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Three-row versus two-row circular staplers for left-sided colorectal anastomosis: a propensity score-matched analysis of the iCral 2 and 3 prospective cohorts

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Background: Since most anastomoses after left-sided colorectal resections are performed with a circular stapler, any technological change in stapling devices may influence the incidence of anastomotic adverse events. The aim of the present study was to analyze the effect of a three-row circular stapler on anastomotic leakage and related morbidity after left-sided colorectal resections.

Materials and methods: A circular stapled anastomosis was performed in 4255 (50.9%) out of 8359 patients enrolled in two prospective multicenter studies in Italy, and, after exclusion criteria to reduce heterogeneity, 2799 (65.8%) cases were retrospectively analyzed through a 1:1 propensity score-matching model including 20 covariates relative to patient characteristics, to surgery and to perioperative management. Two well-balanced groups of 425 patients each were obtained: group (A) – true population of interest, anastomosis performed with a three-row circular stapler; group (B) – control population, anastomosis performed with a two-row circular stapler. The target of inferences was the average treatment effect in the treated (ATT). The primary endpoints were overall and major anastomotic leakage and overall anastomotic bleeding; the secondary endpoints were overall and major morbidity and mortality rates. The results of multiple logistic regression analyses for the outcomes, including the 20 covariates selected for matching, were presented as odds ratios (OR) and 95% confidence intervals (95% CI).

Results: Group A versus group B showed a significantly lower risk of overall anastomotic leakage (2.1 vs. 6.1%; OR 0.33; 95% CI 0.15–0.73; $P = 0.006$), major anastomotic leakage (2.1 vs. 5.2%; OR 0.39; 95% CI 0.17–0.87; $P = 0.022$), and major morbidity (3.5 vs. 6.6% events; OR 0.47; 95% CI 0.24–0.91; $P = 0.026$).

Conclusion: The use of three-row circular staplers independently reduced the risk of anastomotic leakage and related morbidity after left-sided colorectal resection. Twenty-five patients were required to avoid one leakage.

Keywords: anastomotic leakage, circular staplers, colorectal surgery

Introduction

The last decade has witnessed a significant evolution in colorectal surgery, due to the diffusion of minimally invasive approaches (either laparoscopic or robotic) and the implementation of enhanced recovery pathways (ERP)[1], allowing optimal oncological, physiological, and cosmetic results associated with shorter postoperative stay[2]. However, early anastomotic adverse events, such as leakage (AL) and bleeding (AB), remain the Achille's heel of any colorectal anastomosis, leading to prolonged postoperative stay, increased costs, risk of reoperation, and permanent colostomy, together with an increase in overall morbidity and mortality rates[3,4]. Furthermore, AL has been shown to

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affect long-term outcomes being associated with a higher risk of recurrence and shortened survival in colorectal cancer[5].

Nearly 50 years have passed since the first description of mechanical circular staplers (CS) to facilitate colorectal anastomosis[6], and the double-stapling technique for colorectal end-to-end anastomosis has rapidly become a standard practice that is still widely used today[7], having demonstrated safety and efficacy equivalent to the hand-sewn anastomosis with the advantages of shorter anastomotic time, less contamination, and greater reproducibility[8,9].

Beyond well-known patient-related, disease-related, and procedure-related risk factors[10], successful healing of any anastomosis relies on an effective blood supply and micro-perfusion of the anastomotic tissue and on the mechanical strength of the newly formed anastomosis[11]. Consequently, any technological improvement in CS may represent a target for AL risk reduction, and during the last 5 years, two significant developments have been commercially available for this purpose. The powered two-row circular stapler (Ethicon, Somerville, New Jersey, USA) decrease the force needed for firing, improving stability at the anastomotic site, reduces the compressive forces on tissues and their slippage, and utilizes two rows of staples with three-dimensional architecture[12]. The three-row circular stapler (Covidien, New Haven, Connecticut, USA) is based on three circular rows of conventional, B-shaped staples, varying in height: the staples of the inner row, closest to the anastomotic lumen, have the shortest height to provide the greatest occlusion and barrier to leak and to bleed, while the second and third rows, each with incrementally longer staples' height, contribute strength to the closure line, enhancing both tissue micro-perfusion[13] and pressure resistance[14]. Despite several animal models and clinical and artificial intelligence studies[14–17], the effectiveness of the three-row CS in reducing the AL risk has not been fully examined or demonstrated mainly because of the small sample size, small number of considered conditioning variables, and lack of comparison with two-row CS of different producers. Although highly advisable[18], administrative, economic, and ethical reasons have hindered, to date, a randomized clinical trial on this issue, and the Italian ColoRectal Anastomotic Leakage (iCral) study group decided to estimate the treatment effects of the three-row CS on data derived from two prospective open-label observational multicenter studies[19,20].

Material and methods

Study design

This was a retrospective analysis of a prospective database of patients who underwent colorectal resection and anastomosis for malignant and benign diseases. The aim of the present study was to evaluate the effectiveness of the three-row CS in reducing the risk of early adverse events in a population of patients who underwent left colectomy and/or anterior resection with end-to-end stapled colorectal anastomosis, compared to a control population in which a two-row CS was used. Propensity score-matching analysis (PSMA) was used to adjust for heterogeneity between the two groups.

Patient population and data collection

Patients were enrolled in two consecutive studies: iCral2[19] and iCral3[20]. Both studies, designed to investigate the effects of ERP

adherence rates on several outcomes, were based on prospective enrollment on a voluntary basis in Italy, carried out from January 2019 to June 2020 in 38 surgical centers (iCral2) and from October 2020 to September 2021 in 76 surgical centers (iCral3). A total of 78 centers were involved in one (42 centers) or both (36 centers) of the studies. All patients who underwent colorectal resection with anastomosis (laparoscopic, robotic, open, or converted approach, including planned Hartmann's reversals) were assessed according to explicit inclusion/exclusion criteria shared by both studies. Inclusion criteria were: American Society of Anesthesiologists (ASA) class I, II, or III; elective or delayed urgency setting (defined > 48 h from admission in iCral2 and > 24 h from admission in iCral3); patient's written informed consent for inclusion in the study and processing of sensitive data. Exclusion criteria were: pregnancy; hyperthermic chemotherapy (HIPEC) for carcinomatosis; incomplete data. The iCral2 study excluded patients with a protective stoma proximal to the anastomosis; conversely, these cases were included in the iCral3 study.

Each center was defined as a high volume (≥ 4) or low volume (< 4) according to the median number of enrolled cases per month. All data of the included patients were prospectively uploaded to a web-based database via an electronic case report form, specifically designed for both studies and protected by access credentials for each center/investigator. Continuous and discrete variables related to biometric data, patient-related risk factors, indications and types of surgical procedures, adherence to ERP items, and outcomes were recorded in all cases. When anastomosis was performed with a CS, complete data regarding the manufacturer, model, and diameter were recorded. Quality control of the data for consistency, plausibility, and completeness was performed on each record by local investigators and subsequently validated by the study coordinator, resolving any discrepancies through strict cooperation. During the perioperative period, patients were examined daily by local investigators, who recorded and graded any adverse event and were free to decide on complementary imaging and any further action according to their local criteria.

