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Research article

Indocyanine green in left side colorectal surgery segmental resection to decrease anastomotic leak: A parallel retrospective cohort study of 115 patients

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A R T I C L E I N F O

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Anastomotic leak
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Observational study

A B S T R A C T

Background: We investigated the impact of Indocyanine Green (ICG) angiography on reducing anastomotic leakage (AL) after elective left segmental colon resection, including transverse resection. While ICG is widely used in colorectal surgery to assess vascularization, its true effect on AL, particularly in left segmental resections, remains unclear.
Study design: This retrospective, monocentric cohort study included patients undergoing left and transverse colon resection from January 2017 to July 2023. Patients were divided into ICG and no-ICG groups. The primary outcome was AL, with secondary outcomes including postoperative morbidity and length of stay.
Results: Of the 115 patients enrolled, 53 received ICG and 63 did not. AL occurred in 6 patients in the no-ICG group, but none in the ICG group. No significant correlation was found between ICG use and other confounding factors. Postoperative length of stay was also shorter in the ICG group.
Conclusions: The use of ICG was associated with a reduction in AL, with no cases in the ICG group. These findings suggest a potential benefit of ICG, warranting confirmation in future large-scale studies.
Clinical trial registration: clinicaltrial.gov (NCT05981937).

1. Introduction

Anastomotic leakage (AL) is a significant complication following colorectal surgery, impacting patient quality of life and survival [1]. It is defined as an intestinal wall defect at the anastomotic site, creating communication between intra- and extraluminal compartments [2]. Reported incidence varies between 1 % and 30 %, depending on surgical procedures and definitions used [1,3,4]. Key modifiable risk factors include excessive anastomosis tension and inadequate vascularization, with other contributors being

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Abbreviations

Anastomotic Leak (AL)
American Society of Anesthesiologist (ASA)
Computer Tomography (CT)
Confidence Interval (CI)
Interquartile range (IQR)
Odds Ratio (OR)
Randomized Controlled Trials (RCTs)
Indocyanine Green (ICG)

patient-related factors such as age, obesity, and preoperative treatment [1,4]. The presence of AL increases morbidity, delays adjuvant therapy, and negatively impacts oncological outcomes [5].

Indocyanine Green (ICG) is a widely used fluorophore that aids in assessing anastomotic vascularization during surgery. Introduced in 1976 [6], its utility in colorectal surgery has been confirmed by systematic reviews and meta-analyses, though these studies often exclude specific types of surgeries or do not focus exclusively on left-sided resections [7,8]. The European Association for Endoscopic Surgery recommends ICG use in colorectal surgery, but its effectiveness in preventing AL in left-sided segmental resections remains under-explored [9].

Left-sided colorectal surgery carries an increased risk of AL due to the variability of the marginal artery, particularly when vessel sectioning does not occur at its origin [10]. Although Randomized Controlled Trials (RCTs) have explored ICG use in rectal and rectosigmoid surgeries, results have been inconclusive regarding AL reduction [11–15]. Moreover, no trials specifically address segmental colon resections. This study investigates the role of ICG in reducing AL during elective segmental colon resections, aiming to provide more targeted insights into its protective effect and influence on surgical outcomes.

2. Methods

2.1. Design, inclusion and exclusion criteria, and sample recruitment

A parallel, monocentric, retrospective cohort study conducted according to the protocol registered at clinicaltrial.gov (NCT05981937) was authorized by our local ethics committee. A consecutive series of patients who underwent colorectal surgery at our institution (Guglielmo da Saliceto Hospital, Piacenza, Italy) between January 1, 2017, and July 31, 2023, were screened. We reviewed the risk factors for AL and identified variables of interest and confounding factors to assess the relationship of each covariate, including current smoker [16] and surgeon experience in colorectal surgery [17].

The primary endpoint of the study was AL at 30 days after surgery. Secondary endpoints were postoperative mortality and morbidity [18] within 30 days after surgery, defined as medical and surgical morbidity, including surgical site infection, readmission, redo surgery, and any other complication related to surgery. Moreover, any morbidity with Clavien-Dindo Score ≥ III, postoperative length of stay, rate of laparoscopic surgical procedure, and rate of protection stoma were collected and reported. AL was defined as a defect of the intestinal wall at the anastomotic site leading to a communication between the intra- and extraluminal compartments [2]. Sex, body mass index, smoking, diabetes mellitus, cardiovascular disease, and tumor stage according to the American Joint Committee on Cancer 8th edition [19] were considered as confounding factors for the onset of AL, in line with the evidence available in the literature [4].

An electronic database was created from the extracted medical records. The operating room log and all digital medical records were scanned, including perioperative outcomes and 30-day postoperative follow-up data. Inclusion criteria were elective surgery, left segmental colon resection including transverse colon resection for benign or malignant pathology, at least 30 days of postoperative follow-up available from medical documentation, primary colocolic or colorectal anastomosis with or without preventing ostomy, and ≥18 years of age.

Exclusion criteria were terminal colonic stoma without anastomosis creation after resection, extended transverse right hemi-colectomy, hartmann's reversal, left hemicolectomy with high-inferior mesenteric artery ligation, associated bowel or other splanchnic resection (i.e. neoplastic infiltration), previous colon surgery, synchronous neoplasm, missing data regarding vascular ligation or primary outcomes, stage IV cancer, American Society of Anesthesiologist(ASA) score = IV, less than 18 years old, and emergency/urgency surgery.

