2 rectal cancer per year in the Netherlands
TME, total mesorectal excision.

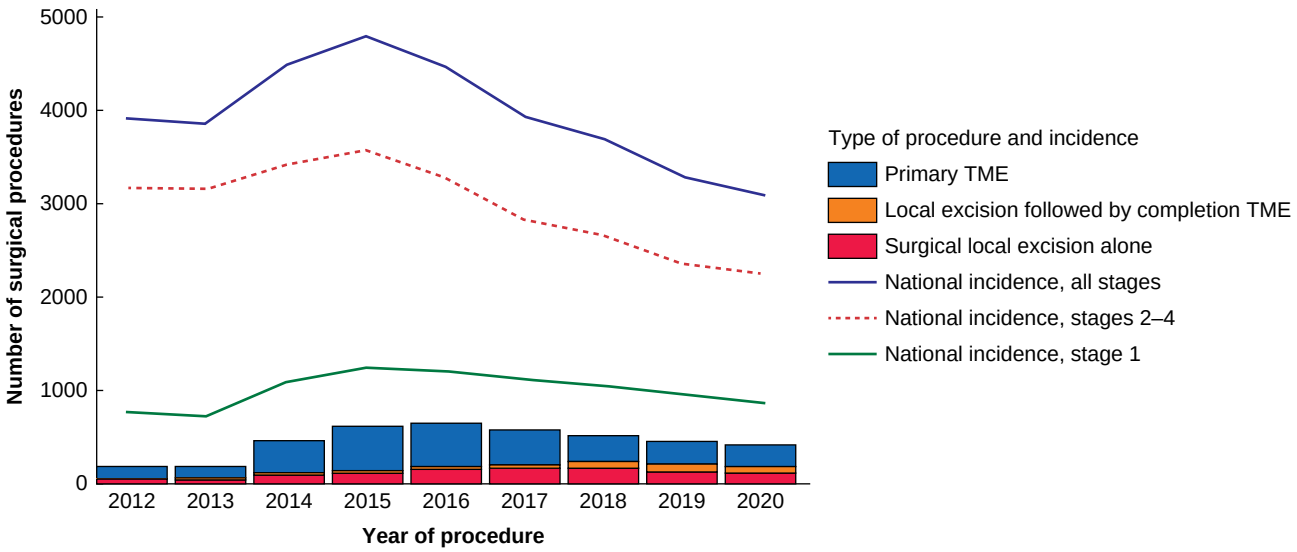

Fig. 3 Number of surgical procedures for cT1–2 rectal cancer per year in the Netherlands relative to the national incidence (all stages, stages 2–4, and stage 1)
TME, total mesorectal excision.

The proportions of each treatment group per year are presented in *Fig. 4*. For primary TME, percentages varied over the years: 64.2% in 2012 compared with 56.1% in 2020. The same applies for LE only: 31.6% in 2012 compared with 28.8% in 2020. Although the primary TME and LE percentages vary (in opposite directions) and with no clear trend over the years, the percentage of patients treated with LE + cTME seems to have increased from 2015 onwards; the percentages were 3.1% and 15.1% in 2015 and 2020 respectively.

In addition, when separating groups into one-stage (primary TME) and two-stage (surgical LE only and LE + cTME) approaches, a decreasing trend regarding the one-stage approach can be observed from 2015 onwards (77.7% in 2015 and 56.1% in 2020), as well as an increase in the two-stage approach (22.3% in 2015 and 43.9% in 2020) (*Fig. 5*). In particular, from 2018 to 2020, the percentages for both approaches are close to 50% (*Fig. 5*). Similar charts for cT1 and cT2 tumours are presented in *Figure S1* and *Figure S2* respectively. From 2015 to 2020, an increase in the two-stage approach can be seen for cT1 and cT2 tumours: 54.7% in 2015 and 87.2% in 2020 for cT1 tumours and 8.3% in 2015 and 24.1% in 2020 for cT2 tumours.

Primary total mesorectal excision *versus* completion total mesorectal excision

Table 1 shows the patient and tumour characteristics of the primary TME group and LE + cTME group before and after

propensity score matching with corresponding standardized mean differences (SMDs).

Before matching, the primary TME group included older patients (68 *versus* 66.4 years) and more cT2 tumours (85.7% *versus* 42.3%). For the primary TME group, the tumours were located more proximally, with a mean distance from the anorectal junction of 90.6 mm *versus* 59.5 mm for the LE + cTME group ($P < 0.001$). After propensity matching for age, distance to the anorectal junction, ASA grade, and cT category, the primary TME group comprised 740 patients and the LE + cTME group comprised 322 patients. After matching, differences in cT category and distance from the anorectal junction remained significant. Univariable logistic regression analyses with corresponding ORs after propensity score matching of the primary and secondary outcomes are shown in *Table 2*.