Both studies were conducted in accordance with the Declaration of Helsinki and the guidelines for good clinical practice E6 (R2). The study protocols were approved by the ethics committee of the coordinating center and registered at ClinicalTrials.gov. Subsequently, all other centers were authorized to participate in their local ethics committees. Both studies followed the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guidelines[21]. Individual participant-level anonymized datasets were made available for both studies upon reasonable request by contacting the study coordinator.

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To control for data heterogeneity derived from several treatment confounders, PSMA included 2799 patients (65.8%) out of 4255 cases in which anastomosis was performed using a CS, based on explicit exclusion criteria: any resection different from left colectomy or anterior resection, neo-adjuvant therapy, any anastomosis different form end-to-end, any anastomosis located less than 5 cm from the external anal verge, any anastomosis performed with a 25 mm diameter CS, and any anastomosis protected by a proximal stoma (Fig. 1). The variables and outcomes recorded for the study population are shown in Table 1. To optimize the effectiveness of the PSMA by reducing the number of unmatched cases, continuous variables were categorized according to their median values.

Adverse events

All the enrolled patients were followed-up for 8 weeks after surgery, recording and grading any adverse event according to Clavien–Dindo[23] and the Japanese Clinical Oncology Group (JCOG) extended criteria[24], as well as any unplanned readmission, reoperation, or death, calculated at 60 days after surgery. AL was defined according to the international consensus[25,] and AB was defined as persistent rectal bleeding associated with at least a 20 g/l decrease in hemoglobin concentration[26]. Adverse events and their grading are reported in Table 2.

Outcomes

The primary endpoints were overall AL (any AL), major AL (any AL grade > II), and AB, and the secondary endpoints were overall morbidity (any adverse event), major morbidity (any adverse event grade > II), and mortality (any death).

Statistical analysis

No missing data were observed in the database of 2799 patients. A propensity score-matching model[27] was used for analysis (Fig. 1). Based on its original theory[28], the propensity score is a variable that groups several covariates and represents the conditional probability of receiving a protective treatment effect on the outcomes using or not using the treatment variable. The theory requires the following assumptions: no unmeasured confounding variable; the propensity score should not be exactly 0 or 1; the treatment should be well-defined and homogeneous; sufficient overlap in subgroups of covariates; and balance model specifications. Adjusted logistic regression was used to estimate the propensity scores of the treatment and control groups. Based on the conditioning categorical variables selected, each patient was assigned a propensity score estimated by the standardized mean difference (a standardized mean difference less than 0.1 typically indicates a negligible difference between the means of the groups). The treatment (exposure) variable was end-to-end anastomosis performed using the three-row CS, and 20 confounding variables (covariates), potentially affecting the treatment were selected: age, sex, American Society of Anesthesiologists (ASA) class, body mass index (BMI), diabetes, chronic renal failure, chronic liver disease, surgery for malignancy, left colectomy as a type of resection, operation length (minutes), center volume, open surgery, intracorporeal or extracorporeal anastomosis, the diameter of the circular stapler, preoperative blood transfusion(s), intraoperative and/or postoperative blood transfusion(s), and overall,
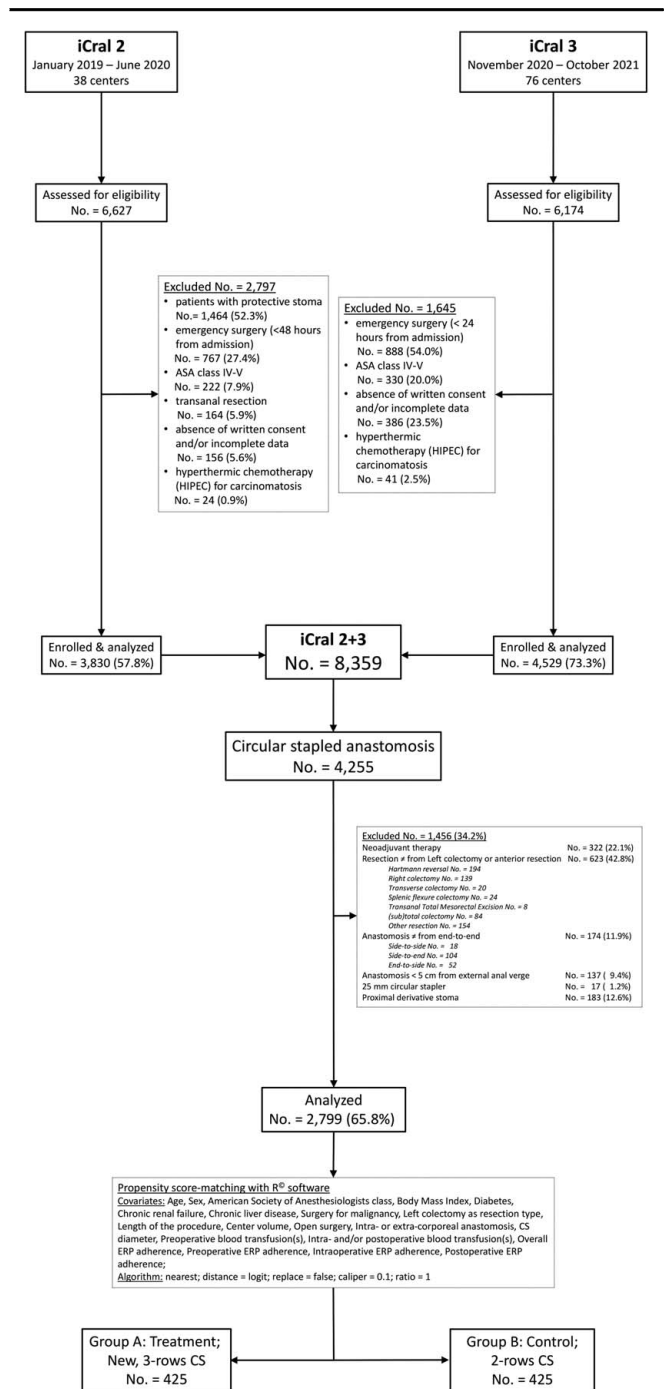
Figure 1. Study flowchart according to the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) guidelines[21] and to the Reporting and Guidelines in Propensity Score Analysis[22]. iCral, Italian ColoRectal Anastomotic Leakage study group; ERP, enhanced recovery pathway.

preoperative, intraoperative, and postoperative ERP items adherence rates. No outcome variable was included[29].

As the balance is the main goal of PSMA, the analysis was performed using the software 'R' (Version 4.2.2, The R Foundation for Statistical Computing, Vienna, Austria, 2022) with the following specifications: seed 100 for the reproducibility of the analysis; method for distance metric = nearest, distance = logit, caliper = 0.1, replace = false (without sampling replacement),

Table 1

Descriptive analysis of the study population variables.

