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Original Article

Stoma-free survival after anastomotic leak following rectal cancer resection: worldwide cohort of 2470 patients

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Members of the TENTACLE-Rectum Collaborative Group are co-authors of this study and are listed under the heading Collaborators.

Abstract

Background: The optimal treatment of anastomotic leak after rectal cancer resection is unclear. This worldwide cohort study aimed to provide an overview of four treatment strategies applied.

Methods: Patients from 216 centres and 45 countries with anastomotic leak after rectal cancer resection between 2014 and 2018 were included. Treatment was categorized as salvage surgery, faecal diversion with passive or active (vacuum) drainage, and no primary/secondary faecal diversion. The primary outcome was 1-year stoma-free survival. In addition, passive and active drainage were compared using propensity score matching (2 : 1).

Results: Of 2470 evaluable patients, 388 (16.0 per cent) underwent salvage surgery, 1524 (62.0 per cent) passive drainage, 278 (11.0 per cent) active drainage, and 280 (11.0 per cent) had no faecal diversion. One-year stoma-free survival rates were 13.7, 48.3, 48.2, and 65.4 per cent respectively. Propensity score matching resulted in 556 patients with passive and 278 with active drainage. There was no statistically significant difference between these groups in 1-year stoma-free survival (OR 0.95, 95 per cent c.i. 0.66 to 1.33), with a risk difference of −1.1 (95 per cent c.i. −9.0 to 7.0) per cent. After active drainage, more patients required secondary salvage surgery (OR 2.32, 1.49 to 3.59), prolonged hospital admission (an additional 6 (95 per cent c.i. 2 to 10) days), and ICU admission (OR 1.41, 1.02 to 1.94). Mean duration of leak healing did not differ significantly (an additional 12 (−28 to 52) days).

Conclusion: Primary salvage surgery or omission of faecal diversion likely correspond to the most severe and least severe leaks respectively. In patients with diverted leaks, stoma-free survival did not differ statistically between passive and active drainage, although the increased risk of secondary salvage surgery and ICU admission suggests residual confounding.

Introduction

A feared complication after restorative rectal cancer resection is anastomotic leak (AL), owing to its significant impact on morbidity[1–4]. The incidence of AL remains high, with rates of up to 20 per cent[5], despite developments in surgical technique and perioperative care. AL is associated with prolonged hospital stay, reintervention, a stage-dependent decrease in survival, bowel dysfunction, and a high risk of a permanent stoma[6–10]. Although the consequences of AL are evident, international consensus and standardization of treatment strategies is

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lacking[11], possibly because of heterogeneity of both the AL as well as the patients it affects.

Treatment of AL mostly depends on the patient's clinical symptoms and severity of AL[12,13], which varies from occult leaks in patients with a diverting stoma, to faecal peritonitis with multiple organ failure[14,15]. Traditionally, patients with AL have been treated with faecal diversion, either with or without abscess drainage, and in a minority of patients the anastomosis is dismantled with creation of an end-colostomy[16–18]. These treatment strategies are associated with high rates of non-healing, particularly in irradiated patients[16]. Moreover, persistent leakage might give rise to a chronic presacral sinus that can cause long-term problems, such as fistula formation, fasciitis, and bleeding. Pelvic sepsis originating from a non-healed leak is a serious condition, contributing to hospital admission and multiple interventions, often requiring extensive salvage surgery[19,20].

In the past decade, active treatment strategies have emerged starting with the introduction of endoscopic vacuum therapy (EVT)[21]. This strategy was subsequently modified by closing the anastomotic defect as soon as appropriate granulation of the cavity was observed. This so-called endoscopic vacuum-assisted transanal closure (EVAC) can yield high success rates in experienced hands[16,21,22]. The main objective of EVAC is more effective and faster healing of the anastomosis with preservation of bowel continuity[23–25]. However, substantial heterogeneity exists among ALs, and clinical decision-making is also dependent on various patient, clinical, and surgical characteristics (for example, co-morbidity, time from diagnosis, defect circumference)[12,26,27]. No large studies have evaluated different AL treatment strategies, simultaneously considering all these various characteristics.

This worldwide cohort study aimed to evaluate four different treatment strategies, with 1-year stoma-free survival as the main outcome. In the TENTACLE-Rectum study, detailed data were collected from a large number of patients who developed AL after rectal cancer resection with at least 1 year of follow-up[17]. In the present explorative study, outcomes after AL were analysed according to the following predefined primary treatment strategies: salvage surgery, faecal diversion with passive drainage, faecal diversion with active drainage, and no faecal diversion. The outcomes encompassed the need for secondary salvage surgery, total duration of hospital stay, ICU admission, time to healing of the leak, and 1-year stoma-free survival. Moreover, as robust comparative studies are scarce, the aforementioned outcomes were additionally compared among patients with a diverted leak who underwent either active (EVT) or passive drainage of the perianastomotic abscess.

Methods

Study design

This was an international retrospective cohort study encompassing 216 centres from 45 countries. The TENTACLE-Rectum study protocol was approved by the institutional board at Radboud University Medical Centre On 17 October 2019[17]. All collaborating centres adhered to the regulations of their own ethical committees. The study was registered at ClinicalTrials.gov (NCT04127734), and was conducted in agreement with the STROBE guidelines for reporting of observational studies[28].

Patient selection

Patients with rectal cancer who underwent surgery between 1 January 2014 and 31 December 2018 in the participating centres were included if they were diagnosed with AL within 1 year after index surgery. AL was defined as 'a defect of the intestinal wall at the anastomotic site (including suture and staple lines of neorectal reservoirs) leading to a communication between the intra- and extraluminal compartments'[29]. Included patients were: aged 18 years or older; diagnosed with rectal cancer, defined as an adenocarcinoma with its lower border below the level of the sigmoid take-off[30]; and underwent surgical resection with creation of a primary anastomosis for either primary cancer, salvage resection for regrowth, or completion total mesorectal excision (TME) after local excision. Patients were excluded if they underwent surgery for benign or recurrent disease, or had an emergency resection. Patients with missing data regarding treatment of AL were also excluded.

