



# Transanal total mesorectal excision: how are we doing so far?

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Received 14 September 2018; accepted 25 February 2019; Accepted Article Online 7 March 2019

## Abstract

**Aim** This subgroup analysis of a prospective multicentre cohort study aims to compare postoperative morbidity between transanal total mesorectal excision (TaTME) and laparoscopic total mesorectal excision (LaTME).

**Method** The study was designed as a subgroup analysis of a prospective multicentre cohort study. Patients undergoing TaTME or LaTME for rectal cancer were selected. All patients were followed up until the first visit to the outpatient clinic after hospital discharge. Postoperative complications were classified according to the Clavien–Dindo classification and the comprehensive complication index (CCI). Propensity score matching was performed.

**Results** In total, 220 patients were selected from the overall prospective multicentre cohort study. After propensity score matching, 48 patients from each group were compared. The median tumour height for TaTME was 10.0 cm (6.0–10.8) and for LaTME was 9.5 cm (7.0–12.0) ( $P = 0.459$ ). The duration of surgery and anaesthesia were both significantly longer for TaTME (221 *vs* 180 min,  $P < 0.001$ , and 264 *vs* 217 min,

$P < 0.001$ ). TaTME was not converted to laparotomy whilst surgery in five patients undergoing LaTME was converted to laparotomy (0.0% *vs* 10.4%,  $P = 0.056$ ). No statistically significant differences were observed for Clavien–Dindo classification, CCI, readmissions, reoperations and mortality.

**Conclusion** The study showed that TaTME is a safe and feasible approach for rectal cancer resection. This new technique obtained similar postoperative morbidity to LaTME.

**Keywords** rectal cancer, minimal invasive surgery, laparoscopic, transanal

### What does this paper add to the literature?

Transanal total mesorectal excision (TaTME) is an emerging surgical technique for rectal cancer resection. This study is the first to provide results of a prospective multicentre cohort study comparing TaTME and laparoscopic total mesorectal excision. TaTME is a safe and feasible approach for rectal cancer resection. TaTME obtained similar postoperative morbidity and required fewer conversions.

## Introduction

Total mesorectal excision (TME) is the gold standard for rectal resection. This surgical technique, involving resection of the fatty envelope surrounding the rectum, has substantially contributed to local control and survival of rectal cancer [1,2].

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Minimally invasive techniques have been introduced for rectal surgery. Several randomized controlled trials have shown that oncological outcomes are comparable for open and laparoscopic surgery for rectal cancer. The COREAN trial has shown short-term benefits for laparoscopic surgery compared to open surgery and an equivalent quality of oncological resection [3]. In the long term, disease-free survival was similar for the two techniques [4]. In addition, The COLOR-II trial has confirmed that

laparoscopic and open surgery for rectal cancer provide similar long-term outcomes [5].

Recently, it has been shown that age above 65 years, a body mass index (BMI) greater than 25 and tumour location close to the anal verge are risk factors for the conversion from laparoscopic to open surgery [6]. In addition, factors such as a narrow pelvis or limited views of the distal rectum make the laparoscopic approach difficult. These considerations emphasize the need for a new minimally invasive technique that overcomes the limitations of laparoscopy.

Transanal total mesorectal excision (TaTME) may be the solution. Since its introduction in 2010, TaTME has been shown to be a feasible and safe technique for rectal cancer resections and has subsequently achieved widespread acceptance [7,8]. Nevertheless, to date, most evidence has been obtained from cohort studies with small sample sizes and retrospective design [9–13]. Therefore, this study is important because it is the first to provide results of a prospective multicentre cohort study. The aim of the study was to compare postoperative morbidity between TaTME and laparoscopic total mesorectal excision (LaTME).