Variable	Pattern	Number	%
Age (year)	< 65.2	1399	49.9
	≥ 65.2	1400	50.1
Sex	Male	1363	48.7
	Female	1436	51.3
ASA class	I–II	2053	73.3
	III	746	26.7
Body mass index (kg/m^2)	≤ 25.0	1389	49.6
	> 25.0	1410	50.4
Diabetes	Yes	298	10.6
	No	2501	89.4
Chronic renal failure	Yes	77	2.8
	No	2722	97.2
Chronic liver disease	Yes	22	0.8
	No	2777	99.2
Surgery for malignancy	Yes	1684	60.2
	No	1115	39.8
	Diverticular disease	758	
	Endometriosis	246	
	Polyps	74	
	Inflammatory bowel disease	6	
	Other	31	
Type of resection	Anterior resection	894	31.9
	Left colectomy	1905	68.1
Type of circular stapler	Three-row	488	17.4
	Two-row	2311	82.6
	Covidien – DST EEA	938	
	Ethicon ECHELON Powered Stapler – CDHP	172	
	Ethicon Circular Stapler – ECS	122	
	Ethicon Circular Stapler – CDH	764	
	Touchstone Endoscopic Circular Stapler – ECSC	128	
	Touchstone Circular Stapler – CSC	139	
	Other	48	
Diameter of the circular stapler	< 30 mm	1929	68.9
	≥ 30 mm	870	31.1
Anastomosis	Intracorporeal	2457	87.8
	Extracorporeal	342	12.2
Operation length (minutes)	≤ 180	1268	45.3
	> 180	1531	54.7
Center volume	Low; <4 enrolled cases/month	676	24.2
	High; ≥ 4 enrolled cases/month	2123	75.8
Open surgery	Yes	154	5.5
	No	2645	94.5
	Laparoscopic	2288	
	Robotic	249	
	Converted	108	
Preoperative blood transfusion(s)		53	1.9
Intraoperative/postoperative blood transfusion(s)		100	3.6
Overall ERP adherence (%)	≤ 75.0	1290	46.1
	> 75.0	1509	53.9
Nutritional screening		1917	68.5
Prehabilitation		977	34.9
Counseling		1770	63.2
Immune enhancing nutrition		769	27.5
Antithrombotic prophylaxis		2611	93.3
Antibiotic prophylaxis		2643	94.4
No mechanical bowel preparation		1623	58.0
Preoperative carbohydrates load		1533	54.8
Preoperative ERP adherence (%)	≤ 57.1	1029	36.8
	> 57.1	1770	63.2

Table 1

(Continued)

Variable	Pattern	Number	%
No preanesthesia		1970	70.4
Standard anesthesia protocol		2088	74.6
Normothermia		2466	88.1
Goal-directed or restrictive fluid therapy		1994	71.2
Postoperative nausea/vomit prophylaxis		2340	83.6
Multimodal analgesia		2433	86.9
No nasogastric tube		2483	88.7
Minimally invasive surgery		2645	94.5
No drains		861	30.8
Intraoperative ERP adherence (%)	≤ 88.9	2247	80.3
	> 88.9	552	19.7
Urinary catheter <24–48 h		2053	73.3
Early mobilization		1628	58.2
Early oral feeding		1672	59.7
Predischarge check		2179	77.8
Postoperative ERP adherence (%)	≤ 75.0	1141	40.8
	> 75.0	1658	59.2
Overall morbidity		731	26.1
Major morbidity		191	6.8
Anastomotic leakage		140	5.0
Major anastomotic leakage		111	4.0
Anastomotic bleeding		102	3.6
Mortality		22	0.8

ASA, American Society of Anesthesiologists; ERP, enhanced recovery pathway.

ratio = 1; adjusted logistic regression to estimate the association between the exposure/treatment variable and the outcomes. The following R libraries/programs have been used: 'matchit', 'glm',

Table 2

Adverse events and grading in the study population.

Adverse event	Clavien–Dindo and JCOG grade						
	I	II	IIIa	IIIb	IVa	IVb	Total
Anastomotic leakage	9	20	6	94	6	5	140
Superficial surgical site infections	25	34	0	0	0	0	59
Abdominal collection/abscess	2	14	14	1	0	0	31
Small bowel obstruction	1	10	1	15	0	0	27
Anastomotic bleeding	45	19	29	6	3	0	102
Abdominal bleeding	3	6	6	12	0	0	27
Small bowel perforation	0	0	0	3	0	0	3
Deep wound dehiscence	0	3	0	2	0	0	5
Trocar/wound site bleeding	8	1	1	1	0	0	11
Anemia	7	59	0	0	0	0	66
Paralytic ileus	33	36	0	0	0	0	69
Fever	34	59	0	0	0	0	93
DVT/pulmonary embolism	0	4	0	1	0	0	5
Neurologic	7	4	0	1	0	1	13
Pneumonia and pulmonary failure	8	33	9	0	7	5	62
Urinary retention	27	25	0	0	0	0	52
Urinary tract infection	2	3	0	0	0	0	5
Acute renal failure	3	2	0	0	1	0	6
Acute mesenteric ischemia	0	0	0	3	0	0	3
Acute peptic ulcer/erosive gastritis	0	0	2	0	0	0	2
Other	51	40	9	5	1	1	107
Total	265	372	77	143	19	12	888

DVT, deep venous thrombosis; JCOG, Japanese Clinical Oncology Group.

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Table 3

Details of the circular staplers used for end-to-end colorectal anastomosis in the treatment and control groups.

Treatment Group (A): three-row CS				Control Group (B): two-row CS			
Producer	**Model**	**Number**	**%**	**Producer**	**Model**	**Number**	**%**
Covidien	TRIEEA28MT	157	37.0	Ethicon	CDH29A	68	16.0
	TRIEEA28XT	19	4.5		ECS29A	9	2.1
	TRIEEA31MT	216	50.8		CDH33A	35	8.2
	TRIEEA31XT	30	7.5		CDH29P	14	3.3
	TRIEEA33MT	3	0.7		CDH31P	26	6.1
				Covidien	DSTEEA28	49	11.5
					DSTEEA28XL	7	1.6
					DSTEEA31	105	24.7
					DSTEEA31XL	31	7.3
					DSTEEA33	5	1.2
					DSTEEA33XL	42	9.9
				Touchstone	CSC29A	14	3.3
					ECSC29	12	2.8
					CSC33A	1	0.2
					ECSC33	1	0.2
				Other	Not available	6	1.4

CS, circular stapler.

'publish', 'Tablone', 'Plot', and 'cobalt'[30]. Balance in the matched groups was assessed by calculating the standardized mean difference (SMD) and general variance ratio (a variance ratio close to 1 indicates that variances are equal in the two groups). For outcome modeling, an adjusted logistic regression based on the use of the three-row CS as the treatment variable and on the same 20 covariates selected for the PSMA was performed, presenting odds ratios (OR) and 95% confidence intervals (95% CI). The eventual effect of any unobserved confounder was tested through a sensitivity analysis[31], using the library 'SensitivityR5' of the software 'R' (Version 4.2.2, The R Foundation for Statistical Computing, Vienna, Austria, 2022) and presenting the Γ values (each 0.1 increment of Γ values representing a 10%-odds of differential assignment to treatment due to any unobserved variable).

Results

After propensity score-matching, 1949 patients were excluded (63 treated with the three-row CS and 1886 with the two-row CS), and two groups of 425 patients each were generated: group A (treatment, true population of interest), using the new three-row CS, and group B (control population), using a two-row CS. This population of 850 patients includes data deriving from 62 (79.5%) of the original 78 centers: group A included data deriving from 45 (57.7%) centers, and group B from 54 (69.2%) centers. The details of the CS models used in both groups are shown in Table 3. A good balance between the two groups was achieved (Table 4 and Fig. 2), with a model variance ratio of 1.049. AL diagnosis was established by intravenous contrast CT scan in 57 (40.7%), clinical criteria in 49 (35.0%), endoluminal contrast CT scan in 26 (18.6%), endoluminal contrast enema in 4 (2.8%), and gross findings at reoperation in the remaining four cases (2.8%).