Treatment strategies for anastomotic leak after rectal cancer resection

Four main treatment strategies for AL were defined based on a case-vignette study among international experts, in which the use of basic treatment principles was evaluated for different leak scenarios[27]. These four strategies comprised salvage surgery, faecal diversion with passive drainage, faecal diversion with active drainage, and no faecal diversion. Salvage surgery included dismantling of the anastomosis and formation of an end-colostomy, or immediate or delayed (Turnbull–Cutait) redo anastomosis. Faecal diversion could be accomplished using a primary diverting stoma that was constructed during index surgery, or a secondary diverting stoma after diagnosis of AL. Passive drainage comprised solely faecal diversion, or a combination of faecal diversion and transabdominal or transgluteal drain placement, endoscopic or surgical washout of the abscess cavity, or abdominal lavage. Active drainage comprised faecal diversion and EVT (Endo-SPONGE®) with or without transanal closure. In the fourth strategy (no faecal diversion), no primary or secondary diverting stoma was created, and treatment could consist of any of the following modalities alone or in combination: antibiotics, drainage (transabdominal or transgluteal drain placement, endoscopic or surgical abscess drainage, abdominal or colonic lavage), endoscopic clipping or stenting, or transanal surgical closure. Primary treatment was defined as the first treatment strategy after diagnosis of AL, and was considered to have failed if another secondary treatment strategy was used afterwards. All patients were categorized and subsequently analysed based on the primary treatment modality, according to the intention-to-treat principle.

Definitions

Healing of the leak was confirmed by CT, MRI, endoscopy or contrast enema, and time to healing calculated in patients with an anastomosis *in situ*. The healed anastomosis could either be a primary or secondary anastomosis, the latter being created by excision of the leaking primary anastomosis by either an immediate or delayed (Turnbull–Cutait) redo procedure. Presacral abscess present more than 1 year after index surgery was defined as a chronic sinus. A chronic sinus was considered a non-healed anastomosis.

Outcomes

The primary outcome of this study was 1-year stoma-free survival, defined as being alive without a temporary or permanent ileostomy or colostomy 1 year after index surgery. Secondary outcomes were: failure of first treatment necessitating salvage surgery, number of secondary anastomoses, total duration of hospital stay, ICU admission, total duration of ICU stay, and time to leak healing.

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Statistical analysis

Patient, tumour, index treatment, and leak characteristics were evaluated for the four treatment strategies using descriptive statistics. Baseline characteristics are presented as numbers with percentages, and continuous data according to their distribution as mean(s.d.) or median (i.q.r.). All missing data were considered to be missing at random, and multiple imputation using chained equations was performed[31,32]. Additional information about handling of missing data and multiple imputation can be found in the *supplementary material*. Owing to the explorative nature of this study, a sample size calculation was not performed.

A comparative analysis was undertaken among patients who underwent primary or secondary faecal diversion, with either primary passive or primary active drainage of the perianastomotic abscess, and propensity score matching (PSM) was used to minimize confounding bias (*supplementary material* and *Table S1*). Multivariable logistic regression modelling was used to calculate propensity scores, including the following known confounders: age, sex, BMI, ASA fitness grade, clinical metastatic disease category, neoadjuvant therapy, abdominal approach, transanal approach (transanal TME), multivisceral resection, presence of a primary diverting stoma, clinical setting of AL diagnosis, postoperative day of AL diagnosis, presence of severe clinical symptoms, anastomotic defect circumference, ischaemic afferent colon, anastomotic fistula, retraction of the afferent colon, abdominal contamination, and reactivation leakage[33]. Cases were matched using the nearest-neighbour method, with a caliper of 0.2 and a 2 : 1 ratio[34,35]. To assess the covariate balance between the two treatment strategies before and after PSM, standardized mean differences (SMDs) were calculated. There was considered to be sufficient balance between cohorts when the SMD was below 0.1.

In patients with a diverted leak who underwent passive or active drainage as initial treatment for the perianastomotic abscess, the primary outcome was assessed using logistic regression by estimating an OR with 95 per cent confidence interval and a risk difference (RD) between treatment strategies. Secondary outcomes were evaluated using logistic regression (OR with 95 per cent c.i.) and RD, or linear regression (mean difference with 95 per cent c.i.). To assess the effect of annual case volume on outcomes, a sensitivity analysis was performed including annual case volume (low, below 20; middle, 20–49; high, 50 or more) in the multivariable logistic regression model. PSM and the subsequent comparative analyses were performed in each data set, and these results were pooled according to Rubin's rule. All analyses were carried out in R version 4.1.3 (R Foundation for Statistical Computing, Vienna, Austria) using packages mice and MatchIt.

Results

In total, 2710 patients were included in the database. After exclusion of 240 patients because of incorrect year of index surgery (189), AL diagnosis beyond 1 year (21), absence of AL (1), and missing primary treatment modality (29), 2470 patients remained for analysis. Based on the primary treatment strategy for AL, these patients were categorized into salvage surgery (388 patients, 16.0 per cent), faecal diversion with passive drainage (1524 patients, 62.0 per cent), faecal diversion with active drainage (278 patients, 11.0 per cent) and no faecal diversion (280

