Original article

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An international multicentre prospective audit of elective rectal cancer surgery; operative approach versus outcome, including transanal total mesorectal excision (TaTME)

The 2017 European Society of Coloproctology (ESCP) collaborating group

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Abstract

Introduction Transanal total mesorectal excision (TaTME) has rapidly emerged as a novel approach for rectal cancer surgery. Safety profiles are still emerging and more comparative data is urgently needed. This study aimed to compare indications and short-term outcomes of TaTME, open, laparoscopic, and robotic TME internationally.

Methods A pre-planned analysis of the European Society of Coloproctology (ESCP) 2017 audit was performed. Patients undergoing elective total mesorectal excision (TME) for malignancy between 1 January 2017 and 15 March 2017 by any operative approach were included. The primary outcome measure was anastomotic leak.

Results Of 2579 included patients, 76.2% (1966/2579) underwent TME with restorative anastomosis of which 19.9% (312/1966) had a minimally invasive approach (laparoscopic or robotic) which included a transanal component (TaTME). Overall, 9.0% (175/1951, 15 missing outcome data) of patients suffered an anastomotic leak. On univariate analysis both laparoscopic TaTME (OR 1.61, 1.02–2.48, $P = 0.04$) and robotic TaTME (OR 3.05, 1.10–7.34, $P = 0.02$) were associated with a higher risk of anastomotic leak than non-transanal laparoscopic TME. However this association was lost in the mixed-effects model controlling for patient and disease factors (OR 1.23, 0.77–1.97, $P = 0.39$ and OR 2.11, 0.79–5.62, $P = 0.14$ respectively), whilst low rectal anastomosis (OR 2.72, 1.55–4.77, $P < 0.001$) and male gender (OR 2.29, 1.52–3.44, $P < 0.001$) remained strongly associated. The overall positive circumferential margin resection rate was 4.0%, which varied between operative approaches: laparoscopic 3.2%, transanal 3.8%, open 4.7%, robotic 1%.

Conclusion This contemporaneous international snapshot shows that uptake of the TaTME approach is widespread and is associated with surgically and pathologically acceptable results.

Keywords Rectal cancer, laparoscopic surgery, TME, transanal TME, TaTME, robotic surgery

What does this paper add to the literature?
Approaches to rectal cancer resection vary internationally. One in five patients is undergoing a TaTME approach, with results suggesting equivalent anastomotic leak and positive resection margin rates. Both robotic and TaTME approaches need further evidence to support their impact on major complications. Anastomotic leak rates in low rectal anastomoses remain high, regardless of operative approach.

Introduction

The best technique to achieve safe and effective total mesorectal excision (TME) for rectal cancer continues to pose a significant challenge for surgeons and patients. The ideal technique aims for an intact TME with clear circumferential and distal resection margins [1]. When reconstruction is planned, an anastomotic technique that minimises the risk of leak whilst promoting good function is needed. A significant challenge is posed by cancers in the lowest third of the rectum, particularly in a narrow pelvis. From an abdominal approach, the ability to pass a stapler safely below the tumour is vital to avoid an involved distal resection margin. Similarly, the

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need for multiple firings of a cross-stapler predisposes to anastomotic leak [2]. Finally, precise placement of circular stapling devices through cross-stapled rectal stumps can be challenging.

Transanal TME (TaTME) has been proposed as a method to improve surgery of mid and low rectal lesions [3,4]. It is typically performed as a hybrid procedure with a minimally invasive (laparoscopic or robotic) abdominal approach, with dissection and ultralow colorectal/coloanal anastomosis through the transanal port to improve visualisation and avoid cross stapling [5] or multiple firings [2,5]. It has the potential to be safer for the distal resection margin by improving access and precision of dissection and stapler placement [2].

TaTME is still evolving (IDEAL Phase 2b) with moderate stability of its components [6,7]. A prolonged learning curve [8] for transanal surgery has been described, with worse outcomes seen in as many as the first fifty cases performed [9]. Consistent with this, early series report anastomotic leak rates as high as 43% [10], with concerning rates of urethral and other solid organ injury. Concerns also exist about circumferential resection margin (CRM) involvement and suboptimal TME specimen grades in its early adoption [9,11]. There is not yet randomised evidence for the benefit of TaTME. A recent large and comprehensive registry study has identified baseline data and showed acceptable leak rates and safety profiles from the included centres [12]. However, it did not have comparative groups to benchmark current practice, and so to supplement this, we planned a study from a wide range of centres to gather comparative data. The primary aim of this study was to describe the safety profile of TaTME compared to other surgical approaches to manage rectal cancer. The secondary aim was to additionally describe the current landscape in terms of uptake of TaTME and the alternate operative approaches for rectal cancer, including open, laparoscopic, and robotic TME.

Method

Protocol and centres

This prospective, observational, multicentre study was conducted in line with a pre-specified protocol (http://www.escp.eu.com/research/cohort-studies). An external pilot of the protocol and data capture system was conducted in five international centres prior to launch, allowing refinement of the study tool and delivery. Any unit performing gastrointestinal surgery was eligible to register to enter patients into the study. No minimum case volume, or centre-specific limitations were applied. The study protocol was disseminated to registered members European Society of Coloproctology (ESCP), and through national surgical or colorectal societies, and represents a pre-planned analysis of the European Society of Coloproctology 2017 audit database.

Study approvals

All participating centres were responsible for compliance to local approval requirements for ethics approval or indemnity as required. In the UK, the National Research Ethics Service tool recommended that this project was not classified as research, and the protocol was registered as clinical audit in all participating centres.

Patient eligibility

Adult patients (> 16 years) undergoing elective (planned) rectal resection with or without a primary anastomosis were extracted from the main audit database. Only operations performed for a malignant pathology within the rectum, up to the rectosigmoid junction were included. For the abdominal component, open, laparoscopic and robotic procedures were all eligible. Transanal and non-transanal approaches were acceptable. Rectal resections performed as part of a more extensive resection (e.g. panproctocolectomy) were excluded.

Data capture

Consecutive sampling was performed of eligible patients over an 8-week study period in each included centres. Local investigators commenced data collection on any date between the 1 January 2017 and 15 March 2017, with the last eligible patient being enrolled on 10 May 2017. This study adopted the UK National Research Collaborative model for data collection and follow-up. Small teams of up to five surgeons or surgical trainees worked together to collect prospective data on all eligible patients at each centre. Quality assurance was provided by at least one consultant or attending-level surgeon. Data was recorded contemporaneously and stored on a secure, user-encrypted online platform (REDCap) without using patient identifiable information. Centres were asked to validate that all eligible patients during the study period had been entered, and to attain > 95% completeness of data field entry prior to final submission.