The results of the adjusted logistic regression and sensitivity analyses are reported in Table 5 for the primary endpoints and Table 6 for the secondary endpoints.

Group A versus group B showed a significantly lower risk of overall anastomotic leakage [9 (2.1%) vs. 26 (6.1%) events; OR

0.33; 95% CI 0.15–0.73; $P = 0.006$] and major anastomotic leakage [9 (2.1%) vs. 22 (5.2%) events; OR 0.39; 95% CI 0.17–0.87; $P = 0.022$]. Concerning the risk of AB, no difference was recorded between the two groups (Table 5), whereas it was significantly lower for adherence to preoperative ERP items above its median value [4/573 (0.7%) vs. 8/277 (2.9%) events; OR 0.10; 95% CI 0.02–0.48, $P = 0.004$].

Regarding secondary endpoints, a significantly lower risk of major morbidity was recorded in group A than in group B [15 (3.5%) vs. 28 (6.6%) events; OR 0.47; 95% CI 0.24–0.91; $P = 0.026$], while no significant difference between the two groups was recorded in terms of the risk of overall morbidity and mortality (Table 6). The use of CS diameter at least 30 mm versus less than 30 mm significantly reduced the risk of major morbidity [14/495 (2.8%) vs. 29/355 (8.2%) events; OR 0.33; 95% CI 0.16–0.65; $P = 0.002$] and the risk of overall morbidity [95/495 (19.2%) vs. 93/355 (26.2%) events; OR 0.66; 95% CI 0.47–0.94, $P = 0.02$]. The sensitivity analysis showed $\Gamma = 1.5$ for overall anastomotic leakage, meaning that 50% of patients should have been treated with a two-row CS instead of a three-row CS because of unknown and/or unmeasured confounding variables to alter the result (association of three-row CS use and lower risk of anastomotic leakage) or to lose statistical significance (30% for major anastomotic leakage and 20% for major morbidity).

Discussion

To our best knowledge, this is the first clinical study based on a large, prospective, multicenter database, comparing three-row CS with several two-row CS of different producers, evaluating the risk of early anastomotic adverse events after left-sided colorectal resection for malignant and benign diseases with stapled end-to-end colorectal anastomosis. The use of the three-row CS significantly and independently reduced AL and major morbidity rates. From a practical point of view, the use of a three-row CS determined a 4% absolute risk reduction for overall AL (3% for major AL and major

Table 4

Variables distribution in treatment and control groups before and after propensity score-matching.

| Variable | Pattern | Before propensity score-matching | | | | After propensity score-matching | | | |
		Three-row CS No. = 488 (17.4%)	Two-row CS No. = 2,311 (82.6%)	ᵃP	SMD	Three-row CS No. = 425 (50.0%)	Two-row CS No. = 425 (50.0%)	ᵃP	SMD
Age	< 65.2 years	198	1201	0.001	0.91	160	170	0.58	0.03
	≥ 65.2 years	290	1110	0.001	− 0.25	265	255	0.64	− 0.03
Sex	Male	266	1097	0.001	0.74	237	234	0.91	− 0.008
	Female	222	1214	0.001	0.89	188	191	0.91	0.008
ASA class	I–II	321	1732	0.001	1.23	274	267	0.75	− 0.02
	III	167	579	0.001	0.44	151	158	0.71	0.02
Body mass index	≤ 25 kg/m²	215	1174	0.001	0.86	183	175	0.68	− 0.02
	> 25 kg/m²	273	1137	0.001	0.76	242	250	0.71	0.02
Diabetes	Yes	60	238	0.001	0.29	50	40	0.33	− 0.05
	No	428	2073	0.001	1.47	375	385	0.66	0.02
Chronic renal failure	Yes	19	58	0.001	0.12	14	14	1.00	0.00
	No	469	2253	0.001	1.66	411	411	1.00	0.00
Chronic liver disease	Yes	7	15	0.13	0.05	5	4	1.00	− 0.02
	No	481	2296	0.001	1.70	420	421	1.00	0.002
Surgery for malignancy	Yes	319	1365	0.001	0.89	284	277	0.76	− 0.02
	No	169	946	0.001	0.74	141	148	0.70	0.02
Type of resection	Anterior resection	97	797	0.001	0.73	92	74	0.16	− 0.07
	Left colectomy	391	1514	0.001	0.93	333	351	0.40	0.04
Diameter of CS	< 30 mm	177	1,752	0.001	1.47	176	179	0.90	0.01
	≥ 30 mm	311	559	0.001	0.25	249	246	0.92	− 0.01
Anastomosis	Intracorporeal	470	1987	0.001	1.30	407	402	0.85	− 0.01
	Extracorporeal	18	324	0.001	0.47	18	23	0.53	0.04
Operation length	≤ 180 min	248	1020	0.001	0.70	202	217	0.43	0.04
	> 180 min	240	1291	0.001	0.93	223	208	0.44	− 0.04
Center volume	Low	76	600	0.001	0.60	75	86	0.41	0.04
	High	412	1711	0.001	1.09	350	339	0.62	− 0.03
Open surgery	Yes	13	141	0.001	0.28	12	14	0.84	0.02
	No	475	2170	0.001	1.53	413	411	0.96	− 0.005
Preoperative BT	Yes	17	36	0.01	0.07	13	10	0.67	− 0.03
	No	471	2275	0.001	1.69	412	415	0.92	0.01
Intraoperative and postoperative BT	Yes	14	86	0.001	0.20	12	11	1.00	− 0.01
	No	474	2225	0.001	1.61	413	414	1.00	0.002
Overall ERP adherence	≤ 75.0%	68	1222	0.001	1.12	67	67	1.00	0.00
	> 75.0%	420	1089	0.001	0.56	358	358	1.00	0.00
Preoperative ERP adherence	≤ 57.1%	67	962	0.001	0.91	66	60	0.64	− 0.03
	> 57.1%	421	1349	0.001	0.76	359	365	0.81	0.01
Intraoperative ERP adherence	≤ 88.9%	320	1927	0.001	1.44	274	284	0.64	0.03
	> 88.9%	168	384	0.001	0.26	151	141	0.56	− 0.03
Postoperative ERP adherence	≤ 75.0%	87	1054	0.001	0.95	83	74	0.50	− 0.04
	> 75.0%	401	1257	0.001	0.71	342	351	0.69	0.02
Overall morbidity	Yes	106	625	0.001	0.57	89	99	0.49	0.04
	No	382	1686	0.001	1.10	336	326	0.65	− 0.02
Major morbidity	Yes	19	172	0.001	0.30	15	28	0.06	0.10
	No	469	2139	0.001	1.49	410	397	0.56	− 0.03
Overall AL	Yes	13	127	0.001	0.26	9	26	0.01	0.14
	No	475	2184	0.001	1.55	416	399	0.44	− 0.04
Major AL	Yes	12	99	0.001	0.22	9	22	0.03	0.11
	No	476	2212	0.001	1.58	416	403	0.56	− 0.03
Overall AB	Yes	4	98	0.001	0.25	4	8	0.38	0.06
	No	484	2213	0.001	1.57	421	417	0.88	− 0.01
Mortality	Yes	4	18	0.005	0.08	3	4	1.00	0.02
	No	484	2293	0.001	1.69	422	421	1.00	− 0.002

ᵃStudent's test for proportions.
AB, anastomotic bleeding; AL, anastomotic leakage; ASA, American Society of Anesthesiologists; BT, blood transfusion(s); CS, circular stapler; ERP, enhanced recovery pathway; SMD, standardized mean difference.