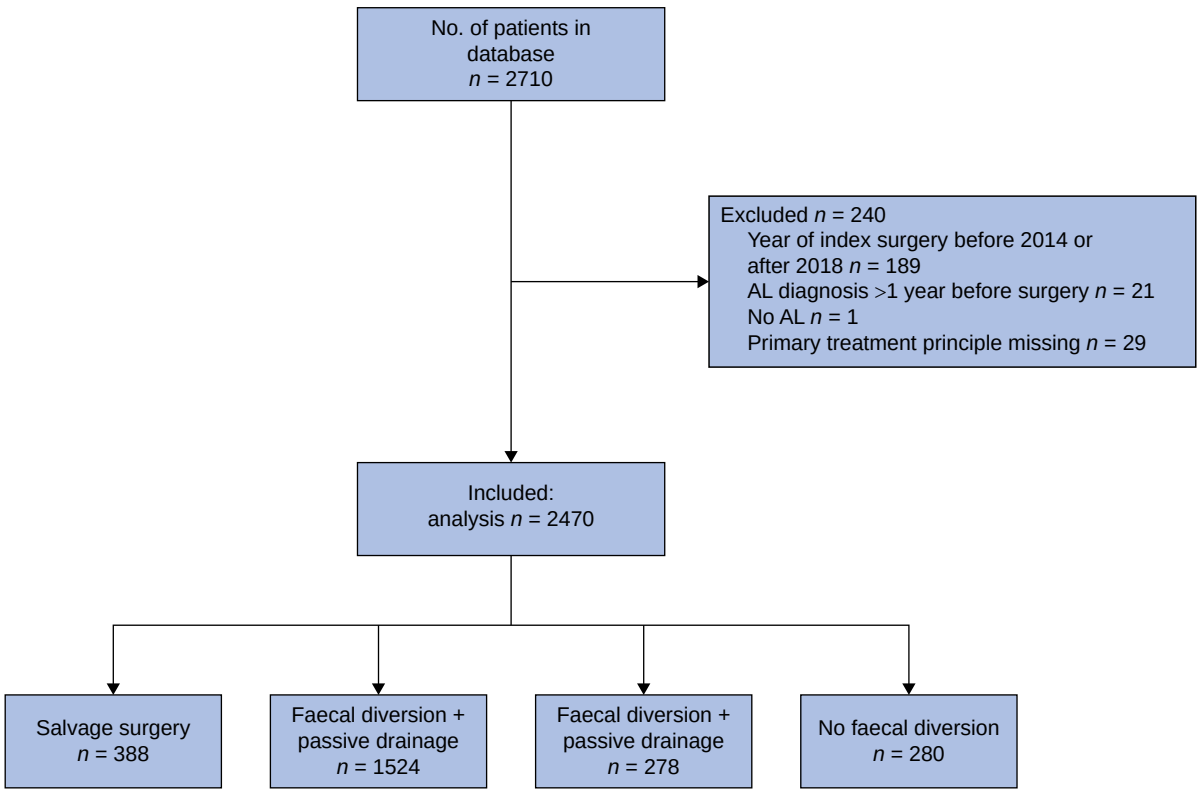


Fig. 1 Study flow chart

AL, anastomotic leak.

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Table 1 Baseline characteristics for the four predefined treatment strategies

	Salvage surgery (*n* = 388)	Faecal diversion + passive drainage (*n* = 1524)	Faecal diversion + active drainage (*n* = 278)	No faecal diversion (*n* = 280)	SMD
Age (years), median (i.q.r.)	65 (59–73)	66 (57–71)	64 (56–72)	65 (57–74)	0.099
Sex ratio (M : F)	256 : 132	1104 : 420	229 : 49	192 : 88	0.199
ASA fitness grade					0.172
I	48 (12.7)	246 (16.4)	47 (17.3)	36 (13.5)	
II	196 (51.9)	863 (57.7)	165 (60.7)	150 (56.2)	
III–IV	134 (35.4)	387 (25.9)	60 (22.1)	81 (30.3)	
Missing	10	28	6	13	
BMI (kg/m²)					0.157
Underweight (< 18.5)	26 (7.4)	68 (4.8)	8 (3.0)	16 (6.6)	
Normal (18.5–24.9)	120 (34.0)	449 (31.9)	88 (32.8)	83 (34.0)	
Overweight (25.0–29.9)	124 (35.1)	599 (42.6)	103 (38.4)	96 (39.3)	
Obese (≥ 30.0)	83 (23.5)	291 (20.7)	69 (25.7)	49 (20.1)	
Missing	35	117	10	36	
Clinical metastasis category					0.036
cM0	303 (89.4)	1202 (91.4)	234 (91.1)	201 (91.4)	
cM1	36 (10.6)	113 (8.6)	23 (8.9)	19 (8.6)	
Missing	49	209	21	60	
Neoadjuvant therapy					0.323
None	209 (53.9)	575 (37.7)	111 (39.9)	176 (62.9)	
Radiotherapy	34 (8.8)	202 (13.3)	37 (13.3)	18 (6.4)	
Chemotherapy	10 (2.6)	23 (1.5)	6 (2.2)	7 (2.5)	
Chemoradiation	135 (34.8)	724 (47.5)	124 (44.6)	79 (28.2)	
Clinical setting of AL diagnosis					0.281
Surgical ward	296 (76.3)	1030 (67.6)	182 (65.5)	182 (65.5)	
ICU/HC	35 (9.0)	50 (3.3)	11 (4.0)	11 (4.0)	
Emergency department	28 (7.2)	149 (9.8)	28 (10.1)	41 (14.7)	
Outpatient clinic	29 (7.5)	294 (19.3)	57 (20.5)	44 (15.8)	
Missing	0	1	0	2	
POD of AL diagnosis, median (i.q.r.)	6 (4–10)	8 (5–20)	10 (5–19)	8 (5–17)	0.098
Abdominal approach					0.283
Laparoscopic	223 (57.5)	962 (63.1)	170 (61.2)	159 (57.0)	
Robot-assisted	26 (6.7)	134 (8.8)	53 (19.1)	20 (7.2)	
Laparotomy	139 (35.8)	428 (28.1)	55 (19.8)	100 (35.8)	
Missing	0	0	0	1	
Transanal TME					0.179
No	331 (85.3)	1240 (81.4)	201 (72.3)	239 (85.4)	
Yes	57 (14.7)	284 (18.6)	77 (27.7)	41 (14.6)	
Multivisceral resection					0.080
No	352 (92.4)	1393 (93.6)	255 (94.1)	249 (90.2)	
Yes	29 (7.6)	96 (6.4)	16 (5.9)	27 (9.8)	
Missing	7	35	7	4	
Primary defunctioning stoma					1.353
No	204 (52.6)	310 (20.8)	65 (23.4)	280 (100)	
Yes	184 (47.4)	1214 (79.2)	213 (76.6)	0 (0)	
Fistula					0.154
No	332 (90.0)	1351 (93.0)	262 (96.7)	226 (90.0)	
Yes	37 (10.0)	101 (7.0)	9 (3.3)	25 (10.0)	
Missing	19	72	7	29	
Retraction of afferent colon					0.268
No	245 (86.9)	1161 (96.8)	212 (92.2)	191 (98.5)	
Yes	37 (13.1)	39 (3.2)	18 (7.8)	3 (1.5)	
Missing	106	324	48	86	
Abdominal contamination					0.535
No	117 (31.6)	965 (69.3)	191 (79.3)	167 (67.6)	
Yes	253 (68.4)	428 (30.7)	50 (20.7)	80 (32.4)	
Missing	18	131	37	33	
Bowel wall ischaemia					0.447
No	197 (60.1)	1141 (92.6)	226 (91.5)	200 (93.9)	
Yes	131 (39.9)	91 (7.4)	21 (8.5)	13 (6.1)	
Missing	60	292	31	67	
Anastomotic defect circumference (%)					0.629
0–24.9	54 (23.8)	368 (62.8)	80 (48.5)	60 (70.6)	
25–49.9	81 (35.7)	145 (24.7)	60 (36.4)	20 (23.5)	
50–100	92 (40.5)	73 (12.5)	25 (15.2)	5 (5.9)	
Missing	161	938	113	195	

(continued)

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Table 1 (continued)

	Salvage surgery (*n* = 388)	Faecal diversion + passive drainage (*n* = 1524)	Faecal diversion + active drainage (*n* = 278)	No faecal diversion (*n* = 280)	SMD
Reactivation leakage					0.129
No	155 (91.7)	1071 (89.9)	178 (91.8)	184 (96.3)	
Yes	14 (8.3)	120 (10.1)	16 (8.2)	7 (3.7)	
Missing	219	333	84	89	
Severe clinical symptoms					0.267
No	185 (47.7)	878 (73.8)	185 (82.6)	158 (73.5)	
Yes	128 (40.9)	312 (26.2)	39 (17.4)	57 (26.5)	
Missing	75	334	54	65	
Annual procedure volume of hospital					0.263
Low (<20)	24 (6.2)	120 (7.9)	13 (4.7)	44 (15.7)	
Middle (20–49)	150 (38.7)	592 (38.8)	92 (33.1)	121 (43.2)	
High (>50)	214 (55.2)	812 (53.3)	173 (62.2)	115 (41.1)	

Values are *n* (%) unless otherwise indicated. SMD, standardized mean difference; AL, anastomotic leak; HC, high care; POD, postoperative day; TME, total mesorectal excision.