## Method

The study was designed as a subgroup analysis of a prospective multicentre cohort study, the APPEAL-II study. Ten hospitals in the Netherlands and Belgium participated. The study was approved by the medical ethics committee of the Erasmus University Medical Center in the Netherlands and of the University Hospital Leuven in Belgium. We also obtained approval from local ethics committees of the participating hospitals. This prospective cohort was established between August 2015 and October 2017. Patients aged 18 years and older who underwent partial mesorectal excision (PME) or TME with construction of a colorectal or coloanal anastomosis were eligible for inclusion. We excluded pregnant women and patients who underwent emergency procedures. All patients received a pelvic drain during surgery that was kept in place for at least the first three postoperative days. Drain fluid was obtained for further analysis according to the study protocol (<https://doi.org/10.1186/isrc.tn84052649>). Follow-up, for the purposes of this study, was completed at the first visit at the outpatient clinic after hospital discharge. Informed consent was obtained from all patients. For this subgroup analysis, we selected patients who underwent TaTME or LaTME for rectal cancer. Patient selection for TaTME or LaTME was at discretion of the surgeon.

Baseline characteristics [age, gender, BMI, smoking, alcohol abuse (> 14 units per week), American Society of

Anesthesiologists (ASA) score, tumour location, neoadjuvant radiotherapy, neoadjuvant chemotherapy, pathological TNM staging] and surgical characteristics [duration of surgery, duration of anaesthesia, conversion, construction of anastomosis, configuration of anastomosis, diverting ileostomy, circumferential resection margin (CRM), distal resection margin (DRM)] were prospectively registered. CRM was considered positive when the margin was < 1 mm and for the DRM this was < 1 cm [14].

## Outcome measures

The outcome measures of this analysis were postoperative complications, readmissions, reoperations, conversions and mortality. Stoma reversals were not considered as reoperations unless they were due to stoma complications. Anastomotic leakage was defined as clinically manifest insufficiency of the anastomosis leading to a clinical state requiring re-intervention (i.e. Grade B/C) [15]. Anastomotic leakage was confirmed by endoscopy, CT scan and/or contrast enema or reoperation. Re-intervention for anastomotic leakage consisted of therapeutic antibiotics, (endoscopic) drainage or a surgical re-intervention. Presacral abscesses were classified as anastomotic leakage if extravasation of the colonic contrast was visible on radiological imaging. Fistulas attached to the anastomosis on CT scan were also classified as anastomotic leakage. Postoperative complications were classified according to the Clavien–Dindo classification system and Grade II or higher was considered to be a severe complication [16,17]. In addition, the comprehensive complication index (CCI) for every patient was calculated using [www.assessurgery.com](http://www.assessurgery.com) [18].

## Statistical analysis

Continuous variables were described as median  $\pm$  interquartile range and compared with the Mann–Whitney *U* test. Categorical variables were described as percentages and compared using the chi-squared test or Fisher's exact test when needed. Patients were matched based on the propensity score derived from a logistic regression model with approach as dependent covariate and baseline characteristics with *P* value < 0.1 as independent covariates. In addition, a multivariate penalized logistic/linear regression model was built to investigate the adjusted association between the surgical approach and the outcome measures adjusted for the aforementioned risk factors in the unmatched dataset (age, gender, BMI, tumour location, pathological tumour stage, neoadjuvant radiotherapy, neoadjuvant chemotherapy, diverting ileostomy, approach). All clinically relevant variables were added to the model. Statistical significance was defined as

$P$  value  $< 0.050$ . All analyses were performed using SPSS® software 21.0 (IBM, Armonk, New York, USA) or (R software, <http://www.r-project.org>).

## Results

This prospective cohort study of patients undergoing PME or TME included 301 patients. For this analysis, we excluded 74 patients who underwent PME or who had an open approach and seven patients who were operated upon for reasons other than rectal cancer. In total, 220 patients were selected (Fig. 1). The median follow-up was 27.0 days (interquartile range 19.0–34.0 days).