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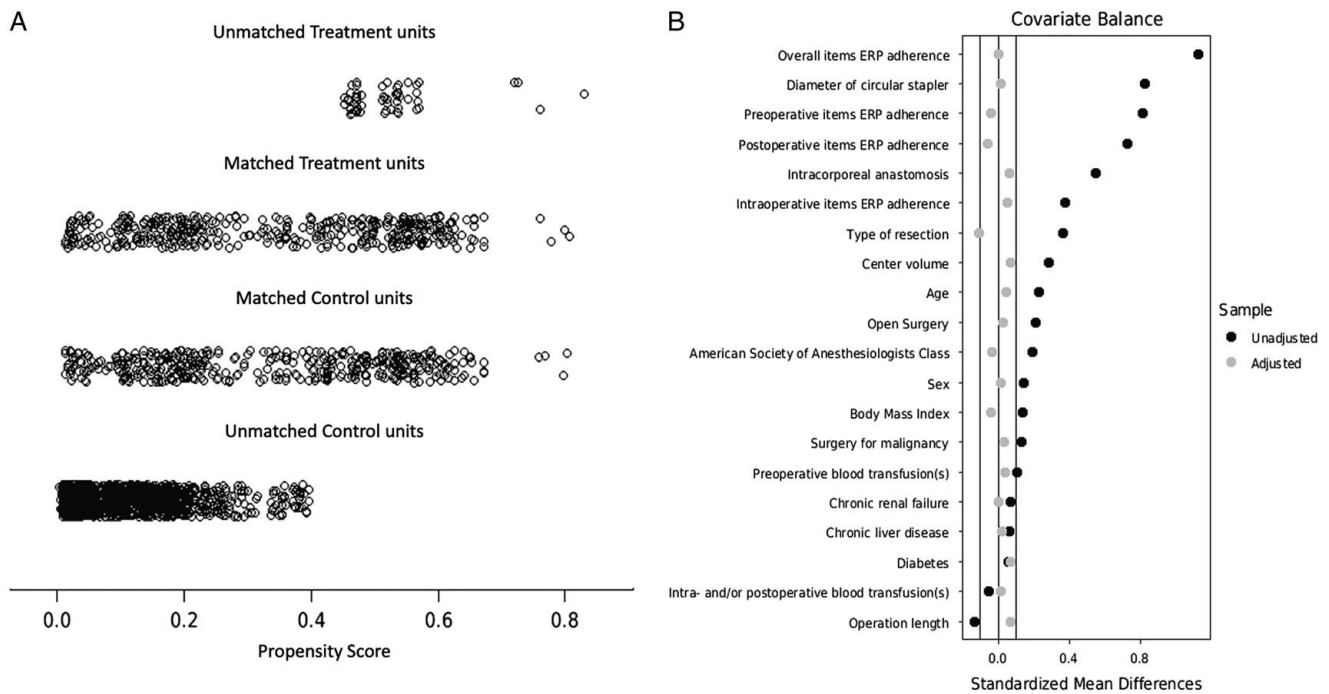
Figure 2. (A) Jitter plot distribution of propensity scores in treatment and control groups. (B) Love plot of covariates' standardized mean differences between treatment and control groups before and after matching; the vertical lines represent the interval of ±0.1 within which balance is considered acceptable. ERP, enhanced recovery pathway.

morbidity), corresponding to the need to treat 25 patients to avoid one AL (33 patients to avoid one major AL and/or one major adverse event). The finding that a CS diameter of at least 30 mm is linked to a significantly lower risk of overall and major morbidity deserves further investigation since the available evidence is controversial[32,33].

The main strength of this study is its methodology: a large database gathered during two prospective multicenter studies was analyzed through a PSMA that perfectly responded to the EQUATOR (Enhancing the QUAlity and Transparency Of Health Research) network reporting guidelines[22]. Although observational studies cannot be regarded as a replacement for randomized studies, data generated from large observational cohorts have been increasingly used to evaluate important clinical questions where data from randomized trials are limited or do not exist[34], mainly because of the lower barriers and cost to subject recruitment. PSMA offers an alternative approach for estimating treatment effects with observational data when randomized trials are not feasible or unethical or when researchers need to assess treatment effects based on real-life data collected through the observation of systems as they operate in normal practice without any intervention implemented by randomized assignment rules, responding to the frequent need to draw conditioned casual inferences from quasi-experimental studies. To account for the conditional probability of treatment selection, thus reducing confounding bias, PSMA presents analytical and interpretation challenges that need to be addressed to maintain the reproducibility of its results, which in recent years has been recognized as a crucial element of high-quality research[35].

The relevant quality of the PSMA used in the present study is based on: (1) a rigorous patients' selection from the parent population, performed upon explicit criteria: to limit data heterogeneity, several potential confounders[36–39] related to the surgical procedure or to the anastomosis itself (any resection different from left colectomy and/or anterior resection, and any anastomosis different from end-to-end), as well as any variable exclusively impacting on subgroups of patients (anastomosis located <5 cm from external anal verge, neoadjuvant therapy, CS diameter 25 mm, proximal protective stoma) were excluded; (2) a reasoned inclusion of 20 conditioning variables (covariates): resections for both malignant and benign diseases in consideration that the stapled end-to-end anastomosis is the same, despite different resection and vascular control criteria; center volume to account for the potential heterogeneity of multicenter, clustered data; adherence to the ERP to account for the potential heterogeneity of medical, anesthesiological, and surgical perioperative management and its impact on the measured outcomes[2]; type of resection in relation to the heterogeneity of the treatment for malignant and benign diseases; intracorporeal or extracorporeal anastomosis, although no difference in the AL risk has recently been reported[40]; CS diameter because its association with the AL risk is still unclear[32,33]; (3) a clear, sheer and restrictive balance algorithm (Fig. 1), particularly regarding caliper = 0.1, matching ratio = 1:1, complete balance assessment, a covariate to number of patients per treatment arm ratio = 1:21; (4) complete description of software package and of its related analytic details; (5) evaluation of the treatment effect through an adjusted multiple regression model including the same 20 covariates used for matching; (6) accounting for unmeasured confounders by a sensitivity analysis.

Another strength of this study is the large number of enrolled patients in a well-defined time-lapse in a large number of centers,

Table 5

Adjusted multiple regression analysis for primary endpoints.