Perioperative outcomes

Perioperative outcomes are presented in *Table 3*. After matching, the end-ostomy rate was significantly higher for patients who underwent LE + cTME compared with the patients who underwent primary TME (29.6% *versus* 16.8%; OR 2.21 (95% c.i. 1.59 to 3.05); $P < 0.001$). In addition, the mean time interval between diagnosis and first surgery was longer for the LE + cTME group compared with the primary TME group (LE + cTME 48.0 days *versus* primary TME 42.6 days; $P = 0.025$). Conversion rates were comparable for the two groups: 4.7% and 5.0% for the primary TME group and the LE + cTME group respectively (OR 1.04 (95% c.i. 0.52 to 2.08); $P = 0.911$). The diverting ostomy rate was similar for the two groups (22.7% for the primary TME group *versus* 19.2% for the LE + cTME group; OR 0.815 (95% c.i. 0.56 to 1.18); $P = 0.266$).

Histopathological outcomes

Histopathological outcomes are presented in *Table 4*. After matching, the primary TME group included slightly more pT1 tumours (39.9% *versus* 35.4%; $P = 0.001$) and pT3 tumours (19.0% *versus* 16.4%; $P < 0.001$), whereas the LE + cTME group included slightly more pT2 tumours (38.1% *versus* 37.6%; $P = 0.003$) and pN1 tumours (20.1% *versus* 17.9%; $P = 0.046$). Also, the LE + cTME group included more tumours with a poor differentiation grade (6.9% *versus* 1.7%; $P < 0.001$) and more mucinous carcinomas (5.4% *versus* 2.6%; $P = 0.038$). All other histopathological outcomes, including the rate of R0 resections, were comparable for the two groups (*Table 4*).

Postoperative outcomes

Table 5 shows the postoperative outcomes of both groups. Complications within 90 days occurred in 32.6% of primary TME patients and in 30.0% of LE + cTME patients (OR 0.89 (95% c.i. 0.66 to 1.21); $P = 0.448$). More detailed analyses revealed that pulmonary events occurred more frequently in primary TME patients (4.6% *versus* 1.6%; $P = 0.023$), whereas more LE + cTME patients developed an ileus (5.4% *versus* 2.4%; $P = 0.019$). Primary TME patients required more re-interventions (16.7% *versus* 11.8%; OR 0.67 (95% c.i. 0.45 to 1.00); $P = 0.047$). No differences between primary TME patients and LE + cTME patients were observed with regard to anastomotic leakage (13.0% *versus* 10.6% respectively; $P = 0.381$), pelvic sepsis (13.8% *versus* 11.5% respectively; $P = 0.418$), surgical complications (24.0% *versus* 21.4% respectively; $P = 0.365$), readmissions (12.8% *versus* 13.2% respectively; $P = 0.877$), and deaths within 90 days (1.1% *versus* 0.6% respectively; $P = 0.463$).

Discussion

This nationwide population study evaluated treatment strategies in early rectal cancer between 2012 and 2020 and compared the short-term outcomes of primary TME with those of LE + cTME. An increased incidence of two-stage procedures for both cT1 and cT2 rectal cancer was noted since 2015. Matched comparison revealed a significantly higher end-ostomy rate of 29.6% for the LE + cTME group *versus* 16.8% for the primary TME group (OR 2.21 (95% c.i. 1.59 to 3.05)). Although more re-interventions were observed for patients who underwent primary TME compared with patients who underwent LE + cTME, complication rates within 90 days were similar for both groups of patients.

Since the introduction of the bowel cancer screening programme in the Netherlands in 2014, the number of surgical procedures for both rectal carcinomas in general (stages 1–4) and early-stage carcinomas has increased temporarily. From 2015, there has been a steep decline in the total number of surgical interventions for all stages; however, this is not seen for early-stage rectal tumours, for which the number of procedures has decreased minimally. A previous study comparing the effect of colorectal screening programmes in European countries showed a similar peak and subsequent decline in Denmark, Belgium, and Slovenia[24]. These countries showed a rapid screening uptake and a high screening coverage. In contrast, colorectal cancer incidence either grew or remained steady in nations without extensive screening programmes, including Bulgaria, Estonia, and Norway[24]. Besides the relative increase in treatment of early-stage rectal cancer from 2015 to 2020, it seems that the treatment approach has changed, reflecting the demand for organ preservation and the expanding possibilities in piecemeal and *en-bloc* resection techniques. Whereas, in 2012, about two-thirds of patients with early-stage tumours were treated using a one-stage approach (primary TME), the two-stage approach (LE only or LE + cTME) has gained popularity over recent years and accounted for nearly half of all procedures in 2020. Nevertheless, the safety of the two-stage approach is still under debate.