Table 2 Outcomes for the four predefined treatment strategies

	Salvage surgery (*n* = 388)	Faecal diversion + passive drainage (*n* = 1524)	Faecal diversion + active drainage (*n* = 278)	No faecal diversion (*n* = 280)
1-year stoma-free survival	53 (13.7)	736 (48.3)	134 (48.2)	183 (65.4)
Patients requiring secondary salvage surgery	–	79 (5.2)	29 (10.4)	8 (2.9)
No. of secondary anastomoses created	48 (12.4)	28 (1.8)	6 (2.2)	1 (0.4)
Total duration of hospital stay within 1 year (days), median (i.q.r.)	29 (20–43)	22 (15–35)	30 (20–45)	20 (12–30)
Patients admitted to ICU within 1 year	239 (61.6)	532 (34.9)	119 (42.8)	101 (36.1)
Duration of ICU stay within 1 year (days), median (i.q.r)	4 (2–10)	3 (1–6)	2 (1–4)	3 (1–7)
Time to healing AL within 1 year (days), median (i.q.r.)	148 (77–260)	154 (83–252)	155 (92–224)	125 (38–251)

Values are *n* (%) unless otherwise indicated. AL, anastomotic leak.

patients, 11.0 per cent) cohorts (*Fig. 1*). Baseline characteristics of the participating centres are summarized in *Tables S2* and *S3*.

Characteristics and outcomes of the four treatment strategies

Table 1 shows the patient, tumour, surgical, and leak characteristics; several proportional differences were observed between cohorts. In the primary salvage cohort, fewer patients received a primary diverting stoma at index surgery than in the passive and active drainage cohorts (47.4, 79.2, and 76.6 per cent respectively). Patients who required salvage surgery had proportionally more severe clinical symptoms at the time of AL diagnosis (40.9, 26.2, 17.4, and 26.5 per cent in salvage surgery, faecal diversion with passive drainage, faecal diversion with active drainage, and no faecal diversion cohorts), and differences in leak characteristics including abdominal contamination (68.4, 30.7, 20.7, and 32.4 per cent), and ischaemic afferent colon (39.9, 7.4, 8.5, and 6.1 per cent). More patients had moderate-to-severe anastomotic dehiscence (more than 25 to 100 per cent) in the salvage surgery and faecal diversion with active drainage cohorts (76.2, 37.2, 51.6, and 29.4 per cent). In the faecal diversion with active drainage cohort, proportionally more patients originated from a high-volume hospital (55.2, 53.3, 62.2, and 41.1 per cent).

Table 2 shows outcomes for the four primary treatment strategies. The 1-year stoma free survival rate was 13.7 per cent after salvage surgery, 48.3 per cent after faecal diversion with passive drainage, 48.2 per cent after faecal diversion with active drainage, and 65.4 per cent with no faecal diversion group. The percentage of patients requiring secondary salvage surgery was 5.2 per cent after faecal diversion with passive drainage, 10.4 per cent after faecal diversion with active drainage, and 2.9 per cent after no faecal diversion. The proportion of secondary anastomoses created was 12.4, 1.8, 2.2, and 0.4 per cent in the salvage surgery, faecal diversion with passive drainage, faecal diversion with active drainage, and no faecal diversion groups. The median total duration of hospital stay was 29 (i.q.r. 20–43), 22 (15–35), 30 (20–45), and 20 (12–30) days respectively. Some 61.6, 34.9, 42.8, and 36.1 per cent of patients respectively were admitted to ICU within 1 year of index surgery, for a median of 4 (2–10), 3 (1–6), 3 (1–6), and 3 (1–7) days. If an anastomosis was present, median time to healing of the leak in the four groups was 148 (77–260), 154 (83–252), 155 (92–224), and 125 (38–251) days.

Outcomes after passive *versus* active drainage

Baseline characteristics of patients with a diverted leak who were treated with either primary passive drainage or primary active drainage, before and after PSM, are presented in *Table 3*. Several

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Table 3 Baseline characteristics for groups with passive and active drainage, before and after propensity score matching