Table 1 shows prematching baseline characteristics of the overall study population of 220 patients. Age, tumour location, pathological T staging and neoadjuvant chemotherapy were used to calculate the propensity score. After matching for propensity score, 96 patients were eligible for analysis.

Table 2 shows postmatching baseline characteristics of 48 patients undergoing TaTME and 48 patients undergoing LaTME. Patients undergoing LaTME received neoadjuvant radiotherapy more often (43.8% *vs* 64.6%,  $P = 0.041$ ). The other baseline characteristics were not statistically significantly different for TaTME and LaTME. Duration of surgery and anaesthesia were both significantly longer for TaTME (221 *vs* 180 min,  $P < 0.001$ ; 264 *vs* 217 min,  $P < 0.001$ ). TaTME was not converted to laparotomy whilst surgery in five

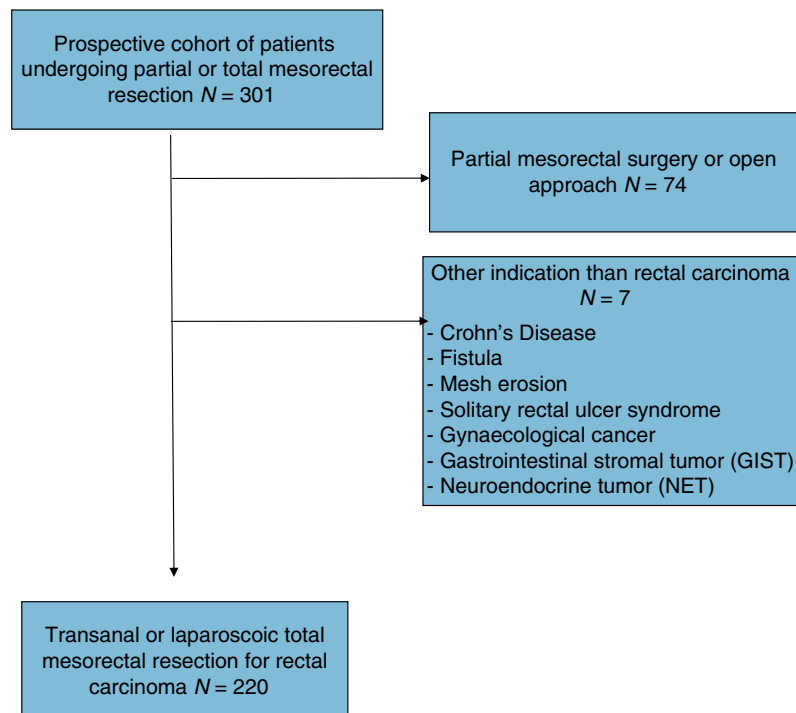
patients undergoing LaTME was converted to laparotomy (0.0% *vs* 10.4%,  $P = 0.056$ ; Table 3). Reasons for conversion were adhesions, obesity, bleeding and insufficient bowel length for stoma creation.

No statistically significant differences were observed for hospital stay, anastomotic leakage, ileus, cardiopulmonary complications, wound infections, Clavien–Dindo classification, CCI, readmissions, reoperations and mortality (Table 4). Readmissions were due to anastomotic leakage, high output stoma, ileus, pancreatic pseudocyst and iatrogenic small bowel perforation. The indications for reoperations were anastomotic leakage and replacement of diverting ileostomy. In the LaTME group, one patient died 2 days after discharge of an unknown reason as autopsy was not performed.

In the overall study population of 220 patients, multivariate penalized regression analyses showed that surgical approach is not associated with Clavien–Dindo classification  $> II$  (OR 1.02, 95% CI 0.41–2.51,  $P = 0.970$ ), CCI (estimate  $-0.77$ , 95% CI  $-6.84$  to  $5.31$ ,  $P = 0.805$ ), readmission (OR 1.13, 95% CI 0.43–2.99,  $P = 0.802$ ) and reoperation (OR 1.33, 95% CI 0.49–3.64,  $P = 0.574$ ; Table 5).