This study showed a significantly higher end-ostomy rate within 90 days after surgery for LE + cTME patients compared with primary TME patients after propensity score matching (29.6% *versus* 16.8%). A potential explanation might be impaired healing of the anastomosis due to the fibrotic scar or local inflammation caused by the prior LE, which may contribute to the complexity of cTME[15]. A nationwide study performed in Norway also showed an increased end-colostomy rate after LE + cTME for early-stage rectal cancer. However, the reported ostomy rates were much higher in both groups (53% for the LE + cTME group and 32% for the primary TME group) and the reported difference was no longer significant after propensity score matching[25]. Another study showed a significantly higher ostomy rate for LE + cTME patients compared with primary TME patients (50.8% *versus* 45.9%; $P = 0.006$)[26]. The reported differences in ostomy rates could possibly be explained by the inclusion of abdominoperineal resections and Hartmann's procedures, the prolonged follow-up of 5 years compared with 90 days, and the inclusion of advanced stages of rectal cancer. It is important to acknowledge that the increased ostomy rate may be due to multiple factors, including the tumour's location, the patient's initial wish for organ preservation, surgeons' preferences, and the selection of tumours with unfavourable prognostic factors for the two-stage approach. Unfortunately,

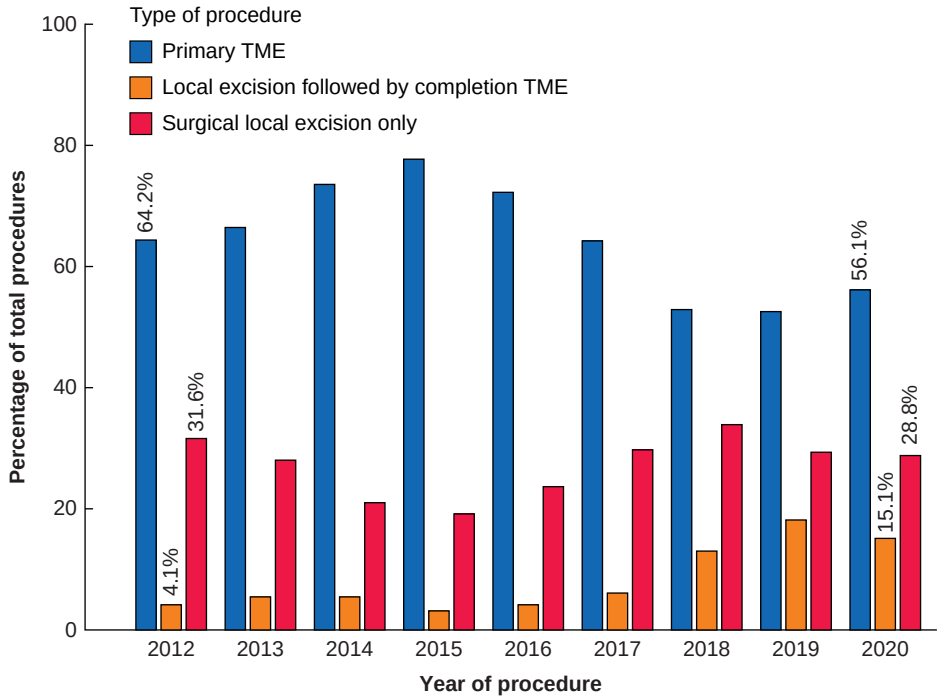

Fig. 4 Distribution of different surgical procedures for cT1–2 rectal cancer over time: primary TME *versus* local excision followed by completion TME *versus* surgical local excision only

TME, total mesorectal excision.

information on the shared decision process was not available in the DICA registry.

The comparable overall complication rates for the two groups is in line with previous studies showing no significant differences between primary TME and LE + cTME[15,17–21,27]. However, the higher rate of re-interventions for primary TME patients compared with LE + cTME patients (16.7% *versus* 11.8%) is in contrast with the latest meta-analysis, which showed a higher rate for LE + cTME compared with primary TME (11.6% *versus* 6.4%; OR 4.28 (95% c.i. 1.10 to 16.76); $P < 0.04$)[19]. This difference may be caused by the anastomosis rate for the primary TME group compared with the LE + cTME group and the small numbers of studies and patients included in the meta-analysis. Another possible explanation is the difference in type of LE before cTME. The meta-analysis focused on surgical full-thickness excisions only, whereas the present study included both full-thickness excisions and excisions that used more superficial and less invasive LE techniques, such as submucosal and intermuscular dissections, which may explain the lower rate of re-interventions for the LE + cTME group, due to less scar tissue and fewer anastomotic problems. Besides one study showing more surgical complications for the LE + cTME group (57.1% *versus* 20%; $P = 0.048$)[20], other studies correspond to the present data, showing no differences between the two groups[15,18]. Although percentages of diverting ileostomies differ widely among studies (ranging between 15.3% and 100%), no differences were found between primary TME and LE + cTME[14,15,20,21,26]. In addition, the comparable rates of conversion, R0 resections, anastomotic leakage, readmissions, and death between primary TME and LE + cTME are consistent with previous studies[14,15,17–21,25,27].