Variable	Pattern	Overall AL OR (95% CI)	P	Major AL OR (95% CI)	P	Overall AB OR (95% CI)	P
Circular stapler	Three-row	0.33 (0.15–0.73)	0.006	0.39 (0.17–0.87)	0.022	0.32 (0.08–1.23)	0.098
	Two-row	Reference		Reference		Reference	
Age	< 65.2 years	Reference		Reference		Reference	
	≥ 65.2 years	0.95 (0.43–2.11)	0.91	0.89 (0.38–2.07)	0.79	1.31 (0.34–5.04)	0.69
Sex	Male	0.91 (0.45–1.87)	0.81	0.71 (0.33–1.50)	0.37	3.93 (0.92–16.78)	0.06
	Female	Reference		Reference		Reference	
ASA class	I–II	Reference		Reference		Reference	
	III	1.63 (0.73–3.63)	0.24	1.35 (0.56–3.24)	0.50	0.22 (0.03–1.40)	0.11
Body mass index	≤ 25 kg/m^2	Reference		Reference		Reference	
	> 25 kg/m^2	1.11 (0.54–2.29)	0.78	1.19 (0.55–2.58)	0.66	0.65 (0.19–2.18)	0.49
Diabetes	Yes	1.28 (0.41–4.00)	0.68	1.36 (0.41–4.46)	0.62	1.23 (0.13–12.13)	0.86
	No	Reference		Reference		Reference	
Chronic renal failure	Yes	Not estimable	–	Not estimable	–	Not estimable	–
	No						
Chronic liver disease	Yes	Not estimable	–	Not estimable	–	Not estimable	–
	No						
Surgery for malignancy	Yes	0.87 (0.39–1.95)	0.74	0.96 (0.42–2.20)	0.92	0.35 (0.09–1.45)	0.15
	No	Reference		Reference		Reference	
Type of resection	Anterior resection	Reference		Reference		Reference	
	Left colectomy	1.18 (0.45–3.09)	0.74	1.60 (0.52–4.94)	0.42	1.29 (0.14–11.81)	0.82
Diameter of CS	< 30 mm	Reference		Reference		Reference	
	≥ 30 mm	0.74 (0.36–1.52)	0.41	0.64 (0.30–1.38)	0.26	1.04 (0.28–3.82)	0.95
Anastomosis	Intracorporeal	0.65 (0.12–3.56)	0.62	0.67 (0.11–3.91)	0.65	1.37 (0.03–73.55)	0.88
	Extracorporeal	Reference		Reference		Reference	
Operation length	≤ 180 min	Reference		Reference		Reference	
	> 180 min	1.80 (0.86–3.75)	0.12	1.73 (0.80–3.74)	0.17	0.54 (0.15–1.91)	0.34
Center volume	Low	Reference		Reference		Reference	
	High	0.66 (0.28–1.54)	0.33	0.62 (0.25–1.53)	0.30	1.97 (0.34–11.54)	0.45
Open surgery	Yes	Reference		Reference		Reference	
	No	0.32 (0.04–2.33)	0.26	0.44 (0.05–4.05)	0.47	0.16 (0.00–9.34)	0.38
Preoperative BT	Yes	0.82 (0.08–8.01)	0.86	2.95 (0.52–16.67)	0.22	9.60 (0.79–115.88)	0.08
	No	Reference		Reference		Reference	
Intraoperative/postoperative BT	Yes					Ref	
	No	Not estimable	–	Not estimable	–	5.25 (0.40–68.71)	0.21
Overall ERP adherence	≤ 75.0%	Reference		Reference		Reference	
	> 75.0%	1.25 (0.26–6.00)	0.78	2.26 (0.41–12.58)	0.35	11.7 (0.81–169.61)	0.07
Preoperative ERP adherence	≤ 57.1%	Reference		Reference		Reference	
	> 57.1%	1.44 (0.42–4.97)	0.56	1.31 (0.35–4.91)	0.69	0.10 (0.02–0.48)	0.004
Intraoperative ERP adherence	≤ 88.9%	Reference		Reference		Reference	
	> 88.9%	1.18 (0.53–2.61)	0.56	1.31 (0.35–4.91)	0.69	0.60 (0.14–2.59)	0.49
Postoperative ERP adherence	≤ 75.0%	Reference		Reference		Reference	
	> 75.0%	0.85 (0.23–3.08)	0.80	0.60 (0.17–2.20)	0.44	0.23 (0.03–1.62)	0.14
Sensitivity analysis		Γ		Γ		Γ	
		1.5	0.06	1.3	0.07	1.0	0.19

AB, anastomotic bleeding; AL, anastomotic leakage; ASA, American Society of Anesthesiologists; BT, blood transfusion(s); CS, circular stapler; ERP, enhanced recovery pathway; OR (95% CI), odds ratio and 95% confidence intervals.

representing a very wide sample of surgical units performing colorectal resections in Italy. Although the multicenter nature of the considered data may be a definite source of a clustering bias, it is undoubtedly representative of real-life data.

However, this study had several limitations, and the results should be interpreted with caution. First, several controversial risk factors for AL were not measured or recorded in the parent studies: disease stage[41], single surgeon's experience[42,43], level of vascular control[44], splenic flexure mobilization[45], rectal stump management[46], intraoperative anastomotic testing, and reinforcement[47]. The second limitation is represented by the impact of potential residual, known or unknown, confounding factors which are intrinsic to observational studies. This impact seems to be not relevant in this study. Actually, according to the sensitivity analysis (Tables 5, 6), a potential model deviation from random assignment due to unknown and/or unmeasured confounders, which can alter the results, was estimated at 50% (Γ = 1.5) for overall AL risk, 30% (Γ = 1.3) for major AL risk, and 20% (Γ = 1.2) for major morbidity risk. On the other hand, lower values (Γ = 1.0) were recorded for overall morbidity (Table 6), indicating that unknown and/or unmeasured confounders may account for the controversial findings regarding CS diameter. Another limitation is the lack of testing for the same hypothesis by using the powered two-row CS as the treatment variable. A PSMA has not been performed because only

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Table 6

Adjusted multiple regression analysis for secondary endpoints.