## Discussion and conclusions

This propensity score matched study of a prospective multicentre cohort study aimed to compare postoperative morbidity between TaTME and LaTME. Our



**Figure 1** Flowchart of patient selection.

**Table 1** Demographic characteristics for patients undergoing LaTME and TaTME.

	TaTME 119 (54.1%)	LaTME 101 (45.9%)	Missing (%)	<i>P</i> value
Baseline characteristics				
Age, median (IQR), year	62.0 (56.0–67.0)	66.0 (59.5–73.0)	0 (0.0)	<b>0.003</b>
Gender				
Male	86 (72.3%)	64 (63.4%)	0 (0.0)	0.158
Female	33 (27.7%)	37 (36.6%)		
BMI, median (IQR), kg/m <sup>2</sup>	26.6 (23.7–29.7)	25.2 (23.2–28.7)	1 (0.5)	0.162
Smoking				
Yes	15 (12.7%)	11 (11.5%)	6 (2.7)	0.780
No	103 (87.3%)	85 (88.5%)		
Alcohol abuse				
Yes	16 (13.6%)	11 (11.7%)	8 (3.6)	0.687
No	102 (86.4%)	83 (88.3%)		
Bowel preparation				
Yes	116 (97.5%)	82 (92.1%)	12 (5.5)	<b>0.102*</b>
No	3 (2.5%)	7 (7.9%)		
Previous abdominal surgery				
Yes	37 (31.1%)	35 (35.0%)	1 (0.5)	0.540
No	82 (68.9%)	65 (65.0%)		
ASA score				
I	11 (9.2%)	16 (16.0%)	1 (0.5)	<b>0.355*</b>
II	77 (64.7%)	64 (64.0%)		
III	30 (25.2%)	19 (19.0%)		
IV	1 (0.8%)	1 (1.0%)		
Tumour distance to anal verge, median (IQR), cm	5.0 (2.1–10.0)	12.0 (9.0–15.0)	12 (5.5)	<b>&lt; 0.001</b>
pT stage				
pT0	21 (17.8%)	6 (6.0%)	7 (3.1)	<b>0.027*</b>
pT1	16 (13.6%)	19 (19.0%)		
pT2	36 (30.5%)	26 (26.0%)		
pT3/4	42 (35.6%)	47 (47.0%)		
pN stage				
pN0	83 (69.7%)	68 (67.3%)	7 (3.1)	0.292
pN1	17 (14.3%)	22 (21.8%)		
pN2	14 (11.8%)	8 (7.9%)		
pN3	0 (0.0%)	1 (1.0%)		
Neoadjuvant radiotherapy				
Yes	67 (56.3%)	60 (60.0%)	1 (0.5)	0.581
Short-course	14	34		
Long-course	47	25		
No	52 (43.7%)	40 (40.0%)		
Neoadjuvant chemotherapy				
Yes	52 (43.7%)	28 (28.0%)	1 (0.5)	<b>0.016</b>
No	67 (56.3%)	72 (72.0%)		

ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; LaTME, laparoscopic total mesorectal excision; TaTME, transanal total mesorectal excision.

\*Fisher's exact test.

Bold values indicates *P* value <0.05.

results suggest that TaTME is a safe and feasible approach for rectal cancer resection and has similar postoperative morbidity to LaTME.