Current histological risk stratification manages to recognize a substantial proportion of T1 tumours as low risk. As a result of the two-stage approach, these patients are treated sufficiently using LE only and benefit from lesser morbidity and functional complaints compared with primary TME treatment[8,28,29]. However, for the remaining proportion of patients, for whom histopathological assessment reveals a high-risk pT1 or pT2 tumour, completion surgery is recommended and appears to be associated with an increased risk of end colostomy compared with primary TME. This is controversial and concerning, as end colostomies are known to be associated with an impaired quality of life, whereas the two-stage approach aims to result in improved quality of life[30,31]. Moreover, another study showed that the risk of an ostomy is one of the main reasons for patients with rectal cancer not to opt for surgery[32]. Despite the fact that accurate preoperative staging of early rectal cancer is challenging, it is important to be aware that LE before TME surgery increases the risk of an end colostomy and to inform patients on this matter before the start of treatment[29]. For patients with very low rectal cancers requiring abdominal perineal resection as primary surgery, LE may be particularly suitable, as concerns about the increased risk of end-ostomy are not applicable. Although not included in this study, it is crucial to emphasize the significance of long-term oncological outcomes, alongside morbidity and ostomy rates, for informed shared decision-making. This study focuses solely on short-term morbidity and ostomy rates, as previously published studies showed compromised short-term outcomes after two-stage procedures. Limited data are available regarding long-term outcomes of cTME; however, a recent study showed that cTME does not compromise oncological outcomes compared with primary resection[33]. Valuable insights are expected from the ongoing TESAR trial, a large randomized national study that will assess oncological outcomes, including local recurrence rate and overall survival, after cTME surgery in comparison with those after adjuvant chemotherapy after LE and

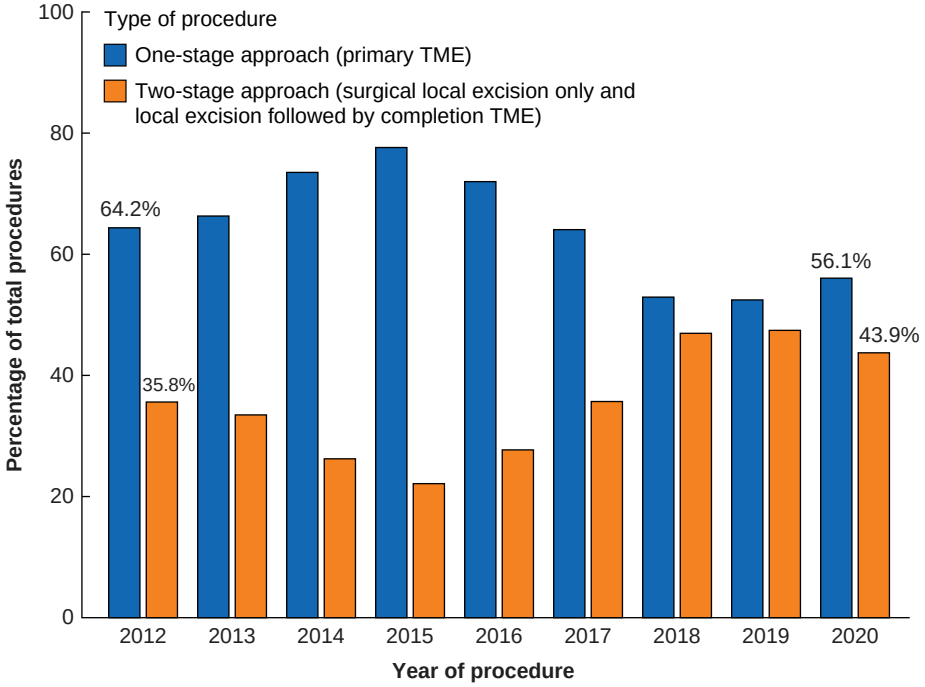

Fig. 5 Distribution of the one-stage approach and the two-stage approach for cT1–2 rectal cancer over time

TME, total mesorectal excision.

Table 1 Patient and tumour characteristics before and after propensity score matching

	Unmatched cohort				Matched cohort			
	Primary TME ($n = 2706$)	Local excision followed by completion TME ($n = 345$)	P	SMD	Primary TME ($n = 740$)	Local excision followed by completion TME ($n = 322$)	P	SMD
Female	1082 (40.0)	148 (42.9)	0.302	0.059	322 (43.5)	138 (42.8)	0.817	0.016
Age (years), mean (95% c.i.)	68.0 (67.7,68.4)	66.4 (65.4,67.3)	0.002*	0.181	66.8 (65.9,67.8)	66.4 (65.4,67.4)	0.544	0.046
BMI (kg/m^2), mean (95% c.i.)	26.5 (26.3,26.7)	26.3 (25.9,26.7)	0.449	0.044	26.4 (26.0,26.8)	26.4 (25.9,26.8)	0.874	0.012
ASA grade			0.683	0.024			0.415	0.055
I–II	2187 (80.8)	282 (81.7)			152 (20.6)	56 (17.3)		
III–IV	519 (19.2)	63 (18.3)			465 (62.9)	206 (64.1)		
Distance from ARJ (mm), mean (95% c.i.)	90.6 (89.0,92.3)	59.5 (54.6,64.3)	<0.001*	0.686	71.2 (67.0,75.3)	64.5 (59.7,69.3)	0.040*	0.156
cT			<0.001*	1.013			<0.001*	0.252
cT1	387 (14.3)	199 (57.7)			312 (42.2)	176 (54.7)		
cT2	2319 (85.7)	146 (42.3)			427 (57.8)	146 (45.3)		
cN			0.004*	0.141			0.104	0.132
cN0	2665 (98.5)	332 (96.2)			728 (98.4)	310 (96.3)		
cNx	41 (1.5)	13 (3.8)			12 (1.6)	12 (3.7)		