Variable	Pattern	Overall morbidity		Major morbidity		Mortality	
		OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Circular stapler	Three-row	0.87 (0.63–1.21)	0.42	0.47 (0.24–0.91)	0.026	0.97 (0.20–4.72)	0.97
	Two-row	Reference		Reference		Reference	
Age	< 65.2 years	Reference		Reference		Reference	
	≥ 65.2 years	1.05 (0.73–1.53)	0.78	0.80 (0.38–1.66)	0.54	0.44 (0.07–2.80)	0.39
Sex	Male	1.01 (0.72–1.42)	0.97	0.67 (0.35–1.28)	0.23	0.70 (0.14–3.51)	0.67
	Female	Reference		Reference		Reference	
ASA class	I–II	Reference		Reference		Reference	
	III	1.02 (0.68–1.52)	0.93	1.45 (0.68–3.03)	0.33	1.25 (0.17–9.18)	0.82
Body mass index	≤ 25 kg/m^2	Reference		Reference		Reference	
	> 25 kg/m^2	1.04 (0.74–1.46)	0.82	0.81 (0.43–1.55)	0.53	1.07 (0.21–5.38)	0.93
Diabetes	Yes	0.87 (0.48–1.56)	0.63	1.36 (0.51–3.60)	0.54	Not estimable	–
	No	Reference		Reference			
Chronic renal failure	Yes	Reference		Reference		Not estimable	–
	No	1.57 (0.65–3.77)	0.32	0.60 (0.07–5.01)	0.64		
Chronic liver disease	Yes	1.80 (0.42–7.68)	0.43	Not estimable	–	Not estimable	–
	No	Reference					
Surgery for malignancy	Yes	1.02 (0.70–1.49)	0.92	2.05 (0.95–4.41)	0.07	2.80 (0.47–16.53)	0.26
	No	Reference		Reference		Reference	
Type of resection	Anterior resection	Reference		Reference			
	Left colectomy	0.95 (0.61–1.48)	0.83	1.30 (0.54–3.15)	0.56	Not estimable	–
Diameter of CS	< 30 mm	Reference		Reference		Reference	
	≥ 30 mm	0.66 (0.47–0.92)	0.02	0.33 (0.16–0.65)	0.002	0.33 (0.05–2.03)	0.23
Anastomosis	Intracorporeal	1.23 (0.44–3.43)	0.69	1.56 (0.19–13.10)	0.68	Not estimable	–
	Extracorporeal	Reference		Reference			
Operation length	≤ 180 min	Reference		Reference		Reference	
	> 180 min	0.85 (0.61–1.20)	0.36	1.65 (0.85–3.21)	0.14	2.68 (0.47–15.24)	0.27
Center volume	Low	Reference		Reference		Reference	
	High	0.81 (0.52–1.25)	0.35	1.05 (0.44–2.48)	0.91	0.89 (0.13–6.19)	0.91
Open surgery	Yes	Reference					
	No	0.56 (0.17–1.84)	0.34	Not estimable	–	Not estimable	–
Preoperative BT	Yes	0.73 (0.24–2.29)	0.59	1.04 (0.13–8.63)	0.97	Not estimable	–
	No	Reference		Reference			
Intraoperative/postoperative BT	Yes	1.34 (0.50–3.60)	0.57	Not estimable	–	Not estimable	–
	No	Reference					
Overall ERP adherence	≤ 75.0%	Reference		Reference		Reference	
	> 75.0%	1.59 (0.74–3.43)	0.24	1.41 (0.37–5.42)	0.62	0.94 (0.06–15.95)	0.97
Preoperative ERP adherence	≤ 57.1%	Reference		Reference		Reference	
	> 57.1%	0.72 (0.41–1.25)	0.24	0.74 (0.28–1.93)	0.54	1.29 (0.13–12.45)	0.82
Intraoperative ERP adherence	≤ 88.9%	Reference		Reference		Reference	
	> 88.9%	1.05 (0.73–1.52)	0.80	1.93 (0.93–3.98)	0.08	2.04 (0.24–17.03)	0.51
Postoperative ERP adherence	≤ 75.0%	Reference		Reference		Reference	
	> 75.0%	1.17 (0.62–2.20)	0.64	0.44 (0.15–1.30)	0.14	0.09 (0.09–1.03)	0.05
Sensitivity analysis		Γ		Γ		Γ	
		1	0.23	1.2	0.09	1	0.50

ASA, American Society of Anesthesiologists; BT, blood transfusion(s); CS, circular stapler; ERP, enhanced recovery pathway; OR (95% CI), odds ratio and 95% confidence intervals.

172 cases treated with the powered two-row CS were available in the examined population (Table 1), and this small number of cases would not have allowed the use of the same PSMA algorithm used for the three-row CS. Moreover, two previous PSMAs were performed on the same topic: the first[48] using the powered two-row CS and the second[16] using the three-row CS in the treatment arm. According to PSMA reporting guidelines[22], both were deeply biased regarding a limited number of cases, retrospective data, matching ratio = 1:2, caliper = 0.2, the inclusion of a limited (8–11) number of covariates, and an incomplete description of the matching algorithm. As a consequence, the 10% AL absolute risk reduction using these devices recorded by both studies appears at least unrealistic, considering that any stapling device is not a 'magic bullet' and that there is always a human being firing it[9].

Finally, although data quality control was performed and repeated at various levels, potential measurement errors by the participating investigators could not be ruled out.

Conclusions

This study clearly highlighted that technological change in stapling devices might play a definite role in limiting the risk of anastomotic leakage and its related morbidity.

Ethical approval

Both studies were conducted in accordance with the Declaration of Helsinki and the guidelines for good clinical practice E6 (R2). The study protocols were approved by the ethics committee of the coordinating center (Marche Regional Ethics Committee – CERM – 2018/334 released on 28 November 2018 for iCral2; CERM – 2020/192 released on 30 July 2020 for iCral3) and registered at ClinicalTrials.gov (NCT03771456 for iCral2 and NCT04397627 for iCral3).

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Author contributions

M.C., S.G., G.R., M.G.V., F.B., G.B., and M.S.: concept and design; M.C., S.G., F.M., G.R., M.G.V., F.B, G.B., and M.S.: acquisition, analysis, or interpretation of data; M.C., S.G., and F.M.: drafting of the manuscript; M.C., S.G., F.M., G.R., M.G.V., F.B., G.B., and M.S.: critical revision of the manuscript for important intellectual content; F.M. and S.G.: statistical analysis.

Conflicts of interest disclosure

Dr Catarci reports personal fees from Baxter Spa outside the submitted work. Dr Guadagni, Masedu, Ruffo, Viola, Borghi, Baldazzi, and Scatizzi have no competing interests.

Research registration unique identifying number (UIN)

None.

Guarantor

Marco Catarci, iCral Study Group coordinator, had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

Data availability statement

Individual participant-level anonymized datasets were made available for both parent studies and presented analysis upon reasonable request by contacting the study coordinator.

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References

[1] Mlambo B, Shih IF, Li Y, et al. The impact of operative approach on postoperative outcomes and healthcare utilization after colectomy. Surgery 2022;171:320–7.

[2] Ripollés-Melchor J, Ramírez-Rodríguez JM, Casans-Francés R, et al. Association between use of enhanced recovery after surgery protocol and postoperative complications in colorectal surgery: the Postoperative Outcomes Within Enhanced Recovery After Surgery Protocol (POWER) Study. JAMA Surg 2019;154:725–36.

[3] Boccola MA, Buettner PG, Rozen WM, et al. Risk factors and outcomes for anastomotic leakage in colorectal surgery: a single-institution analysis of 1576 patients. World J Surg 2011;35:186–95.

[4] La Regina D, Di Giuseppe M, Lucchelli M, et al. Financial impact of anastomotic leakage in colorectal surgery. J Gastrointest Surg 2019;23:580–6.

[5] Bashir Mohamed K, Hansen CH, Krarup P-M, et al. The impact of anastomotic leakage on recurrence and long-term survival in patients with colonic cancer: a systematic review and meta-analysis. Eur J Surg Oncol 2020;46:439–47.

[6] Ravitch MM, Steichen FM. A stapling instrument for end-to-end inverting anastomosis in the gastrointestinal tract. Ann Surg 1979;189:791–7.

[7] Italian ColoRectal Anastomotic Leakage (iCral) study group. Colorectal surgery in Italy: a snapshot from the iCral study group. Updates Surg 2019;71:339–47.

[8] Griffen FD, Knight CD Sr, Whitaker JM. The double stapling technique for low anterior resection. Results, modifications, and observations. Ann Surg 1990;211:745–51.

[9] Slieker JC, Daams F, Mulder IM, et al. Systematic review of the technique of colorectal anastomosis. JAMA Surg 2013;148:190–201.

[10] Sparreboom CL, van Groningen JT, Lingsma HF, et al. Different risk factors for early and late colorectal anastomotic leakage in a nationwide audit. Dis Colon Rectum 2018;61:1258–66.