Nowadays, high conversion rates from laparoscopic to open surgery are reported for rectal resection

especially in elderly patients and obese patients contributing to postoperative morbidity [6]. Even in the most recent clinical trials comparing laparoscopic vs robotic assisted TME for rectal cancer, conversions were up to 10% in both arms [19]. This is one of the main

**Table 2** Postmatching baseline characteristics.

	TaTME 48	LaTME 48	Missing (%)	<i>P</i> value
Age, median (IQR), year	65.0 (56.8–71.0)	64.0 (59.3–73.0)	0 (0.0)	0.752
Gender				
Male	33 (68.8%)	32 (66.7%)		0.827
BMI, median (IQR), kg/m <sup>2</sup>	27.0 (24.5–30.7)	26.1 (24.0–29.0)	1 (1.0)	0.221
Smoking	5 (10.4%)	6 (12.5%)	5 (5.2)	0.661
Alcohol abuse	7 (14.6%)	2 (4.2%)	5 (5.2)	0.164*
ASA score				
I	4 (8.3%)	6 (12.5%)	0 (0.0)	0.953*
II	29 (60.4%)	28 (58.3%)		
III	14 (29.2%)	13 (27.1%)		
IV	1 (2.1%)	1 (2.1%)		
Tumour location, median (IQR), cm	10.0 (6.0–10.8)	9.5 (7.0–12.0)	0 (0.0)	0.459
Neoadjuvant radiotherapy	21 (43.8%)	31 (64.6%)	0 (0.0)	<b>0.041</b>
Short-course	5 (10.4%)	16 (33.3%)		
Long-course	15 (31.3%)	14 (29.2%)		
Neoadjuvant chemotherapy	14 (29.2%)	16 (33.3%)	0 (0.0)	0.660
pT stage				
pT0	3 (6.3%)	2 (4.2%)	0 (0.0)	0.973*
pT1	7 (14.6%)	7 (14.6%)		
pT2	15 (31.3%)	14 (29.2%)		
pT3/4	23 (47.9%)	25 (52.1%)		
pN stage				
pN0	32 (66.7%)	34 (70.8%)	0 (0.0)	0.660
pN+	16 (33.3%)	14 (29.2%)		

ASA, American Society of Anesthesiologists; BMI, body mass index; IQR, interquartile range; LaTME, laparoscopic total mesorectal excision; TaTME, transanal total mesorectal excision.

\*Fisher's exact test.

Bold values indicates *P* value <0.05.

**Table 3** Postmatching surgical characteristics.

	TaTME 48	LaTME 48	Missing (%)	<i>P</i> value
Duration of surgery, median (IQR), min	221.0 (187.50–263.50)	180.0 (141.0–205.0)	3 (3.1)	< <b>0.001</b>
Duration of anaesthesia, median (IQR), min	264.0 (228.8–313.3)	217.0 (176.5–244.3)	8 (8.3)	< <b>0.001</b>
Conversion	0 (0.0%)	5 (10.4%)	0 (0.0)	0.056*
Construction of anastomosis				
Hand-sewn	7 (14.6%)	0 (0.0%)	0 (0.0)	<b>0.012*</b>
Stapler	41 (85.4%)	48 (100.0%)		
Configuration of anastomosis				
Side-to-end	26 (54.2%)	41 (85.4%)	3 (3.1)	< <b>0.001*</b>
End-to-end	20 (41.7%)	4 (8.3%)		
End-to-side	0 (0.0%)	2 (4.2%)		
Diverting ileostomy	40 (83.3%)	23 (47.9%)	0 (0.0)	< <b>0.001</b>
CRM involvement	2 (4.2%)	1 (2.1%)	10 (10.4)	1.000*
DRM involvement	5 (10.4%)	8 (16.7%)	8 (8.3)	0.322

CRM, circumferential resection margin; DRM, distal resection margin; IQR, interquartile range; LaTME, laparoscopic total mesorectal excision; TaTME, transanal total mesorectal excision.

\*Fisher's exact test.

Bold values indicates *P* value <0.05.