Values are *n* (%) unless otherwise indicated. *Statistically significant. TME, total mesorectal excision; SMD, standardized mean difference; ARJ, anorectal junction.

the wait-and-see approach, significantly contributing to the decision-making process[34].

Given that all Dutch hospitals are mandated to register their surgical data with the DICA, this study provides a high-quality and realistic reflection of the current surgical treatment of early rectal cancer in the Netherlands. Propensity matching for four relevant factors improved the comparability of primary TME and LE + cTME for a large group of patients. Although there were minor remaining differences in cT category and distance from the anorectal junction in the matched cohort, SMDs dropped significantly, thereby minimizing selection bias.

This study has several limitations. The design of the study based on the national DICA registry and the accompanying lack of data, including the type of LE, tumour diameter, location of the scar, histopathological risk factors of the LE specimen, timing of completion surgery, and information on the decision-making process (surgeon preferences in choice of treatment and patient wishes), causes selection bias and is therefore a limitation of this study. As the DCRA database only contains data for patients who received a surgical intervention, it was not possible to include patients who underwent endoscopic LE only. Therefore, it was not possible to determine

Table 2 Univariable logistic regression analyses of primary and secondary outcomes after propensity score matching

	Primary TME (*n* = 740)	Local excision followed by completion TME (*n* = 322)	Univariable OR (95% c.i.)	*P*
Conversion*	33 (4.7)	16 (5.0)	1.04 (0.52,2.08)	0.911
Anastomosis	603 (81.5)	215 (66.6)	0.45 (0.33,0.62)	<0.001†
Diverting ostomy	168 (22.7)	62 (19.2)	0.81 (0.56,1.17)	0.266
End-ostomy	125 (16.8)	95 (29.6)	2.21 (1.59,3.05)	<0.001†
R0 (>1 mm)	730 (98.7)	318 (98.7)	1.10 (0.201,5.72)	0.904
Surgical complication	178 (24.0)	69 (21.4)	0.86 (0.62,1.20)	0.365
Anastomotic leakage‡	79 (13.0)	23 (10.6)	0.79 (0.47,1.34)	0.381
Readmission <90 days	95 (12.8)	42 (13.2)	1.03 (0.67,1.60)	0.877
Re-intervention	124 (16.7)	38 (11.8)	0.67 (0.45,1.00)	0.047†
Deceased <90 days	8 (1.1)	2 (0.6)	0.55 (0.11,2.72)	0.463
Complication <90 days	241 (32.6)	97 (30.0)	0.89 (0.66,1.21)	0.448

Values are *n* (%). *Primarily open procedures excluded. †Statistically significant. ‡Procedures without anastomosis excluded. TME, total mesorectal excision.

Table 3 Perioperative outcomes after propensity score matching

	Primary TME (*n* = 740)	Local excision followed by completion TME (*n* = 322)	*P*
Time between diagnosis and first surgery (days), mean (95% c.i.)	42.6 (40.3,45.0)	48.0 (43.6,52.5)	0.025*
Conversion†	32.8 (4.7)	15.6 (5.0)	0.911
Diverting ostomy	168 (22.7)	62 (19.2)	0.266
End-ostomy	125 (16.8)	95 (29.6)	<0.001*
Anastomosis	603 (81.5)	215 (66.6)	<0.001*

Values are *n* (%) unless otherwise indicated. *Statistically significant. †Primarily open procedures excluded. TME, total mesorectal excision.