Outcome measure

The primary outcome measure was overall anastomotic leak, pre-defined as either (i) gross anastomotic leakage proven radiologically or clinically, or (ii) the presence of an intraperitoneal (abdominal or pelvic) fluid collection on post-operative imaging. The secondary outcome measures were the postoperative major complication rate; defined as Clavien-Dindo classification grade 3–5 (reoperation, reintervention, unplanned admission to critical care, organ support requirement or death), post-operative length of stay (in whole days); with day of surgery as day zero, the intraoperative serious adverse event (SAE) rate, and the circumferential resection margin involvement rate; defined as tumour tissue ≤ 1 mm from the resection margin.

Statistical analysis

This report has been prepared in accordance to guidelines set by the STROBE (strengthening the reporting of observational studies in epidemiology) statement for observational studies [13]. Patient, disease and operative characteristics were compared by type of surgical approach (open, laparoscopic – transanal (TaTME), laparoscopic – not transanal, robotic – transanal (TaTME), robotic – not transanal) and by the presence or absence of the primary outcome measure (anastomotic leak or intraperitoneal collection) using Student's t-test for normal, continuous data, Mann-Whitney U test for non-normal continuous data or Chi-squared test for categorical data. To test the association between overall anastomotic leak and approach (the main explanatory variable) two models were fitted: the first was a mixed-effects logistic regression model using the whole dataset, the second was a propensity score-matched group of patients who did and did not undergo TaTME in a 1:2 ratio. In the mixed-effects model, clinically plausible patient, disease and operation-specific factors were entered into the model for risk-adjustment, treated as fixed effects. These were defined *a priori* within the study protocol, and included irrespective of their significance on univariate analysis. Hospital was entered into the model as a random-effect, to adjust for hospital-level variation in outcome. Propensity score matching was used to estimate the effect of approach (transanal versus not transanal perineal approach) by accounting for confounding co-variables that might predict patient selection. Nearest neighbour matching was used with scores calculated from variables selected a priori for model adjustment (age, gender, anastomotic height, AJCC stage), and outputs were examined using jitter plots and Chi-squared testing to observe any significant differences between groups. A second propensity-score matched multivariable logistic regression model was then fitted to explore the association of operative approach and anastomotic leak. Effect estimates are presented as odds ratios (OR) with 95% confidence intervals (95% CI) and two-tailed *P*-values. An alpha level of 0.05 was used throughout. Model discrimination was tested by calculating a C-statistic (analogous to the area under the Receiver Operating Curve (AUC); 0.5: no discrimination; 0.6, adequate; 0.7, good; 0.8 excellent). Multiple imputation was not required as the data completeness rate was very high for data points used for propensity score matching. Data analysis was undertaken using R Studio V3.1.1 (R Foundation, Boston, MA, USA).

Results

Patient demographics

Figure 1 shows inclusion of patients within this study. A total of 2579 patients were included from 355 centres across 49 countries. The mean age of the cohort was 66 years (18–98 years), of which 27.7% (715/2579) had low, 26.0% (670/2579) had middle and 46.3% (1194/2579) had high rectal anastomoses. 62.7% were men (1617/2579) and 36.5% (942/2579) underwent neoadjuvant therapy, of which 72.1% (679/942) had long course chemoradiotherapy. A majority of tumours were either T2 (21.8%, 563/2579) or T3 (51.8%, 1337/2579), N0 (58.4%, 1505/2579) and M0 (87.7%, 2262/2579). The abdominoperineal resection rate was 15.4% (396/2579, Fig. 2) and resection with end stoma formation was 8.4% (217/2579). Of those that had an anastomosis (76.2%, 1966/2579), 92.1% (1811/1966) had a stapled anastomosis.

Patient, disease and operative characteristics by operative approach

There was variation in the selection of patients for different approaches to rectal cancer surgery (Table 1). Of patients undergoing restorative surgery, 15.9% (312/1966) of patients from 189 centres underwent surgery with a transanal perineal approach and minimally invasive abdominal approach (TaTME), ranging from one to 15 submitted cases per centre. 6.4% (126/1966) of patients from 40 centres had robotic surgery (ranging from one to 18 submitted case per centre). In patients undergoing TaTME, the anastomosis was was stapled in 73.7% (230/312) and hand-sewn in 26.3% (82/312). The proportion of males undergoing transanal and robotic approaches was

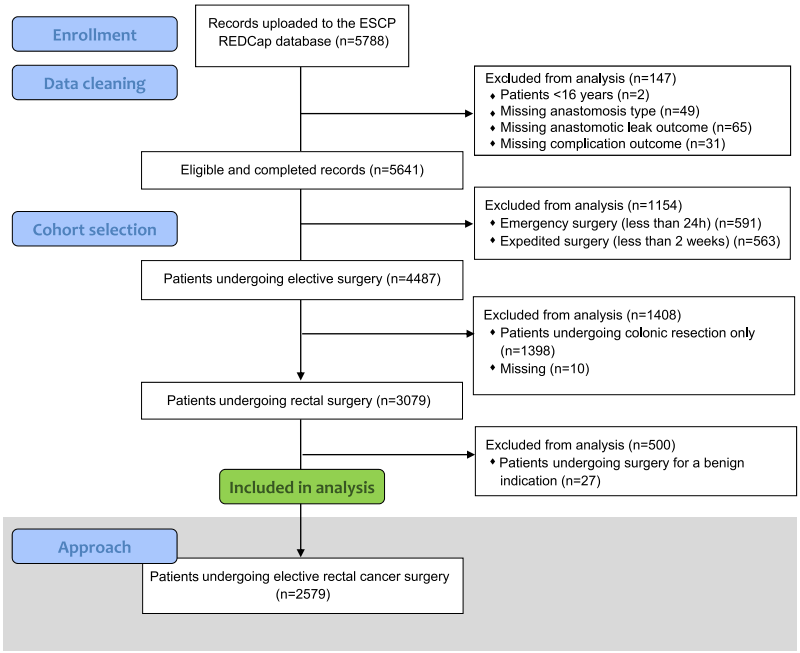


Figure 1 Flowchart for patients included in the analysis of approaches to elective rectal cancer surgery.