	Before PSM			After PSM*		
	Faecal diversion + passive drainage (*n* = 1524)	Faecal diversion + active drainage (*n* = 278)	SMD	Faecal diversion + passive drainage (*n* = 556)	Faecal diversion + active drainage (*n* = 278)	SMD
Age (years), median (i.q.r)	66 (57–71)	64 (56–72))	0.068	65 (57–73)	64 (56–72)	0.018
Sex ratio (M : F)	1104 : 420	229 : 49	0.239	455 : 101	229 : 49	0.014
ASA fitness grade			0.089			0.035
I	246 (16.4)	47 (17.3)		100 (18.0)	47 (16.9)	
II	863 (57.7)	165 (60.7)		331 (59.5)	170 (61.2)	
III–IV	387 (25.9)	60 (22.1)		125 (22.5)	61 (21.9)	
Missing	28	6		0	0	
BMI (kg/m²)			0.156			0.052
Underweight (< 18.5)	68 (4.8)	8 (3.0)		17 (3.1)	8 (2.9)	
Normal (18.5–24.9)	449 (31.9)	88 (32.8)		178 (32.0)	92 (33.1)	
Overweight (25.0–29.9)	599 (42.6)	103 (38.4)		221 (39.7)	104 (37.4)	
Obese (≥ 30.0)	291 (20.7)	69 (25.7)		140 (25.2)	74 (26.6)	
Missing	117	10		0	0	
Neoadjuvant therapy			0.073			0.037
None	575 (37.7)	111 (39.9)		215 (38.7)	111 (39.9)	
Radiotherapy only	202 (13.3)	37 (13.3)		78 (14.0)	37 (13.3)	
Chemotherapy	23 (1.5)	6 (2.2)		14 (2.5)	6 (2.2)	
Chemoradiation	724 (47.5)	124 (44.6)		249 (44.8)	124 (44.6)	
Clinical metastasis category			0.036			0.029
cM0	1202 (91.4)	234 (91.1)		493 (88.7)	252 (89.6)	
cM1	113 (8.6)	23 (8.9)		63 (11.3)	29 (10.4)	
Missing	209	21		0	0	
Clinical setting of AL diagnosis			0.281			0.062
Surgical ward	1030 (67.6)	182 (65.5)		376 (67.6)	182 (65.5)	
ICU/HC	50 (3.3)	11 (4.0)		20 (3.6)	11 (4.0)	
Emergency department	149 (9.8)	28 (10.1)		47 (7.5)	28 (10.1)	
Outpatient clinic	294 (19.3)	57 (20.5)		113 (20.3)	57 (20.5)	
Missing	1	0		0	0	
POD of AL diagnosis, median (i.q.r)	8 (5–20)	10 (5–19)	0.181	9 (5–19)	10 (5–19)	0.040
Abdominal approach			0.283			0.033
Laparoscopic	962 (63.1)	170 (61.2)		347 (62.4)	170 (61.2)	
Robot-assisted	134 (8.8)	53 (19.1)		103 (18.5)	55 (19.8)	
Laparotomy	428 (28.1)	55 (19.8)		106 (19.1)	53 (19.1)	
Transanal TME	284 (18.6)	77 (27.7)	0.179	151 (27.2)	77 (27.7)	0.012
Multivisceral resection			0.080			0.049
Yes	96 (6.3)	16 (5.8)		26 (4.7)	16 (5.8)	
Missing	35	7		0	0	
Primary defunctioning stoma	1214 (79.2)	213 (76.6)	0.074	439 (79.0)	213 (76.6)	0.056
Fistula			0.154			0.039
Yes	101 (3.2)	9 (3.3)		22 (4.0)	9 (3.2)	
Missing	72	7		0	0	
Retraction of afferent colon			0.268			0.059
Yes	39 (3.2)	18 (7.8)		41 (7.4)	25 (9.0)	
Missing	324	48		0	0	
Abdominal contamination			0.535			0.004
Yes	428 (30.7)	50 (20.7)		121 (21.8)	60 (21.6)	
Missing	131	37		0	0	
Bowel wall ischaemia			0.041			0.039
Yes	91 (7.4)	21 (8.5)		44 (7.9)	25 (9.0)	
Missing	292	31		0	0	
Anastomotic defect circumference (%)			0.629			0.059
0–25	368 (62.8)	80 (48.5)		292 (52.5)	138 (49.6)	
25–50	145 (24.7)	60 (36.4)		179 (32.2)	96 (34.5)	
50–100	73 (12.5)	25 (15.2)		85 (15.3)	44 (15.8)	
Missing	938	113		0	0	
Reactivation leakage			0.129			0.068
Yes	120 (10.1)	16 (8.2)		57 (10.3)	23 (8.3)	
Missing	333	84		0	0	
Severe clinical symptoms			0.214			0.033
Yes	312 (26.2)	39 (17.4)		93 (16.7)	50 (18.0)	
Missing	334	54		0	0	

Values are *n* (%) unless otherwise indicated. *Data shown after propensity score matching (PSM) originate from 1 randomly selected data set out of 100 imputation sets. SMD, standardized mean difference; AL, anastomotic leak; HC, high care; POD, postoperative day; TME, total mesorectal excision.

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Table 4 Outcomes for treatment strategies before and after multiple imputation

	Before PSM		After PSM*	
	Faecal diversion + passive drainage (*n* = 1524)	Faecal diversion + active drainage (*n* = 278)	Faecal diversion + passive drainage (*n* = 556)	Faecal diversion + active drainage (*n* = 278)
1-year stoma-free survival	736 (48.3)	134 (48.2)	280 (50.4)	135 (48.6)
Patients requiring secondary salvage surgery	79 (5.2)	29 (10.4)	24 (4.3)	29 (10.4)
No. of secondary anastomoses created	28 (1.8)	6 (2.2)	12 (2.2)	6 (2.2)
Total duration of hospital stay within 1 year (days), median (i.q.r.)	22 (15–35)	30 (20–45)	22 (16–36)	30 (21–45)
Patients admitted to ICU within 1 year	532 (34.9)	119 (42.8)	193 (34.7)	119 (42.8)
Duration of ICU stay within 1 year (days), median (i.q.r.)	3 (1–6)	2 (1–4)	0 (0–1)	0 (0–2)
Time to healing AL within 1 year (days), median (i.q.r.)	154 (83–252)	155 (92–224)	145 (90–219)	152 (90–217)

Values are *n* (%), unless otherwise indicated. *Data shown after propensity score matching (PSM) originate from 1 randomly selected data set out of 100 imputation sets. AL, anastomotic leak.

Table 5 Outcomes after faecal diversion and active drainage compared with faecal diversion and passive drainage, after propensity score matching

	Faecal diversion + active drainage *versus* faecal diversion + passive drainage (reference)*
1-year stoma-free survival	
Risk difference (%)	−1.1 (−9, 7)
OR	0.95 (0.69, 1.33)
Secondary salvage surgery	
Risk difference (%)	5.0 (0.8, 9)
OR	2.32 (1.49, 3.59)
Secondary anastomosis	
Risk difference (%)	0.05 (−2, 2)
OR	1.04 (0.36, 3.02)
Total duration of hospital stay within 1 year (days)	6 (2, 10)
ICU admission within 1 year	
Risk difference (%)	8.0 (0.4, 16)
OR	1.41 (1.02, 1.94)
Duration of ICU stay within 1 year (days)	1 (−2, 3)
Time to healing AL within 1 year (days)	12 (−28, 52)

Values in parentheses are 95% confidence intervals. *Derived from logistic and linear regression; results from linear regression are differences in means. AL, anastomotic leak.

proportional differences with an SMD exceeding 0.1 were observed between the two groups before matching. After PSM, all co-variates had an SMD below 0.1, and were considered to be sufficiently balanced between the two cohorts (*Fig. S1*).

Table 4 shows the raw outcomes for passive and active drainage of the perianastomotic abscess in patients with faecal diversion, before and after matching. The results of the matched comparative analysis between passive and active drainage in patients with faecal diversion are summarized in *Table 5*. There was no statistically significant difference in 1-year stoma-free survival (RD −1.1 (95 per cent c.i. −9 to 7) per cent; OR 0.95, 95 per cent c.i. 0.69 to 1.33). After faecal diversion with active drainage, significantly more patients required secondary salvage surgery (RD 5.0 (0.8 to 9) per cent; OR 2.32, 1.49 to 3.59) and ICU admission (RD 8.0 (0.4 to 16) per cent; OR 1.41, 1.02 to 1.94). The mean total duration of hospital stay within 1 year was 36 days following faecal diversion with active drainage, and 30 days after faecal diversion with passive drainage, which differed significantly by 6 (95 per cent c.i. 2 to 10) days. There was no statistically significant difference in the number of secondary anastomoses created (RD 0.05 (−2 to 2) per cent; OR 1.04, 0.36 to 3.02). The mean total duration of ICU stay was 6 days after faecal diversion with active drainage and 5 days after faecal diversion with passive drainage, with no significant difference (1 (−2 to 3) days). The mean time to healing of the leak was 234 days after faecal diversion with active drainage, and 222 days after faecal diversion with passive drainage, again with no significant difference (12 (−28 to 52) days).