Table 4 Histopathological outcomes after propensity score matching

	Primary TME (*n* = 740)	Local excision followed by completion TME (*n* = 322)	*P*
pT			
pT0	12 (1.6)	20 (6.1)	Reference
pT1	295 (39.9)	114 (35.4)	0.001*
pT2	277 (37.6)	123 (38.1)	0.003*
pT3	145 (19.0)	53 (16.4)	<0.001*
pT4	6 (0.8)	1 (0.4)	0.079
pTis	1 (0.1)	1 (0.3)	>0.999
pTx	7 (0.9)	3 (0.9)	0.126
Missing	1 (0.1)	7 (2.3)	–
pN			
pN0	563 (76.1)	237 (73.6)	Reference
pN1	132 (17.9)	65 (20.1)	0.046*
pN2	31 (4.2)	9 (2.9)	0.059
pNx	8 (1.1)	2 (0.5)	0.041*
Missing	5 (0.7)	9 (2.9)	–
Venous invasion			
No	309 (41.8)	178 (55.4)	Reference
Yes	72 (9.8)	47 (14.5)	0.599
Missing	358 (48.4)	97 (30.1)	–
CRM			
Not involved	650 (87.9)	221 (68.5)	Reference
Involved	3 (0.4)	1 (0.4)	0.784
Missing	87 (11.7)	100 (31.1)	–
R classification			
>1 mm	724 (97.9)	314 (97.5)	Reference
0–1 mm	1 (0.2)	1 (0.6)	>0.999
Tumour in resection plane	8 (1.1)	2 (0.7)	0.696
Missing	6 (0.9)	4 (1.2)	–
Differentiation grade			
Well to moderate	692 (93.5)	263 (81.7)	Reference
Poor	13 (1.7)	22 (6.9)	<0.001*
Missing	35 (4.8)	37 (11.2)	–
Histological type			
Adenocarcinoma	684 (92.4)	294 (91.2)	Reference
Mucinous carcinoma	20 (2.6)	17 (5.4)	0.038*
Signet cell carcinoma	4 (0.6)	0 (0.0)	0.999
Other	7 (0.9)	4 (1.2)	0.652
Missing	25 (3.4)	7 (2.2)	–

Values are *n* (%). *Statistically significant. TME, total mesorectal excision; CRM, circumferential resection margin.

the percentage of patients who benefitted from the two-stage approach and for whom radical surgery was prevented. For patients treated with LE + cTME, data on both endoscopic and surgical LE were available and both techniques were included. In addition, the DCRA database included missing variables due to alterations in registration protocols during the inclusion interval. Multiple imputation was used to account for the missing data instead of excluding many patients[35]. Moreover, hospital volume and surgeons' experience may influence short-term outcomes, such as end-colostomy rates. Unfortunately, it was not possible to compare outcomes for low- and high-volume centres. Lastly, no distinction could be made between TME approaches (including laparoscopic TME, transanal TME, and robotic TME) due to high percentages of missing variables and relatively small groups. Nevertheless, these population-based data are highly valuable to detect real practice and publication bias present in cohort studies of specialized centres is avoided. As transanal TME may provide a better surgical overview of the tumour or fibrotic scar, future research should focus on whether the TME approach influences the end-ostomy rate.

This nationwide study on early rectal cancer showed an increase in the popularity of the two-stage approach (LE potentially followed by completion surgery) since 2015. Nevertheless, LE followed by completion surgery was associated with a higher end-ostomy rate compared with primary TME. Despite the rate of re-interventions, which was higher for primary TME, other outcomes, including complications, conversion rate, diverting ostomy rate, radical (R0) resection, readmissions, and death rate, were similar for both groups. It is important that clinicians and patients with early rectal cancer are aware of the higher end-ostomy risk associated with the two-stage approach when making a balanced and shared decision with regard to treatment.

Table 5 Postoperative outcomes after propensity score matching

	Primary TME ($n = 740$)	Local excision followed by completion TME ($n = 322$)	*P*
Complication <90 days	241 (32.6)	97 (30.0)	0.448
Surgical complication	178 (24.0)	69 (21.4)	0.365
Complication specified			
Anastomotic leakage*	79 (13.0)	23 (10.6)	0.381
Abscess*	7 (1.2)	3 (1.3)	0.940
Pelvic sepsis*	83 (13.8)	25 (11.5)	0.418
Bleeding	5 (0.6)	5 (1.5)	0.228
Ileus	18 (2.4)	17 (5.4)	0.019†
Fascial dehiscence	3 (0.4)	0 (0.0)	0.994
Bowel perforation	2 (0.2)	3 (0.9)	0.178
Urinary tract damage	0 (0.0)	2 (0.6)	0.991
Surgical-site infection	7 (0.9)	5 (1.5)	0.411
Pulmonary event	34 (4.6)	5 (1.6)	0.023†
Cardiac event	14 (0.2)	7 (2.0)	0.896
Thromboembolism	9 (1.2)	3 (0.9)	0.754
Other infectious event	33 (4.5)	15 (4.7)	0.883
Neurological event	12 (3.2)	3 (0.9)	0.367
Other	63 (8.5)	20 (6.2)	0.200
Re-intervention	124 (16.7)	38 (11.8)	0.047†
Re-intervention type‡			
Laparoscopy	4 (3.2)	18 (47.4)	Reference
Radiological	2 (1.6)	1 (2.6)	0.994
Endoscopic	2 (1.6)	1 (2.6)	0.825
Laparotomic	35 (28.2)	6 (15.8)	<0.001†
Other	15 (12.1)	5 (13.2)	0.405
Re-intervention unknown	66 (53.2)	7 (18.4)	0.082
Readmission <90 days	95 (12.8)	42 (13.2)	0.877
ICU admission	91 (12.3)	28 (8.8)	0.116
Deceased <90 days	8 (1.1)	2 (0.6)	0.463

Values are *n* (%). *Procedures without anastomosis excluded. †Statistically significant. ‡Values are *n* (%) of re-interventions. TME, total mesorectal excision.