**Table 4** Postmatching postoperative course comparison.

	TaTME 48	LaTME 48	Missing (%)	<i>P</i> value
Hospital stay, median (IQR), days	8.0 (6.0–13.5)	7.5 (5.0–13.8)	0 (0.0)	0.596
Anastomotic leakage	10 (20.8%)	9 (18.8%)	0 (0.0)	0.798
Ileus	7 (14.6%)	8 (16.7%)	0 (0.0)	0.779
Cardiopulmonary complications	0 (0.0%)	3 (6.3%)	0 (0.0)	0.242*
Wound infection	2 (4.2%)	1 (2.1%)	0 (0.0)	1.000*
Clavien–Dindo classification > II	9 (18.8%)	10 (20.8%)	0 (0.0)	0.798
Comprehensive complication index, median (IQR)	14.8 (0.0–22.6)	4.4 (0.0–22.6)	0 (0.0)	0.602
Readmission	10 (20.8%)	5 (10.4%)	0 (0.0)	0.160
Reoperation	8 (16.7%)	7 (14.6%)	0 (0.0)	0.779
Mortality	0 (0.0%)	1 (2.1%)	0 (0.0)	1.000*

IQR, interquartile range; LaTME, laparoscopic total mesorectal excision; TaTME, transanal total mesorectal excision.

\*Fisher's exact test.

**Table 5** Multivariate penalized logistic regression to test the association between approach and Clavien–Dindo > II, readmission and reoperation.

	Clavien–Dindo > II		CCI		Readmission		Reoperation	
	OR	<i>P</i> value	Estimate	<i>P</i> value	OR	<i>P</i> value	OR	<i>P</i> value
	95% CI		95% CI		95% CI		95% CI	
Age, median (IQR), years	0.96	<b>0.014</b>	−0.32	<b>0.008</b>	0.97	0.181	0.96	<b>0.032</b>
	0.92–0.99		−0.55 to −0.08		0.94–1.01		0.92–1.00	
Gender	0.77	0.482	−0.76	0.760	0.88	0.770	1.01	0.980
	0.37–1.59		−5.66 to 4.14		0.39–2.02		0.44–2.31	
BMI, median (IQR), kg/m <sup>2</sup>	0.98	0.550	0.06	0.820	0.98	0.618	1.03	0.588
	0.90–1.06		−0.45 to 0.57		0.89–1.07		0.94–1.12	
Location lesion, median (IQR), cm	1.00	0.990	0.23	0.417	1.06	0.171	0.96	0.385
	0.92–1.08		−0.32 to 0.78		0.97–1.16		0.87–1.05	
pT	0.88	0.455	−0.76	0.514	0.94	0.774	1.01	0.952
	0.62–1.24		−3.03 to 1.51		0.64–1.39		0.68–1.50	
Neoadjuvant radiotherapy	0.97	0.939	1.63	0.585	1.05	0.920	0.86	0.748
	0.41–2.26		−4.21 to 7.47		0.41–2.70		0.34–2.16	
Neoadjuvant chemotherapy	0.67	0.391	−7.09	<b>0.026</b>	0.80	0.664	0.45	0.153
	0.26–1.68		−13.30 to −0.88		0.30–2.16		0.15–1.34	
Diverting ileostomy	0.56	0.151	1.12	0.680	2.22	0.107	0.41	0.054
	0.26–1.23		−4.19 to 6.43		0.84–5.83		0.17–1.01	
Approach	1.02	0.970	−0.77	0.805	1.13	0.802	1.33	0.574
	0.41–2.51		−6.84 to 5.31		0.43–2.99		0.49–3.64	

BMI, body mass index; CCI, comprehensive complication index; IQR, interquartile range.

Bold values indicates *P* value <0.05.

drawbacks of conventional laparoscopic surgery for rectal resection. In the present study, TaTME was not converted at all whilst LaTME was converted to laparotomy in 10.4% of cases. A recent single-centre case-matched study reported similar results [20]. This low incidence of conversion seems to be the main advantages of this new technique.