Sensitivity analysis assessing the effect of annual case volume

The effect of annual procedure volume was assessed in a sensitivity analysis (*Tables S2 and S3*). After including annual procedure volume in the multivariable logistic regression modelling, no statistically significant differences were observed in 1-year stoma-free survival between treatment strategies (RD −1.6 (95 per cent c.i. −10 to 6) per cent; OR 0.94, 95 per cent c.i. 0.68 to 1.29). In addition, all secondary outcomes remained comparable to those in the initial analysis without inclusion of annual procedure volume, confirming the robustness of the analysis (*Tables S4 and S5*).

Discussion

This large retrospective international multicentre study explored four predefined treatment strategies for AL after restorative rectal cancer resection. Substantial differences were found in several leak characteristics between the four treatment strategies. Primary salvage surgery resulted in a 1-year stoma-free survival rate of 14 per cent, reflecting the severity of these leaks, whereas non-diverted leaks had a rate of 65 per cent. Patients with a diverted leak who underwent active drainage (EVT) had worse leak characteristics than those who had passive drainage of the perianastomotic abscess. After matching, there was no statistically significant difference in 1-year stoma-free survival, but patients treated with EVT more frequently underwent secondary salvage surgery, were more often admitted to the ICU, and had a longer total hospital stay.

Primary salvage surgery was performed in 16 per cent of the total cohort. Although the proportion of redo anastomoses was highest in this group (12 per cent), salvage surgery mostly consisted of

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dismantling the anastomosis, which explains the low 1-year stoma-free survival rate. Salvage surgery is sometimes the only option (for example, in the event of ischaemic afferent colon). In other instances, immediately deciding that preservation of bowel continuity is no longer the ultimate goal can be a wise decision. This might prevent a patient having a long period of treatment that ultimately ends in a permanent stoma anyway. Conversely, there might have been a subgroup of anastomoses that could have been preserved using an alternative strategy. Further studies are necessary to identify these specific patients.

The group of patients who did not undergo primary or secondary faecal diversion had the highest stoma-free survival rate. Surgeons likely decided this most conservative strategy based on favourable patient and leak characteristics. Remarkably, this group also included several patients with adverse leak characteristics. The abdominal cavity was contaminated in 32 per cent, and an ischaemic afferent colon was identified in 6 per cent. There is inherent heterogeneity within this group, which includes patients with only purulent fluid and an early sealed leak that can be effectively treated with laparoscopic lavage, as well as those with sepsis and substantial anastomotic dehiscence and four-quadrant peritonitis that require more aggressive management.

Over the past few decades, minimally invasive active treatment strategies, such as EVT, have emerged as an alternative to major surgery[21,22,36]. EVT is indicated for extraperitoneal AL, and consists of endoscopic placement of open-cell polyurethane sponges connected to a continuous negative pressure system for drainage and debridement of the perianastomotic abscess. EVT can be used either as a single modality or combined with transanal closure of the defect[21,37,38]. The present study failed to show differences between EVT and passive drainage in patients with diverted leaks in terms of 1-year stoma-free survival after AL, which could be explained by several factors. First, early diagnosis of AL and initiation of EVT is crucial for its success, as the neorectum is still pliant and not impaired by chronic inflammation[16,22]. Borstlap *et al.*[16] showed that, if EVT is initiated within 3 weeks of index surgery, it can lead to acceptable anastomotic healing rates of 73.0 per cent, with corresponding rates of restoration of continuity. A similar trend was observed by the GRECCAR group[39], which showed significantly improved anastomotic healing when EVT was initiated within 15 days of AL compared with after 15 days (72.4 *versus* 27.8 per cent). In the present study, no differentiation was made between early and late initiation of EVT. These results reflect a non-trial setting with application of EVT in non-specialized centres as well. Optimizing EVT treatment with early commencement and combining it with surgical closure could potentially have yielded better outcomes; however, this remains to be proven. Furthermore, the GRECCAR group[39] identified predictive factors for success of EVT, and showed significantly lower success rates in patients who underwent percutaneous transgluteal drainage before initiating EVT. As a result of the present retrospective study design, patients who were referred for EVT after a failed primary passive drainage strategy would have been registered as having primary active drainage.

No RCTs have yet been performed to establish robust evidence for the effectiveness of EVT[36], and comparative studies are scarce. A study by Kühn *et al.*[25] compared patients who underwent EVT with a conventionally treated historical cohort, showing advantageous outcomes for EVT in terms of restoration of continuity (86.7 *versus* 37.5 per cent). Another comparative study was undertaken by Eriksen *et al.*[40], who reported significantly higher stoma rates 1 year after EVT compared with conventional management (33.9 *versus* 13.5 per cent). This could also explain the higher rates of secondary salvage surgery and ICU admission in the present study, as patients treated with EVT had larger anastomotic defects and retraction at baseline compared with those treated conventionally. This hypothesis implies that patients who underwent conventional treatment might have had more favourable baseline leak characteristics. The high rates of secondary salvage surgery could therefore potentially be attributed to the use of EVT to control pelvic sepsis in patients with a large anastomotic dehiscence or significant retraction of the afferent colon. Subsequently, these patients undergo complete dismantling of the anastomosis with creation of a permanent end-colostomy or redo surgery. This course of action may be chosen owing to the unsuitability of EVT as a treatment strategy in these specific situations[41]. Furthermore, salvage surgery can be complex and might necessitate ICU admission or additional readmissions to hospital. Another plausible explanation for these findings could be attributed to matching, a process carried out using previously identified confounding factors for stoma-free survival[33]. Although matching was undertaken to create a homogeneous population with comparable characteristics, the multifaceted nature of stoma-free survival as an outcome introduces complexity, and residual bias may have remained.

Previous studies were impeded by a heterogeneous patient population and small sample sizes[23], whereas the present study encompassed a large sample with robust and detailed data. However, several limitations should be discussed. First, the retrospective study design could have contributed to inconsistencies and missing data. To overcome this issue, data verification and validation was performed. Some missing data remained, but statistical power was preserved by imputing the missing data through multiple imputation[31,32]. Second, participating centres had to include their own patients retrospectively and it is anticipated that not all primary treatment strategies were reported correctly. Third, not all centres from a defined geographical region participated in this study, potentially introducing selection bias from differing referral patterns as it is expected that participating centres are more likely to consist of academic centres, potentially impairing external validity.