Funding

The authors have no funding to declare.

Author contributions

Annabel S. van Lieshout (Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Visualization, Writing—original draft, Writing—review & editing), Lisanne J. H. Smits (Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Visualization, Writing—original draft, Writing—review & editing), Julie M. L. Sijmons (Data curation, Methodology, Resources, Writing—review & editing), Susan van Dieren (Conceptualization, Formal analysis, Methodology, Writing—original draft, Writing—review & editing), Stefan E. van Oostendorp (Conceptualization, Data curation, Methodology, Supervision, Writing—original draft, Writing—review & editing), Pieter J. Tanis (Conceptualization, Formal analysis, Investigation, Methodology, Resources, Supervision, Writing—original draft, Writing—review & editing), and Jurriaan B. Tuynman (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Visualization, Writing—original draft, Writing—review & editing)

Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS Open* online.

Data availability

All data supporting the findings of this study are available from the corresponding author upon reasonable request.

References

1. Integraal Kankercentrum Nederland (IKNL). *Cijfers Darmkanker*. 2022. https://iknl.nl/kankersoorten/darmkanker/registratie (accessed 19 January 2023)
2. Lezoche E, Paganini AM, Fabiani B, Balla A, Vestri A, Pescatori L *et al.* Quality-of-life impairment after endoluminal locoregional resection and laparoscopic total mesorectal excision. *Surg Endosc* 2014;**28**:227–234
3. Traa MJ, Orsini RG, Den Oudsten BL, De Vries J, Roukema JA, Bosman SJ *et al.* Measuring the health-related quality of life and sexual functioning of patients with rectal cancer: does type of treatment matter? *Int J Cancer* 2014;**134**:979–987
4. van der Heijden JAG, Koeter T, Smits LJH, Sietses C, Tuynman JB, Maaskant-Braat AJG *et al.* Functional complaints and quality of life after transanal total mesorectal excision: a meta-analysis. *Br J Surg* 2020;**107**:489–498
5. Borstlap WAA, van Oostendorp SE, Klaver CEL, Hahnloser D, Cunningham C, Rullier E *et al.* Organ preservation in rectal cancer: a synopsis of current guidelines. *Colorectal Dis* 2018;**20**:201–210
6. Backes Y, Elias SG, Groen JN, Schwartz MP, Wolfhagen FHJ, Geesing JMJ *et al.* Histologic factors associated with need for surgery in patients with pedunculated T1 colorectal carcinomas. *Gastroenterology* 2018;**154**:1647–1659
7. Hashiguchi Y, Muro K, Saito Y, Ito Y, Ajioka Y, Hamaguchi T *et al.* Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. *Int J Clin Oncol* 2020;**25**:1–42
8. van Oostendorp SE, Smits LJH, Vroom Y, Detering R, Heymans MW, Moons LMG *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. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A *et al.* Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2017;**28**:iv22–iv40
10. Detering R, Oostendorp SE, Meyer VM, Dieren S, Bos ACRK, Dekker JWT *et al.* MRI cT1–2 rectal cancer staging accuracy: a population-based study. *Br J Surg* 2020;**107**:1372–1382
11. Marusch F, Ptok H, Sahm M, Schmidt U, Ridwelski K, Gastinger I *et al.* Endorectal ultrasound in rectal carcinoma—do the literature results really correspond to the realities of routine clinical care? *Endoscopy* 2011;**43**:425–431
12. Ashraf S, Hompes R, Slater A, Lindsey I, Bach S, Mortensen NJ *et al.* A critical appraisal of endorectal ultrasound and transanal endoscopic microsurgery and decision-making in early rectal cancer. *Colorectal Dis* 2012;**14**:821–826
13. van Groningen JT, van Hagen P, Tollenaar R, Tuynman JB, de Mheen PJM, Doornebosch PG *et al.* Evaluation of a completion total mesorectal excision in patients after local excision of rectal cancer: a word of caution. *J Natl Compr Canc Netw* 2018;**16**:822–828