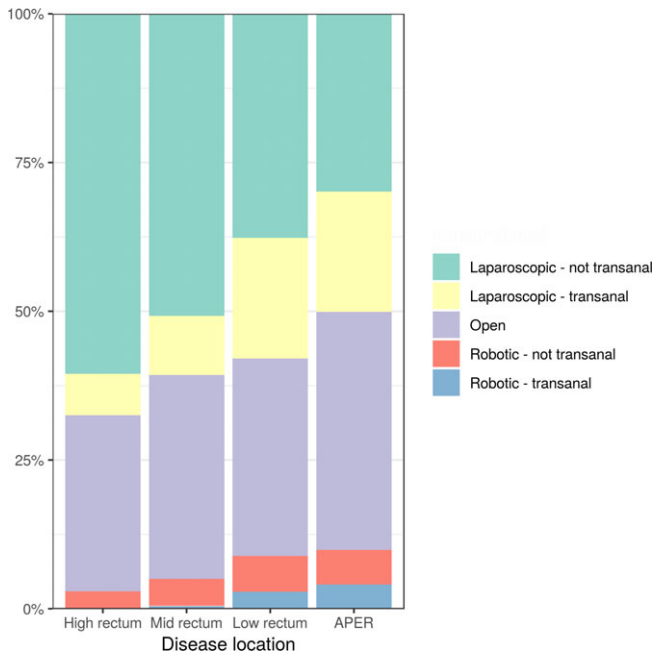


Figure 2 Selection of approach by tumour height in elective rectal cancer surgery.

slightly higher when compared to the other procedures (68.4%, 68.3%, 64.4% *vs* 61.8%, 60.6% respectively; $P = 0.06$). Transanal or robotic approaches were significantly more likely to be selected in low risk ASA 1-2 patients and earlier stage disease.

Anastomotic leak

Within the patients undergoing restorative anastomosis, the overall leak rate was 9.0% (175/1951, with 15 missing outcome data (< 1%)). In the unadjusted data, the

Table 1 Patient, disease and operation characteristics by approach.

Factor	Levels	Laparoscopic not transanal	Laparoscopic transanal	Open	Robotic not transanal	Robotic transanal	*P*-value
Operation type	Primary anastomosis	952 (81.0)	280 (76.3)	608 (70.0)	95 (77.2)	31 (68.9)	< 0.001
	ELAPE	35 (3.0)	25 (6.8)	46 (5.3)	6 (4.9)	1 (2.2)	
	APER	83 (7.1)	51 (13.9)	121 (13.9)	15 (12.2)	13 (28.9)	
	Hartmanns	106 (9.0)	11 (3.0)	93 (10.7)	7 (5.7)	0 (0.0)	
Anastomosis height	High rectum	398 (33.8)	46 (12.5)	195 (22.5)	18 (14.6)	1 (2.2)	< 0.001
	Mid rectum	336 (28.6)	66 (18.0)	227 (26.2)	30 (24.4)	3 (6.7)	
	Low rectum	318 (27.0)	171 (46.6)	280 (32.3)	51 (41.5)	24 (53.3)	
	APER	124 (10.5)	84 (22.9)	166 (19.1)	24 (19.5)	17 (37.8)	
Patient characteristics							
Age	< 55	172 (14.6)	68 (18.5)	135 (15.6)	18 (14.6)	8 (17.8)	0.918
	55–70	521 (44.3)	161 (43.9)	387 (44.6)	57 (46.3)	19 (42.2)	
	70–80	339 (28.8)	103 (28.1)	257 (29.6)	35 (28.5)	13 (28.9)	
	> 80	143 (12.2)	34 (9.3)	89 (10.3)	13 (10.6)	5 (11.1)	
	Missing	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	
Gender	Female	449 (38.2)	116 (31.6)	342 (39.4)	39 (31.7)	16 (35.6)	0.066
	Male	727 (61.8)	251 (68.4)	526 (60.6)	84 (68.3)	29 (64.4)	
ASA class	Missing	20 (1.7)	2 (0.5)	4 (0.5)	0 (0.0)	0 (0.0)	< 0.001
	Low risk (ASA 1-2)	787 (66.9)	261 (71.1)	516 (59.4)	89 (72.4)	32 (71.1)	
	High risk (ASA 3-5)	369 (31.4)	104 (28.3)	348 (40.1)	34 (27.6)	13 (28.9)	
BMI	Normal weight	338 (28.7)	114 (31.1)	274 (31.6)	49 (39.8)	13 (28.9)	0.681
	Underweight	23 (2.0)	9 (2.5)	21 (2.4)	2 (1.6)	0 (0.0)	
	Overweight	504 (42.9)	150 (40.9)	357 (41.1)	45 (36.6)	19 (42.2)	
	Obese	281 (23.9)	87 (23.7)	201 (23.2)	26 (21.1)	13 (28.9)	
	Missing	30 (2.6)	7 (1.9)	15 (1.7)	1 (0.8)	0 (0.0)	
History of IHD/CVA	Missing	2 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.041
	No	998 (84.9)	325 (88.6)	704 (81.1)	103 (83.7)	41 (91.1)	
	Yes	176 (15.0)	42 (11.4)	164 (18.9)	20 (16.3)	4 (8.9)	
History of diabetes mellitus	Missing	3 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.35
	No	995 (84.6)	302 (82.3)	736 (84.8)	111 (90.2)	36 (80.0)	
	Diabetes: any control	178 (15.1)	65 (17.7)	132 (15.2)	12 (9.8)	9 (20.0)	
Smoking history	Non-smoker	997 (84.8)	300 (81.7)	723 (83.3)	107 (87.0)	40 (88.9)	0.122
	Current	167 (14.2)	61 (16.6)	143 (16.5)	16 (13.0)	5 (11.1)	
	Missing	12 (1.0)	6 (1.6)	2 (0.2)	0 (0.0)	0 (0.0)	
Disease characteristics							
Neoadjuvant therapy	Missing	9 (0.8)	2 (0.5)	15 (1.7)	0 (0.0)	0 (0.0)	< 0.001
	Chemotherapy only	36 (3.1)	10 (2.7)	38 (4.4)	1 (0.8)	1 (2.2)	
	Long course CRTx	266 (22.6)	142 (38.7)	215 (24.8)	32 (26.0)	24 (53.3)	
	Short course radiotherapy	74 (6.3)	23 (6.3)	62 (7.1)	17 (13.8)	1 (2.2)	
	None	791 (67.3)	190 (51.8)	538 (62.0)	73 (59.3)	19 (42.2)	
MRI T stage	Missing	45 (3.8)	3 (0.8)	20 (2.3)	1 (0.8)	0 (0.0)	< 0.001
	T1	109 (9.3)	32 (8.7)	56 (6.5)	9 (7.3)	2 (4.4)	
	T2	242 (20.6)	68 (18.5)	196 (22.6)	44 (35.8)	13 (28.9)	
	T3	625 (53.1)	213 (58.0)	421 (48.5)	52 (42.3)	26 (57.8)	
	T4	155 (13.2)	51 (13.9)	175 (20.2)	17 (13.8)	4 (8.9)	

Table 1 (Continued).