[11] Chung RS. Blood flow in colonic anastomoses. Effect of stapling and suturing. Ann Surg 1987;206:335–9.

[12] Herzig DO, Ogilvie JW, Chudzinski A, et al. Assessment of a circular powered stapler for creation of anastomosis in left-sided colorectal surgery: a prospective cohort study. Int J Surg 2020;84:140–6.

[13] Eschbach M, Sindberg GM, Godek ML, et al. Micro-CT imaging as a method for comparing perfusion in graduated-height and single-height surgical staple lines. Med Devices (Auckl) 2018;11:267–73.

[14] Nakanishi R, Fujimoto Y, Sugiyama M, et al. Clinical impact of the triple-layered circular stapler for reducing the anastomotic leakage in rectal cancer surgery: porcine model and multicenter retrospective cohort analysis. Ann Gastroenterol Surg 2021;6:256–64.

[15] Mazaki J, Katsumata K, Ohno Y, et al. A novel predictive model for anastomotic leakage in colorectal cancer using auto-artificial intelligence. Anticancer Res 2021;41:5821–5.

[16] Mazaki J, Katsumata K, Ishizaki T, et al. Effectiveness of a new triple-row circular stapler in reducing the risk of colorectal anastomotic leakage. A historical control and propensity score-matched study. Medicine 2022;101:e29325.

[17] Quero G, Fiorillo C, Menghi R, et al. Preliminary evaluation of two-row versus three-row circular staplers for colorectal anastomosis after rectal resection: a single-center retrospective analysis. Int J Colorectal Dis 2022;37:2501–10.

[18] Folkesson J, Nilsson J, Påhlman L, et al. The circular stapling device as a risk factor for anastomotic leakage. Colorectal Dis 2004;6:275–9.

[19] Catarci M, Ruffo G, Viola MG, et al. ERAS program adherence-insti-tutionalization, major morbidity and anastomotic leakage after elective colorectal surgery: the iCral2 multicenter prospective study. Surg Endosc 2022;36:3965–84.

[20] The Italian Colorectal Anastomotic Leakage (iCral) study group. Patient-reported outcomes and return to intended oncologic therapy after colorectal enhanced recovery pathway: the iCral3 prospective study. Ann Surg Open 2023;4:e267.

[21] Mathew G, Agha R. for the STROCSS Group. STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case–control studies in surgery. Int J Surg 2021;96:106165.

[22] Yao XI, Wang X, Speicher PJ, et al. Reporting and guidelines in propensity score analysis: a systematic review of cancer and cancer surgical studies. J Natl Cancer Inst 2017;109:djw323.

[23] Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13.

[24] Katayama H, Kurokawa Y, Nakamura K, et al. Extended Clavien–Dindo classification of surgical complications: Japan Clinical Oncology Group postoperative complications criteria. Surg Today 2016;46:668–85.

[25] Rahbari NN, Weitz J, Hohenberger W, et al. Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery 2010;147:339–51.

[26] Hébert J, Eltonsy S, Gaudet J, et al. Incidence and risk factors for anastomotic bleeding in lower gastrointestinal surgery. BMC Res Notes 2019;12:378.

[27] Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res 2011;46:399–424.

[28] Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. Biometrika 1983;70:41–55.

[29] Brookhart MA, Schneeweiss S, Rothman KJ, et al. Variable selection for propensity score models. Am J Epidemiol 2006;163:1149–56.

[30] Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat 2011;10:150–61.

[31] Rosenbaum, PR. The power of a sensitivity analysis and its limit. In: Rosenbaum PR, editor. Design of Observational Studies, 2nd ed. Springer Series in Statistics. Springer Nature; 2020:pp. 317–336.

[32] Nagaoka T, Yamaguchi T, Nagasaki T, et al. Safety of small circular staplers in double stapling technique anastomosis for sigmoid colon and rectal cancer. Dis Colon Rectum 2021;64:937–45.

[33] Kim JS, Cho SY, Min BS, et al. Risk factors for anastomotic leakage after laparoscopic intracorporeal colorectal anastomosis with a double stapling technique. J Am Coll Surg 2009;209:694–701.

[34] Silverman SL. From randomized controlled trials to observational studies. Am J Med 2009;122:114–20.

[35] Ioannidis JPA, Greenland S, Hlatky MA, et al. Increasing value and reducing waste in research design, conduct, and analysis. Lancet 2014;383:166–75.

[36] Pommergaard HC, Gessler B, Burcharth J, et al. Preoperative risk factors for anastomotic leakage after resection for colorectal cancer: a systematic review and meta-analysis. Colorectal Dis 2014;16:662–71.

[37] Meyer J, Naiken S, Christou N, et al. Reducing anastomotic leak in colorectal surgery: the old dogmas and the new challenges. World J Gastroenterol 2019;25:5017–25.

[38] McKechnie T, Sharma S, Daniel R, et al. End-to-end versus end-to-side anastomosis for low anterior resection: a systematic review and meta-analysis of randomized controlled trials. Surgery 2021;170:397–404.

[39] Hu MH, Huang RK, Zhao RS, et al. Does neoadjuvant therapy increase the incidence of anastomotic leakage after anterior resection for mid and low rectal cancer? A systematic review and meta-analysis. Colorectal Dis 2017;19:16–26.

[40] Hollandsworth HM, Li K, Zhao B, et al. Robotic left-stapled total intracorporeal bowel anastomosis versus stapled partial extracorporeal anastomosis: operative technical description and outcomes. Surg Endosc 2022;36:3645–52.

[41] Kryzauskas M, Bausys A, Degutyte AE, et al. Risk factors for anastomotic leakage and its impact on long-term survival in left-sided colorectal cancer surgery. World J Surg Onc 2020;18:205.

[42] García-Granero E, Navarro F, Cerdán Santacruz C, et al. Individual surgeon is an independent risk factor for leak after double-stapled colorectal anastomosis: an institutional analysis of 800 patients. Surgery 2017;162:1006–16.

[43] Kelly M, Bhangu A, Singh P, et al. Systematic review and meta-analysis of trainee versus expert surgeon-performed colorectal resection. BJS 2014;101:750–9.

[44] Lange MM, Buunen M, van de Velde CJ, et al. Level of arterial ligation in rectal cancer surgery: low tie preferred over high tie. A review. Dis Colon Rectum 2008;51:1139–45.

[45] Rondelli F, Pasculli A, De Rosa M, et al. Is routine splenic flexure mobilization always necessary in laparotomic or laparoscopic anterior rectal resection? A systematic review and comprehensive meta-analysis. Updates Surg 2021;73:1643–61.

[46] Balciscueta Z, Uribe N, Caubet L, et al. Impact of the number of stapler firings on anastomotic leakage in laparoscopic rectal surgery: a systematic review and meta-analysis. Tech Coloproctol 2020;24:919–25.

[47] Tang G, Du D, Tao J, et al. Effect of indocyanine green fluorescence angiography on anastomotic leakage in patients undergoing colorectal surgery: a meta-analysis of randomized controlled trials and propensity-score-matched studies. Front Surg 2022;9:815753.

[48] Pla-Martí V, Martín-Arévalo J, Moro-Valdezate D, et al. Impact of the novel powered circular stapler on risk of anastomotic leakage in colorectal anastomosis: a propensity score-matched study. Tech Coloproctol 2021;25:279–84.