14. Hompes R, McDonald R, Buskens C, Lindsey I, Armitage N, Hill J *et al.* Completion surgery following transanal endoscopic microsurgery: assessment of quality and short- and long-term outcome. *Colorectal Dis* 2013;**15**:e576–e581
15. Levic K, Bulut O, Hesselfeldt P, Bulow S. 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
16. Serra-Aracil X, Galvez Saldana A, Mora-Lopez LL, Montes N, Pallisera-Lloveras A, Serra-Pla S *et al.* Completion surgery in unfavorable rectal cancer after transanal endoscopic microsurgery: does it achieve satisfactory sphincter preservation, quality of total mesorectal excision specimen, and long-term oncological outcomes? *Dis Colon Rectum* 2021;**64**:200–208
17. Levic Souzani K, Bulut O, Kuhlmann TP, Gögenur I, Bisgaard T. Completion total mesorectal excision following transanal endoscopic microsurgery does not compromise outcomes in patients with rectal cancer. *Surg Endosc* 2022;**36**:1181–1190
18. Coton C, Lefevre JH, Debove C, Creavin B, Chafai N, Tiret E *et al.* Does transanal local resection increase morbidity for subsequent total mesorectal excision for early rectal cancer? *Colorectal Dis* 2019;**21**:15–22
19. Eid Y, Alves A, Lubrano J, Menahem B. Does previous transanal excision for early rectal cancer impair surgical outcomes and pathologic findings of completion total mesorectal excision? Results of a systematic review of the literature. *J Visc Surg* 2018;**155**:445–452
20. Piessen G, Cabral C, Benoist S, Penna C, Nordlinger B. Previous transanal full-thickness excision increases the morbidity of radical resection for rectal cancer. *Colorectal Dis* 2012;**14**:445–452
21. Morino M, Allaix ME, Arolfo S, Arezzo A. Previous transanal endoscopic microsurgery for rectal cancer represents a risk factor for an increased abdominoperineal resection rate. *Surg Endosc* 2013;**27**:3315–3321
22. Pishgar F, Greifer N, Leyrat C, Stuart E. MatchThem:: matching and weighting after multiple imputation. *R J* 2021;**13**:228
23. Ming K, Rosenbaum PR. Substantial gains in bias reduction from matching with a variable number of controls. *Biometrics* 2000;**56**: 118–124
24. Cardoso R, Guo F, Heisser T, Hackl M, Ihle P, De Schutter H *et al.* Colorectal cancer incidence, mortality, and stage distribution in European countries in the colorectal cancer screening era: an international population-based study. *Lancet Oncol* 2021;**22**: 1002–1013
25. Lossius WJ, Stornes T, Myklebust TA, Endreseth BH, Wibe A. Completion surgery vs. primary TME for early rectal cancer: a national study. *Int J Colorectal Dis* 2022;**37**:429–435
26. van Gijn W, Brehm V, de Graaf E, Neijenhuis PA, Stassen LP, Leijtens JW *et al.* Unexpected rectal cancer after TEM: outcome of completion surgery compared with primary TME. *Eur J Surg Oncol* 2013;**39**:1225–1229
27. Overwater A, Kessels K, Elias SG, Backes Y, Spanier BWM, Seerden TCJ *et al.* Endoscopic resection of high-risk T1 colorectal carcinoma prior to surgical resection has no adverse effect on long-term outcomes. *Gut* 2018;**67**:284–290
28. Dekkers N, Dang H, van der Kraan J, le Cessie S, Oldenburg PP, Schoones JW *et al.* Risk of recurrence after local resection of T1 rectal cancer: a meta-analysis with meta-regression. *Surg Endosc* 2022;**36**:9156–9168
29. Smits LJH, van Lieshout AS, Grüter AAJ, Horsthuis K, Tuynman JB. Multidisciplinary management of early rectal cancer—the role of surgical local excision in current and future clinical practice. *Surg Oncol* 2022;**40**:101687
30. Näsvall P, Dahlstrand U, Löwenmark T, Rutegård J, Gunnarsson U, Strigård K. Quality of life in patients with a permanent stoma after rectal cancer surgery. *Qual Life Res* 2017;**26**:55–64
31. Ross L, Abild-Nielsen AG, Thomsen BL, Karlsen RV, Boesen EH, Johansen C. Quality of life of Danish colorectal cancer patients with and without a stoma. *Support Care Cancer* 2007; **15**:505–513
32. van der Valk MJM, van der Sande ME, Toebes RE, Breukink SO, Bröker MEE, Doornebosch PG *et al.* Importance of patient reported and clinical outcomes for patients with locally advanced rectal cancer and their treating physicians. Do clinicians know what patients want? *Eur J Surg Oncol* 2020;**46**: 1634–1641
33. Burghgraef TA, Rutgers ML, Leijtens JWA, Tuyman JB, Consten ECJ, Hompes R. Completion total mesorectal excision: a case-matched comparison with primary resection. *Ann Surg Open* 2023;**4**:e327
34. Borstlap WA, Tanis PJ, Koedam TW, Marijnen CA, Cunningham C, Dekker E *et al.* A multi-centred randomised trial of radical surgery versus adjuvant chemoradiotherapy after local excision for early rectal cancer. *BMC Cancer* 2016;**16**:513
35. Pedersen AB, Mikkelsen EM, Cronin-Fenton D, Kristensen NR, Pham TM, Pedersen L *et al.* Missing data and multiple imputation in clinical epidemiological research. *Clin Epidemiol* 2017;**9**:157–166