Factor	Levels	Laparoscopic not transanal	Laparoscopic transanal	Open	Robotic not transanal	Robotic transanal	*P*-value
MRI N stage	Missing	38 (3.2)	3 (0.8)	17 (2.0)	1 (0.8)	0 (0.0)	< 0.001
	N0	699 (59.4)	248 (67.6)	443 (51.0)	79 (64.2)	36 (80.0)	
	N1	339 (28.8)	91 (24.8)	286 (32.9)	39 (31.7)	5 (11.1)	
	N2	100 (8.5)	25 (6.8)	122 (14.1)	4 (3.3)	4 (8.9)	
MRI M stage	Missing	30 (2.6)	3 (0.8)	17 (2.0)	0 (0.0)	0 (0.0)	0.239
	M0	1022 (86.9)	326 (88.8)	759 (87.4)	112 (91.1)	43 (95.6)	
	M1	124 (10.5)	38 (10.4)	92 (10.6)	11 (8.9)	2 (4.4)	
MRI AJCC stage	Missing	46 (3.9)	4 (1.1)	18 (2.1)	0 (0.0)	0 (0.0)	< 0.001
	Stage 1	301 (25.6)	93 (25.3)	186 (21.4)	44 (35.8)	14 (31.1)	
	Stage 2	357 (30.4)	140 (38.1)	236 (27.2)	29 (23.6)	21 (46.7)	
	Stage 3	348 (29.6)	92 (25.1)	336 (38.7)	39 (31.7)	8 (17.8)	
	Stage 4	124 (10.5)	38 (10.4)	92 (10.6)	11 (8.9)	2 (4.4)	
MRI EMVI	Missing	127 (10.8)	42 (11.4)	80 (9.2)	7 (5.7)	4 (8.9)	0.366
	No	954 (81.1)	295 (80.4)	721 (83.1)	111 (90.2)	36 (80.0)	
	Yes	95 (8.1)	30 (8.2)	67 (7.7)	5 (4.1)	5 (11.1)	
MRI CRM	Missing	136 (11.6)	44 (12.0)	88 (10.1)	7 (5.7)	5 (11.1)	0.353
	No	909 (77.3)	289 (78.7)	674 (77.6)	106 (86.2)	36 (80.0)	
	Yes	131 (11.1)	34 (9.3)	106 (12.2)	10 (8.1)	4 (8.9)	
Other operation characteristics							
Anastomotic technique	No anastomosis	224 (19.0)	87 (23.7)	260 (30.0)	28 (22.8)	14 (31.1)	< 0.001
	Handsewn	19 (1.6)	66 (18.0)	54 (6.2)	1 (0.8)	15 (33.3)	
	Stapled	933 (79.3)	214 (58.3)	554 (63.8)	94 (76.4)	16 (35.6)	
Operator type	Missing	1 (0.1)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	< 0.001
	Colorectal	1010 (85.9)	333 (90.7)	704 (81.1)	105 (85.4)	38 (84.4)	
	General surgery	165 (14.0)	32 (8.7)	164 (18.9)	18 (14.6)	7 (15.6)	

P-value derived from χ^2 test for categorical variables. % shown by column.
CRM, Circumferential resection margin (</> 1 mm); CVA, Cerebrovascular accident; EMVI, Extramural vascular invasion; IHD, Ischemic heart disease; IQR, Interquartile range; MRI, Pre-neoadjuvant therapy, and/or baseline Magnetic Resonance Imaging staging; N/A, Not applicable; SD, Standard deviation.

anastomotic leak rate was higher in TaTME (12.9%, 45/311, one missing outcome data (< 1%)) than non-transanal TME (8.9%, 135/1520; Fig. 3). The highest leak rate was seen in robotic surgery, and more major complications were seen in transanal and robotic surgery (Table 2). In the univariate analysis both laparoscopic TaTME (OR 1.61, 1.02–2.48, $P = 0.04$) and robotic TaTME (OR 3.05, 1.10–7.34, $P = 0.02$) were associated with a higher risk of anastomotic leak than non-transanal laparoscopic TME. Once adjusted for confounders (Table 3, Fig. 4), transanal surgery was no longer significantly associated with leak (OR 1.23, 0.77–1.97, $P = 0.39$ and OR 2.11, 0.79–5.62, $P = 0.14$ respectively), whilst low rectal anastomosis (OR 2.72, 1.55-4.77, $P < 0.001$) and male gender (OR 2.29, 1.52–3.44, $P < 0.001$) were strongly associated. The model demonstrated fair discrimination (AUC: 0.70). Propensity score matching gave balanced groups (Table 4). In the propensity matched multivariable model (Table 5), transanal approach was not associated with overall anastomotic leak (OR 1.14, 0.70–1.81, $P = 0.595$). However, male gender (OR 2.88, 1.64–5.38, $P < 0.001$) and low rectal anastomosis (OR 3.92, 1.74–10.52, $P = 0.002$) again remained strong predictors for anastomotic leak.

Circumferential resection margin

In the unadjusted data, restorative surgery had a lower CRM positivity rate (36/1733, with 232 missing outcome data (11.8%)) than non-restorative (58/549) operations (2.3% versus 10.6%). Overall, there was a low CRM positive rates across all approach types to rectal resection with restorative anastomosis (0–4.7%, Table 2). For the low rectum, robotic surgery had a lower positive margin rate than laparoscopic surgery (0/19 with a transanal perineal approach, and 1/27 with a non-transanal approach;