In conclusion, this large worldwide cohort study has provided detailed insights into patient and leak characteristics of four predefined treatment strategies for AL after restorative rectal cancer surgery. The 1-year stoma-free survival rate was low for patients undergoing primary salvage surgery and high in those with non-diverted anastomoses, and did not differ significantly between matched patients treated with faecal diversion and either EVT or passive drainage. Nonetheless, significantly more patients required secondary salvage surgery and ICU admission within 1 year of EVT, indicating a potential allocation bias.

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Supplementary material

Supplementary material is available at *BJS* online.

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Data availability

Study data are available on reasonable request

References

1. Chiarello MM, Fransvea P, Cariati M, Adams NJ, Bianchi V, Brisinda G. Anastomotic leakage in colorectal cancer surgery. *Surg Oncol* 2022;**40**:101708
2. Bakker IS, Snijders HS, Wouters MW, Havenga K, Tollenaar RA, Wiggers T *et al.* High complication rate after low anterior resection for mid and high rectal cancer; results of a population-based study. *Eur J Surg Oncol* 2014;**40**:692–698
3. Bostrom P, Haapamaki MM, Rutegard J, Matthiessen P, Rutegard M. Population-based cohort study of the impact on postoperative mortality of anastomotic leakage after anterior resection for rectal cancer. *BJS Open* 2019;**3**:106–111
4. Snijders HS, Bakker IS, Dekker JW, Vermeer TA, Consten EC, Hoff C *et al.* High 1-year complication rate after anterior resection for rectal cancer. *J Gastrointest Surg* 2014;**18**:831–838
5. Borstlap WAA, Westerduin E, Aukema TS, Bemelman WA, Tanis PJ; Dutch Snapshot Research Group. Anastomotic leakage and chronic presacral sinus formation after low anterior resection: results from a large cross-sectional study. *Ann Surg* 2017;**266**: 870–877
6. Hammond J, Lim S, Wan Y, Gao X, Patkar A. The burden of gastrointestinal anastomotic leaks: an evaluation of clinical and economic outcomes. *J Gastrointest Surg* 2014;**18**:1176–1185
7. Ashraf SQ, Burns EM, Jani A, Altman S, Young JD, Cunningham C *et al.* The economic impact of anastomotic leakage after anterior resections in English NHS hospitals: are we adequately remunerating them? *Colorectal Dis* 2013;**15**:e190–e198
8. Arron MNN, Greijdanus NG, Bastiaans S, Vissers PAJ, Verhoeven RHA, Ten Broek RPG *et al.* Long-term oncological outcomes after colorectal anastomotic leakage; a retrospective Dutch population based study. *Ann Surg* 2022;**276**:882–889
9. Lindgren R, Hallbook O, Rutegard J, Sjodahl R, Matthiessen P. What is the risk for a permanent stoma after low anterior resection of the rectum for cancer? A six-year follow-up of a multicenter trial. *Dis Colon Rectum* 2011;**54**:41–47
10. Jutesten H, Buchwald PL, Angenete E, Rutegård M, Lydrup ML. High risk of low anterior resection syndrome in long-term follow-up after anastomotic leakage in anterior resection for rectal cancer. *Dis Colon Rectum* 2022;**65**:1264–1273
11. Daams F, Slieker JC, Tedja A, Karsten TM, Lange JF. Treatment of colorectal anastomotic leakage: results of a questionnaire amongst members of the Dutch Society of Gastrointestinal Surgery. *Dig Surg* 2012;**29**:516–521
12. Gessler B, Eriksson O, Angenete E. Diagnosis, treatment, and consequences of anastomotic leakage in colorectal surgery. *Int J Colorectal Dis* 2017;**32**:549–556
13. Thomas MS, Margolin DA. Management of colorectal anastomotic leak. *Clin Colon Rectal Surg* 2016;**29**:138–144
14. Blumetti J, Abcarian H. Management of low colorectal anastomotic leak: preserving the anastomosis. *World J Gastrointest Surg* 2015;**7**:378–383
15. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg* 2007;**245**:254–258
16. Borstlap WAA, Musters GD, Stassen LPS, van Westreenen HL, Hess D, van Dieren S *et al.* Vacuum-assisted early transanal closure of leaking low colorectal anastomoses: the CLEAN study. *Surg Endosc* 2018;**32**:315–327
17. van Workum F, Talboom K, Hannink G, Wolthuis A, de Lacy BF, Lefevre JH *et al.* Treatment of anastomotic leakage after rectal cancer resection: the TENTACLE-Rectum study. *Colorectal Dis* 2021;**23**:982–988
18. Sparreboom CL, Wu ZQ, Ji JF, Lange JF. Integrated approach to colorectal anastomotic leakage: communication, infection and healing disturbances. *World J Gastroenterol* 2016;**22**:7226–7235
19. Musters GD, Borstlap WA, Bemelman WA, Buskens CJ, Tanis PJ. Intersphincteric completion proctectomy with omentoplasty for chronic presacral sinus after low anterior resection for rectal cancer. *Colorectal Dis* 2016;**18**:147–154
20. Sloothaak DA, Buskens CJ, Bemelman WA, Tanis PJ. Treatment of chronic presacral sinus after low anterior resection. *Colorectal Dis* 2013;**15**:727–732
21. Weidenhagen R, Gruetzner KU, Wiecken T, Spelsberg F, Jauch KW. Endoscopic vacuum-assisted closure of anastomotic leakage following anterior resection of the rectum: a new method. *Surg Endosc* 2008;**22**:1818–1825
22. Talboom K, Greijdanus NG, Ponsioen CY, Tanis PJ, Bemelman WA, Hompes R. Endoscopic vacuum-assisted surgical closure (EVASC) of anastomotic defects after low anterior resection for rectal cancer; lessons learned. *Surg Endosc* 2022;**36**:8280–8289
23. Shalaby M, Emile S, Elfeki H, Sakr A, Wexner SD, Sileri P. Systematic review of endoluminal vacuum-assisted therapy as salvage treatment for rectal anastomotic leakage. *BJS Open* 2019;**3**:153–160
24. Kuehn F, Janisch F, Schwandner F, Alsfasser G, Schiffmann L, Gock M *et al.* Endoscopic vacuum therapy in colorectal surgery. *J Gastrointest Surg* 2016;**20**:328–334
25. Kühn F, Janisch F, Schwandner F, Gock M, Wedermann N, Witte M *et al.* Comparison between endoscopic vacuum therapy and conventional treatment for leakage after rectal resection. *World J Surg* 2020;**44**:1277–1282
26. Daams F, Luyer M, Lange JF. Colorectal anastomotic leakage: aspects of prevention, detection and treatment. *World J Gastroenterol* 2013;**19**:2293–2297
27. Talboom K, Greijdanus NG, van Workum F, Ubels S, Rosman C, Hompes R *et al.* International expert opinion on optimal treatment of anastomotic leakage after rectal cancer resection: a case-vignette study. *Int J Colorectal Dis* 2022;**37**: 2049–2059
28. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg* 2014; **12**:1495–1499
29. Rahbari NN, Weitz J, Hohenberger W, Heald RJ, Moran B, Ulrich A *et al.* Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. *Surgery* 2010;**147**:339–351
30. D'Souza N, de Neree Tot Babberich MPM, d'Hoore A, Tiret E, Xynos E, Beets-Tan RGH *et al.* Definition of the rectum: an international, expert-based Delphi consensus. *Ann Surg* 2019; **270**:955–959
31. Buuren SV, Taylor, Francis. *Flexible Imputation of Missing Data* (2nd edn). Boca Raton: CRC Press, 2018
32. Sterne JA, White IR, Carlin JB, Spratt M, Royston P, Kenward MG *et al.* Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;**338**: b2393
33. Greijdanus NG, Wienholts K, Ubels S, Talboom K, Hannink G, Wolthuis A *et al.* Stoma-free survival after rectal cancer resection with anastomotic leakage: development and