With the introduction of minimally invasive techniques, the short-term outcomes of rectal surgery have

improved over recent decades. Despite these advances, the incidence of anastomotic leakage has not been reduced [21]. Anastomotic leakage is one of the major concerns after rectal resection because of associated morbidity and mortality. A recent study demonstrated that large rectal tumours in obese, diabetic male patients who smoke have the highest risk for anastomotic leakage after TaTME [22]. In line with previous literature, we found no difference in leakage rate for TaTME and LaTME

[9–11,13,23–25]. Therefore, the transanal approach does not seem to reduce the incidence of anastomotic leakage after rectal cancer resection.

In contrast to previous studies, our results show that TaTME is associated with more prolonged surgery and anaesthesia [7,8]. Previously, it was suggested that TaTME can be performed by two teams simultaneously; however, not all hospitals have the capacity to perform TaTME in two teams due to lack of personnel. When TaTME is not performed with two teams simultaneously, this may result in prolonged duration of surgery and anaesthesia. Moreover, this study included hospitals in which the TaTME technique was recently introduced. Therefore, a longer duration of surgery might reflect a learning curve [26]. In addition, creation of a diverting ileostomy, which was more often performed in the TaTME group, may also influence duration of surgery and anaesthesia.

After matching for propensity score, patients who underwent LaTME received neoadjuvant radiotherapy more frequently than TaTME patients. The ESMO clinical practice guidelines have recently been updated indicating that specific patients with intermediate risk rectal cancer do not need neoadjuvant treatment in order to minimize local recurrence if good quality TME can be achieved [27]. Since TaTME has recently become more popular, this difference might mirror the update of these guidelines. In addition, this study showed, in the unmatched cohort, that preoperative radiotherapy was not associated with postoperative morbidity (Table 5), and therefore it is unlikely that this difference in baseline characteristics has influenced the results.

In the postmatching TaTME group, more manual and end-to-end anastomoses were observed, even though there were no baseline differences between the two groups on tumour height. A systematic review showed similar results [28].

Diverting ileostomies are common after rectal resection but do not reduce anastomotic leakage or mortality [29]. In fact, diverting ileostomies tend to mitigate the consequences of anastomotic leakage resulting in less invasive treatment strategies. In the present study, patients who underwent TaTME were more often diverted during primary surgery. A recent single-centre case-matched study found similar results [25]. This difference might reflect surgeons' perception to protect the anastomosis following the new approach whilst this risk is unsubstantiated.

In the present study, tumour location was derived from endoscopy. There seems to be a significant difference between the tumour location of colorectal cancers reported by endoscopy and the actual location determined during surgery [30]. Moreover, the anal verge

was the reference for determination of the tumour location. Thus, this distance includes the anal canal of 3–5 cm [31]. This may explain the relatively high tumour location in both the TaTME and the LaTME groups.

Functional outcomes are of interest for future research. TaTME possibly provides better visualization of the distal rectum which may contribute to preservation of pelvic nerves and vascularity resulting in better urinary and sexual function [23,32].

At this moment, this subgroup analysis provides the highest level of evidence on postoperative short-term results after TaTME and LaTME currently available since the results are based on a multicentre prospective cohort study. Nevertheless, we recognize several limitations of the study. First, the TME procedures in both groups were not standardized so different types of laparoscopic assisting techniques (i.e. single-port or multi-port) were used. Second, cohort studies are sensitive to bias and confounding. Nevertheless, both propensity score analysis and penalized multivariate regression analyses were performed to adjust for confounding effects showing similar results.

This propensity score matched study of a prospective multicentre cohort study aimed to compare postoperative morbidity between TaTME and LaTME. It was shown that TaTME is a safe and feasible approach for rectal cancer resection. This new technique obtained similar postoperative morbidity. This study is the first to provide evidence based upon prospective data. However, oncological safety in terms of CRM involvement and local recurrence should be obtained in a well-designed randomized controlled trial.

## Acknowledgements

We would like to thank all patients who participated in the study. We are grateful to everyone at the department of surgery of all participating hospitals.

## Conflicts of interest

No conflicts of interest.

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