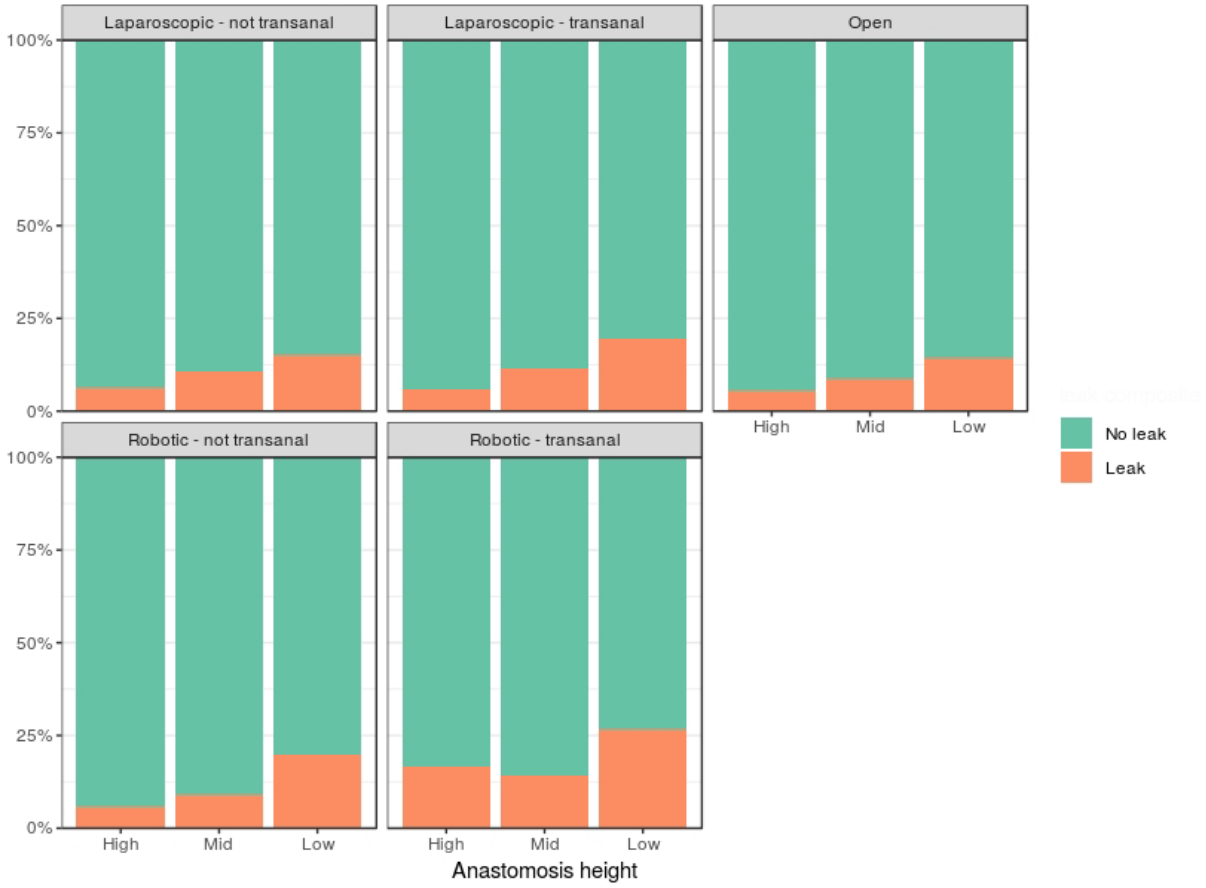


Figure 3 Leak rates by approach and tumour height.

Table 6). However, in a mixed-effects model (Table 7), none of the operative approaches were significantly associated with margin positivity except for non-restorative surgery. The model demonstrated fair discrimination (AUC: 0.72).

Discussion

This study supports the use of a TaTME approach for rectal cancer resection, with comparable postoperative outcomes and pathological safety compared to other approaches. This is in line with recent evidence on TaTME delivery across Europe [12,14,15]. The leak rate was higher than previously reported, at 12.9%, which at univariable level was significantly higher than other techniques. Once adjusted for confounders, this variability was largely a result of anastomosis in the lowest part of the rectum; transanal surgery became non-significant in mixed-effects and propensity-score matched models. By including other techniques within this study, it allows individual surgeons and units to benchmark practice and consider their own selection of patients. TaTME was more commonly used in men, in those undergoing long course chemoradiotherapy and in those with low tumours. This parallels current recommendations for the selection of patients, demonstrating appropriate adoption of this technique within included centres [5,16].

Leak rates after transanal (TaTME) surgery have been reported as 4.7% to 9.1% in recent systematic reviews [5,11] and 6.7% in a subsequent large international registry [17]. We add to this literature by providing an unselected, 'real-world' view of implementation of TaTME internationally in a prospective setting, with risk-adjustment of outcome data with mixed-effects modelling. The higher unadjusted leak rate identified in the present study may reflect learning curve effects from centres being at variable stages of adoption of the technique. It may also reflect the fact that we only included malignant conditions. An important variability between studies still exists in how anastomotic leakage is defined and detected. By comparing leakage to a simultaneous

Table 2 Short-term intraoperative and postoperative outcomes by approach.

Factor	Levels	Laparoscopic not transanal	Laparoscopic transanal	Open	Robotic not transanal	Robotic transanal	*P*-value
Postoperative outcomes							
Anastomotic leak	No leak	873 (74.2)	242 (65.9)	560 (64.5)	87 (70.7)	24 (53.3)	< 0.001
	Leak	79 (6.7)	38 (10.4)	48 (5.5)	8 (6.5)	7 (15.6)	
	No anastomosis	224 (19.0)	87 (23.7)	260 (30.0)	28 (22.8)	14 (31.1)	
Complication grade	Missing	6 (0.5)	1 (0.3)	4 (0.5)	2 (1.6)	2 (4.4)	< 0.001
	Grade 1-2	257 (21.9)	93 (25.3)	241 (27.8)	24 (19.5)	11 (24.4)	
	Grade 3-5	120 (10.2)	58 (15.8)	101 (11.6)	17 (13.8)	8 (17.8)	
	None	793 (67.4)	215 (58.6)	522 (60.1)	80 (65.0)	24 (53.3)	
Pathological margin	CRM involved	38 (3.2)	14 (3.8)	41 (4.7)	1 (0.8)	0 (0.0)	0.134
	CRM not involved	1011 (86.0)	317 (86.4)	750 (86.4)	109 (88.6)	37 (82.2)	
	Missing	127 (10.8)	36 (9.8)	77 (8.9)	13 (10.6)	8 (17.8)	
Length of stay	Mean (SD)	8.4 (5.6)	10 (6.9)	10.7 (5.5)	7.7 (5.8)	9.9 (7.5)	< 0.001
Intraoperative outcomes							
Any intraoperative complication	No	1124 (95.6)	354 (96.5)	834 (96.1)	120 (97.6)	38 (84.4)	0.003
	Yes	52 (4.4)	13 (3.5)	34 (3.9)	3 (2.4)	7 (15.6)	
Vascular injury	No	1161 (98.7)	363 (98.9)	857 (98.7)	121 (98.4)	43 (95.6)	0.455
	Yes	15 (1.3)	4 (1.1)	11 (1.3)	2 (1.6)	2 (4.4)	
Bowel injury	No	1163 (98.9)	365 (99.5)	858 (98.8)	121 (98.4)	42 (93.3)	0.01
	Yes	13 (1.1)	2 (0.5)	10 (1.2)	2 (1.6)	3 (6.7)	
Other organ injury	No	1152 (98.0)	360 (98.1)	854 (98.4)	123 (100.0)	41 (91.1)	0.005
	Yes	24 (2.0)	7 (1.9)	14 (1.6)	0 (0.0)	4 (8.9)	

P-value derived from χ^2 test for categorical variables. % shown by column.
CRM, Circumferential resection margin (</> 1 mm); CVA, Cerebrovascular accident; IHD, Ischemic heart disease; IQR, Interquartile range; N/A, Not applicable; SD, Standard deviation.

cohort of laparoscopic, open and robotic resections from the same centres, we can explore and control for case selection variability by approach and mitigate against concerns of reporting bias. Reassuringly, male gender and low tumour height were strongly predictive factors for leak in our mixed effects models, which is consistent with current knowledge [18–20]. Whilst our data gives evidence for safety in the current dissemination of TaTME, structured training with proctorship from experienced proponents remains essential.