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validation of a prediction model in a large international cohort. *Ann Surg* 2023
34. Austin PC. Statistical criteria for selecting the optimal number of untreated subjects matched to each treated subject when using many-to-one matching on the propensity score. *Am J Epidemiol* 2010;**172**:1092–1097
35. Rassen JA, Shelat AA, Myers J, Glynn RJ, Rothman KJ, Schneeweiss S. One-to-many propensity score matching in cohort studies. *Pharmacoepidemiol Drug Saf* 2012;**21**:69–80
36. Bemelman WA, Arezzo A, Banasiewicz T, Brady R, Espin-Basany E, Faiz O *et al.* Use of sponge-assisted endoluminal vacuum therapy for the treatment of colorectal anastomotic leaks: expert panel consensus. *BJS Open* 2022;**6**: zrac123
37. Kuhn F, Schardey J, Wirth U, Schiergens T, Crispin A, Beger N *et al.* Endoscopic vacuum therapy for the treatment of colorectal leaks—a systematic review and meta-analysis. *Int J Colorectal Dis* 2022;**37**:283–292
38. de Lacy FB, Talboom K, Roodbeen SX, Blok R, Curell A, Tanis PJ *et al.* Endoscopic vacuum therapy and early surgical closure after pelvic anastomotic leak: meta-analysis of bowel continuity rates. *Br J Surg* 2022;**109**:822–831
39. Abdalla S, Cotte E, Epin A, Karoui M, Lefevre JH, Berger A *et al.* Short-term and long-term outcome of endoluminal vacuum therapy for colorectal or coloanal anastomotic leakage: results of a nationwide multicenter cohort study from the French GRECCAR Group. *Dis Colon Rectum* 2020;**63**:371–380
40. Eriksen JD, Emmertsen KJ, Madsen AH, Iversen LH. Anastomotic leakage following restorative rectal cancer resection: treatment and impact on stoma presence 1 year after surgery-a population-based study. *Int J Colorectal Dis* 2022;**37**:1161–1172
41. Slooter MD, Talboom K, Sharabiany S, van Helsdingen CPM, van Dieren S, Ponsioen CY *et al.* IMARI: multi-interventional program for prevention and early management of anastomotic leakage after low anterior resection in rectal cancer patients: rationale and study protocol. *BMC Surg* 2020;**20**:240

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European Colorectal Congress

3 – 6 December 2023, St.Gallen, Switzerland

OVERVIEW
Sun, 3 Dec 2023

MASTERCLASS
PROCTOLOGY DAY
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SCIENTIFIC PROGRAMME
Mon, 4 Dec – Wed, 6 Dec 2023

DIVERTICULAR DISEASE

Gut microbiome and surgery
Phil Quirke, Leeds, UK

Diet in diverticular disease
Pamela Buchwald, Lund, SE

Decision making in the management of acute complicated Diverticulitis beyond the guidelines
Seraina Faes, Zurich, CH

Diverticular Abscess – Always drainage or who benefits from Surgery?
Johannes Schultz, Oslo, NO

Perforated Diverticulitis: Damage Control, Hartmann's Procedure, Primary Anastomosis, Diverting Loop
Reinhold Kafka-Ritsch, Innsbruck, AT

When to avoid protective stoma in colorectal surgery
Antonino Spinelli, Milano, IT

ENDOMETRIOSIS

Endometriosis – what is the role of the abdominal surgeon
Tuynman Juriaan, Amsterdam, NL

Challenges in Surgery of Endometriosis – always interdisciplinary?
Peter Oppelt, Linz, AT; Andreas Shamiyeh, Linz, AT

A gaze in the crystal ball: Where is the role of virtual reality and artificial Intelligence in colorectal surgery
Müller Beat, Basel, CH

MALIGNANT COLORECTAL DISEASE

Cytoreductive Surgery and Intraperitoneal Chemotherapy – facts and hopes
Michel Adamina, Winterthur, CH

Metastatic Colorectal Cancer – surgical approaches and limits
Jürgen Weitz, Dresden, DE

Extended lymph node dissection for rectal cancer, is it still under debate?
Miranda Kusters, Amsterdam, NL

Organ preservation functional outcome in rectal cancer treatment – in line with patient's needs? (Robot – laparoscopic – open surgery?)
Hans de Wilt, Nijmegen, NL

ROBOTICS

Advances in Robotic Surgery and what we learnt so far
Parvaiz Amjad, Portsmouth, UK

Challenging the market: Robotic (assistant) Devices and how to choose wisely (Da Vinci – Hugo Ras – Distalmotion ua)
Khan Jim, London, UK

TAMIS - Robotic Transanal Surgery, does it make it easier?
Knol Joep, Genk, BE

Live Surgery – Contonal Hospital of St.Gallen
Walter Brunner, St.Gallen, CH;
Salvadore Conde Morals, Sevilla, ES;
Friedrich Herbst, Vienna, AUT;
Amjad Parvaiz, Portsmouth, UK

Video Session

Lars Pahlmann Lecture
Markus Büchler, Lisboa, PRT

Honorary Lecture
Bill Heald, Lisboa, PRT

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