Improved pathological and oncological outcomes are a potential benefit of TaTME. The positive resection margin rate in restorative surgery from this study (4.0%) is consistent with previous reports, including the transanal component [5]. Fleshman *et al.* [21] previously reported a significantly lower difference rate of CRM involvement with TaTME when compared with laparoscopic TME. In contrast, the Bordeaux randomized trial found a significantly greater rate of CRM involvement for laparoscopic TME when compared to TaTME (18.0% *vs* 4.0%, $P = 0.025$) although this did not mean a decrease in local recurrence (long term oncological outcomes) [22]. The low positive CRM rates seen with robotic surgery in the lower rectum within the present study are likely to represent a degree of case selection at a site level; results from randomised trials in TaTME and robotic rectal cancer surgery are awaited.

This study also provides valuable information for other resection techniques. Recent randomised trials have suggested laparoscopic TME may lack oncological safety compared to open surgery in the mid and low rectum (ALaCaRT and ACOSOG) [21,22]. The present study shows pathological equivalence of laparoscopic and open approaches, with a selection variability evident that suggests surgeons are carefully and correctly selecting patients for each approach; this is consistent with COLOR II, COREAN and CLASiCC trials [18,19,23]. There were relatively few robotic cases in this cohort. Where robotics was performed, the positive CRM and conversion rates were lower when compared to laparoscopic techniques. The ROLARR trial with 471 patients did not show differences between laparoscopic and robotic for positive resection margin [24]. International registry studies alongside ROLARR reported a rate of conversion from laparoscopic to open or transanal of 6.3%. We found significant differences between laparoscopic transanal that presented the highest rate of conversion (16.2%) and robotic transanal (0%). This is consistent with the findings

Table 3 Univariable and multilevel models for overall anastomotic leak (primary outcome measure).

Factor	Level	Anastomotic leak		OR (univariable)	OR (multilevel)
		No leak	Leak		
Approach	Laparoscopic – not transanal	806 (48.1)	72 (44.2)	– (Reference)	– (Reference)
	Laparoscopic – transanal	223 (13.3)	32 (19.6)	1.61 (1.02–2.48, $P = 0.036$)	1.23 (0.77–1.97, $P = 0.386$)
	Open	538 (32.1)	45 (27.6)	0.94 (0.63–1.37, $P = 0.740$)	0.93 (0.61–1.43, $P = 0.745$)
	Robotic – not transanal	86 (5.1)	8 (4.9)	1.04 (0.45–2.11, $P = 0.917$)	0.81 (0.36–1.78, $P = 0.594$)
	Robotic – transanal	22 (1.3)	6 (3.7)	3.05 (1.10–7.34, $P = 0.019$)	2.11 (0.79–5.62, $P = 0.135$)
Age	< 55	278 (16.6)	29 (17.8)	–	–
	55–70	775 (46.3)	77 (47.2)	0.95 (0.61–1.51, $P = 0.831$)	0.92 (0.58–1.47, $P = 0.729$)
	70–80	481 (28.7)	47 (28.8)	0.94 (0.58–1.54, $P = 0.792$)	0.87 (0.51–1.48, $P = 0.606$)
	> 80	141 (8.4)	10 (6.1)	0.68 (0.31–1.39, $P = 0.311$)	0.70 (0.31–1.58, $P = 0.394$)
Gender	Female	629 (37.6)	34 (20.9)	–	–
	Male	1046 (62.4)	129 (79.1)	2.28 (1.56–3.42, $P < 0.001$)	2.29 (1.52–3.44, $P < 0.001$)
ASA class	Low risk (ASA 1-2)	1150 (68.7)	114 (69.9)	–	–
	High risk (ASA 3-5)	525 (31.3)	49 (30.1)	0.94 (0.66–1.33, $P = 0.736$)	0.99 (0.66–1.49, $P = 0.969$)
BMI	Normal weight	515 (30.7)	53 (32.5)	–	–
	Underweight	30 (1.8)	4 (2.5)	1.30 (0.37–3.44, $P = 0.639$)	1.35 (0.45–4.10, $P = 0.594$)
	Overweight	741 (44.2)	71 (43.6)	0.93 (0.64–1.36, $P = 0.707$)	0.89 (0.60–1.33, $P = 0.577$)
	Obese	389 (23.2)	35 (21.5)	0.87 (0.56–1.36, $P = 0.556$)	0.86 (0.53–1.39, $P = 0.534$)
History of IHD/CVA	No	1420 (84.8)	138 (84.7)	–	–
	Yes	255 (15.2)	25 (15.3)	1.01 (0.63–1.55, $P = 0.969$)	1.16 (0.70–1.94, $P = 0.567$)
History of diabetes mellitus	No	1431 (85.4)	140 (85.9)	–	–
	Diabetes: any control	244 (14.6)	23 (14.1)	0.96 (0.59–1.50, $P = 0.874$)	0.87 (0.53–1.42, $P = 0.584$)
Smoking history	Non-smoker	1436 (85.7)	129 (79.1)	–	–
	Current	239 (14.3)	34 (20.9)	1.58 (1.05–2.34, $P = 0.025$)	1.46 (0.95–2.23, $P = 0.082$)
Operator type	Colorectal	1403 (83.8)	137 (84.0)	–	–
	General surgery	272 (16.2)	26 (16.0)	0.98 (0.62–1.49, $P = 0.924$)	1.11 (0.68–1.81, $P = 0.687$)
Neoadjuvant therapy	Chemotherapy only	69 (4.1)	3 (1.8)	–	–
	Long course CRTx	368 (22.0)	48 (29.4)	3.00 (1.06–12.58, $P = 0.071$)	1.75 (0.51–5.99, $P = 0.371$)
	Short course radiotherapy	80 (4.8)	14 (8.6)	4.02 (1.25–17.98, $P = 0.034$)	2.74 (0.73–10.30, $P = 0.136$)
	None	1158 (69.1)	98 (60.1)	1.95 (0.71–8.05, $P = 0.266$)	1.97 (0.59–6.55, $P = 0.271$)
Anastomosis height	High rectum	525 (31.3)	29 (17.8)	–	–
	Mid rectum	528 (31.5)	40 (24.5)	1.37 (0.84–2.26, $P = 0.209$)	1.33 (0.79–2.23, $P = 0.277$)
	Low rectum	622 (37.1)	94 (57.7)	2.74 (1.80–4.28, $P < 0.001$)	2.72 (1.55–4.77, $P < 0.001$)
Anastomotic configuration	End to End	1271 (75.9)	123 (75.5)	–	–
	Side to Side	83 (5.0)	2 (1.2)	0.25 (0.04–0.80, $P = 0.054$)	0.27 (0.06–1.16, $P = 0.079$)
	Side to End	321 (19.2)	38 (23.3)	1.22 (0.82–1.78, $P = 0.303$)	1.10 (0.73–1.65, $P = 0.662$)
Leak test performed	No	543 (32.4)	54 (33.1)	–	–
	Yes	1132 (67.6)	109 (66.9)	0.97 (0.69–1.37, $P = 0.853$)	1.11 (0.76–1.64, $P = 0.584$)
Defunctioning stoma	Yes	720 (43.0)	93 (57.1)	–	–
	No	955 (57.0)	70 (42.9)	0.57 (0.41–0.78, $P = 0.001$)	1.05 (0.68–1.63, $P = 0.813$)

AUROC:0.70, AIC: 1088.1

Overall anastomotic leak was pre-defined as either (i) gross anastomotic leakage proven radiologically or clinically, or (ii) the presence of an intraperitoneal (abdominal or pelvic) fluid collection on post-operative imaging. Patients with missing outcome or risk adjustment data have been excluded from this model. Odds ratio (OR) presented with 95% confidence intervals. % shown by column.

CRTx, Chemoradiotherapy; CVA, Cerebrovascular accident; IHD, Ischemic heart disease; IQR, Interquartile range; N/A, Not applicable; SD, Standard deviation.

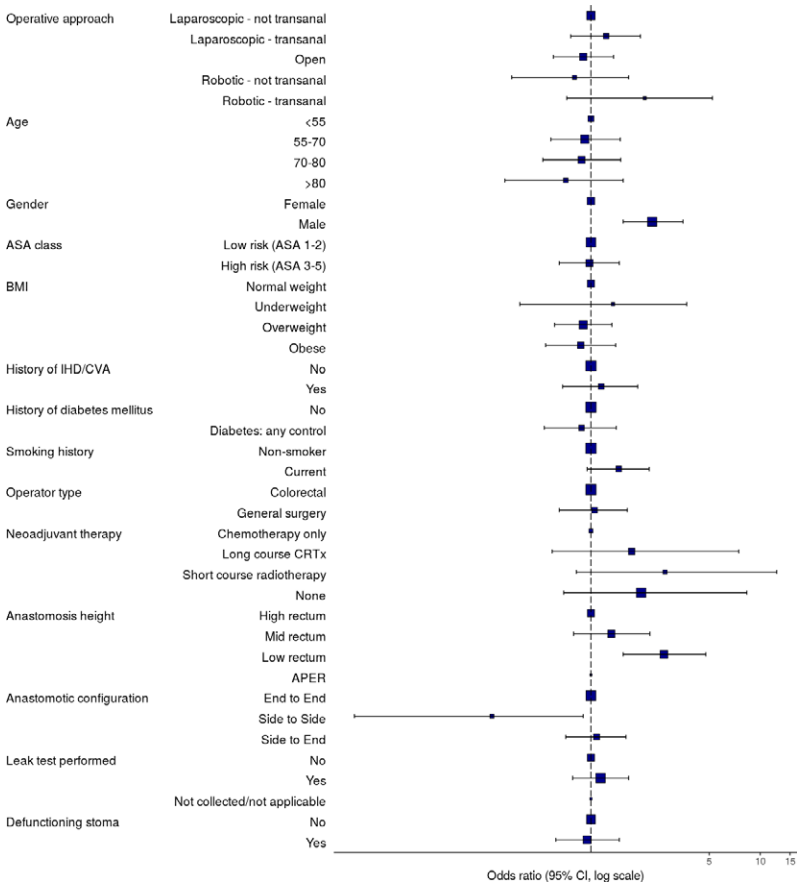


Figure 4 Forest plot for mixed effects model of factors associated with anastomotic leak in elective rectal cancer surgery with restorative anastomosis

Table 4 Balanced characteristics of propensity score matched groups.

		Perineal approach		
Factor	Level	Not transanal	Transanal	*P*-value
Age	< 55	108 (20.1)	56 (20.9)	0.979
	55–70	246 (45.9)	125 (46.6)	
	70–80	146 (27.2)	70 (26.1)	
	> 80	36 (6.7)	17 (6.3)	
Gender	Female	179 (33.4)	90 (33.6)	0.958
	Male	357 (66.6)	178 (66.4)	
Anastomosis height	High rectum	100 (18.7)	46 (17.2)	0.041
	Mid rectum	168 (31.3)	64 (23.9)	
	Low rectum	268 (50.0)	158 (59.0)	
MRI AJCC stage	Stage 1	167 (31.2)	72 (26.9)	0.553
	Stage 2	177 (33.0)	100 (37.3)	
	Stage 3	138 (25.7)	68 (25.4)	
	Stage 4	54 (10.1)	28 (10.4)	

P-value derived from χ^2 test for categorical variables. % shown by column.

Table 5 Summary of propensity score matched multivariable model for overall anastomotic leak.

Factor	Level	OR (multivariable)
Transanal component	No	–
	Yes	1.22 (0.75-1.96, $P = 0.420$)
Age	< 55	–
	55–70	0.92 (0.50-1.73, $P = 0.777$)
	70–80	0.68 (0.34-1.39, $P = 0.282$)
	> 80	0.47 (0.10-1.52, $P = 0.253$)
Gender	Female	–
	Male	2.94 (1.65-5.60, $P < 0.001$)
Anastomosis height	High rectum	–
	Mid rectum	1.81 (0.72-5.16, $P = 0.23$)
	Low rectum	3.75 (1.66-10.10, $P = 0.003$)
MRI AJCC stage	Stage 1	–
	Stage 2	1.18 (0.64-2.25, $P = 0.60$)
	Stage 3	1.55 (0.79-3.05, $P = 0.203$)
	Stage 4	1.03 (0.40-2.47, $P = 0.944$)

Overall anastomotic leak was pre-defined as either (i) gross anastomotic leakage proven radiologically or clinically, or (ii) the presence of an intraperitoneal (abdominal or pelvic) fluid collection on post-operative imaging. Odds ratio (OR) presented with 95% confidence intervals.

Table 6 Circumferential resection margin positive rates (pathological) by approach and height in rectum.

		Laparoscopic		Robotic	
	Open	Transanal	Not transanal	Transanal	Not transanal
Low rectum	19/236	9/163	16/198	0/19	1/27
	8.05%	5.52%	8.08%	0.00%	3.70%
Middle rectum	12/218	5/88	10/267	0/12	0/33
	5.50%	5.68%	3.75%	0.00%	0.00%
High Rectum	10/337	0/80	12/584	0/6	0/50
	2.96%	0.00%	2.05%	0.00%	0.00%

of ROLARR trial about the potential for robotic surgery to decrease the rate of conversion.

Finally the APER rate provides a contemporary permanent stoma rate across a variety of international sites for an operation with known variability between units [25]. Our group plans to produce a future report describing geographic variability in colorectal surgery, exploring differences in patient factors, disease presentations and techniques utilised internationally, across the last three international ESCP audits.

This study has limitations. Unadjusted outcomes showed higher major complication rates with robotic surgery and also transanal surgery, although without risk adjustment for confounding factors this must be interpreted with significant caution. Further research is needed to correctly risk-adjust for individual surgeon, or surgical team experience in TaTME, as well as unmeasured patient, tumour and operation-specific factors. Similarly, standardised definitions of anastomotic leakage and its detection remain uncommonly used between studies. Selection bias is an unavoidable factor in this type of observational research. We have attempted to minimize the effects of this by undertaking adjusted analyses using mixed-effects logistic regression models, but accept that this can never fully counteract the nuances involved in clinical decision-making. This said, the current study was designed to detect safety differences in current practice rather than test efficacy of treatments directly.

Results from randomised trials comparing outcomes after the variety of approaches available for rectal cancer surgery are now needed, particularly evaluating TaTME against laparoscopic TME without a transanal perineal component [26].

Table 7 Univariable and multilevel models for circumferential resection margin involvement.

		Resection margin			
Factor	Level	Negative	Positive	OR (univariable)	OR (multilevel)
Transanal component	No	1709 (79.3)	69 (76.7)	–	–
	Yes	445 (20.7)	21 (23.3)	1.17 (0.69–1.89, $P = 0.540$)	0.96 (0.56–1.65, $P = 0.889$)
Approach	Laparoscopic	1088 (50.5)	40 (44.4)	–	–
	Open	934 (43.4)	49 (54.4)	1.43 (0.93–2.20, $P = 0.102$)	1.50 (0.93–2.42, $P = 0.097$)
	Robotic	132 (6.1)	1 (1.1)	0.21 (0.01–0.96, $P = 0.120$)	0.17 (0.02–1.28, $P = 0.086$)
Age	< 55	335 (15.6)	19 (21.1)	–	–
	55–70	959 (44.5)	32 (35.6)	0.59 (0.33–1.07, $P = 0.074$)	0.57 (0.31–1.05, $P = 0.072$)
	70–80	626 (29.1)	25 (27.8)	0.70 (0.38–1.31, $P = 0.261$)	0.75 (0.39–1.45, $P = 0.393$)
	> 80	234 (10.9)	14 (15.6)	1.05 (0.51–2.14, $P = 0.883$)	1.37 (0.62–3.05, $P = 0.440$)
Gender	Female	781 (36.3)	32 (35.6)	–	–
	Male	1373 (63.7)	58 (64.4)	1.03 (0.67–1.62, $P = 0.892$)	1.08 (0.68–1.73, $P = 0.733$)
ASA class	Low risk (ASA 1-2)	1426 (66.2)	63 (70.0)	–	–
	High risk (ASA 3-5)	728 (33.8)	27 (30.0)	0.84 (0.52–1.31, $P = 0.456$)	0.64 (0.37–1.12, $P = 0.116$)
BMI	Normal weight	672 (31.2)	25 (27.8)	–	–
	Underweight	40 (1.9)	6 (6.7)	4.03 (1.43–9.82, $P = 0.004$)	4.71 (1.74–12.79, $P = 0.002$)
	Overweight	929 (43.1)	39 (43.3)	1.13 (0.68–1.90, $P = 0.644$)	1.32 (0.77–2.26, $P = 0.313$)
	Obese	513 (23.8)	20 (22.2)	1.05 (0.57–1.90, $P = 0.878$)	1.17 (0.62–2.23, $P = 0.626$)
History of IHD/CVA	No	1797 (83.4)	72 (80.0)	–	–
	Yes	357 (16.6)	18 (20.0)	1.26 (0.72–2.09, $P = 0.394$)	1.75 (0.93–3.26, $P = 0.081$)
History of diabetes mellitus	No	1818 (84.4)	80 (88.9)	–	–
	Diabetes: any control	336 (15.6)	10 (11.1)	0.68 (0.33–1.26, $P = 0.251$)	0.62 (0.31–1.25, $P = 0.180$)
Smoking history	Non-smoker	1824 (84.7)	74 (82.2)	–	–
	Current	330 (15.3)	16 (17.8)	1.20 (0.66–2.02, $P = 0.528$)	1.10 (0.61–2.00, $P = 0.756$)
Operator type	Colorectal	1836 (85.2)	79 (87.8)	–	–
	General surgery	318 (14.8)	11 (12.2)	0.80 (0.40–1.46, $P = 0.505$)	0.91 (0.45–1.85, $P = 0.791$)
Neoadjuvant therapy	Chemotherapy only	75 (3.5)	2 (2.2)	–	–
	Long course CRTx	555 (25.8)	40 (44.4)	2.70 (0.81–16.81, $P = 0.176$)	2.17 (0.49–9.60, $P = 0.307$)
	Short course radiotherapy	156 (7.2)	9 (10.0)	2.16 (0.54–14.42, $P = 0.331$)	1.76 (0.35–8.76, $P = 0.491$)
	None	1368 (63.5)	39 (43.3)	1.07 (0.32–6.65, $P = 0.928$)	1.11 (0.25–4.84, $P = 0.891$)
Anastomosis height	High rectum	540 (25.1)	13 (14.4)	–	–
	Mid rectum	574 (26.6)	16 (17.8)	1.16 (0.55–2.47, $P = 0.698$)	1.09 (0.51–2.31, $P = 0.831$)
	Low rectum	714 (33.1)	24 (26.7)	1.40 (0.72–2.85, $P = 0.339$)	1.08 (0.50–2.30, $P = 0.849$)
	APER	326 (15.1)	37 (41.1)	4.71 (2.53–9.33, $P < 0.001$)	3.55 (1.68–7.52, $P = 0.001$)

AUC:0.77, AIC: 731.5

Overall anastomotic leak was pre-defined as either (i) gross anastomotic leakage proven radiologically or clinically, or (ii) the presence of an intraperitoneal (abdominal or pelvic) fluid collection on post-operative imaging. Odds ratio (OR) presented with 95% confidence intervals. % shown by column.

CRTx, Chemoradiotherapy; CVA, Cerebrovascular accident; IHD, Ischemic heart disease; IQR, Interquartile range; N/A, Not applicable; SD, Standard deviation.

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Conflicts of interests

None to declare.

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