2.2. Surgical techniques

The three surgical techniques included in the study (transverse colon resection, splenic flexure resection, and left colectomy including hemicolectomy with lower mesenteric artery ligation [20] and sigmoidectomy) are described in the study protocol and its subsequent modification (Appendix 1, Appendix 2 and Appendix 3).

The ICG anastomosis angiography test has been used at our institute since 2019 using a near-infrared light source and special scope and camera equipped with a xenon light (KARL STORZ SE & Co. KG, Tuttlingen, Germany). Since introduction of the ICG angiography

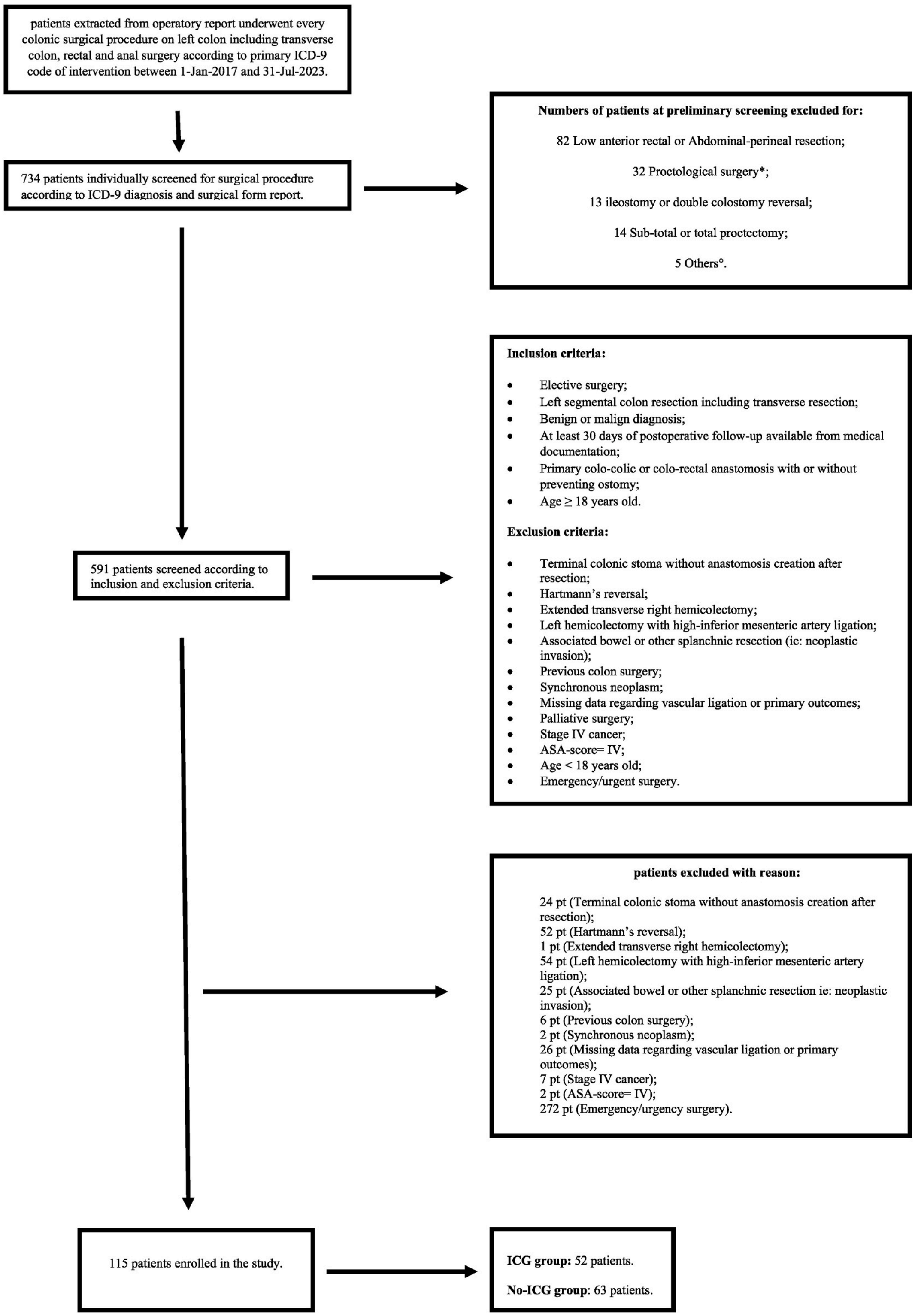

Fig. 1. Patients enrolled flow chart according to preliminary analysis and inclusion/exclusion criteria.
pt: patient
* including anal or rectal procedure with trans-anal approach, TAMIS and endoscopic resection
°including one duplicate case,one tangential transverse colon resection and three palliative surgery.

Table 1
Descriptive analysis and distribution of items of interest.

	Total population n = 115 (100 %)	ICG n = 52 (45.22 %)	No-ICG n = 63 (54.78 %)	p-value
Sex n (%)				
Male	74 (64.35)	35 (67.31)	39 (61.90)	0.684
Female	41 (35.65)	17 (32.69)	24 (38.10)	
Age at surgery (years)[a]	68 [56.50–79.50] (44–88)	68.50 [57–81] (44–88)	67 [55–78.50] (44–86)	**< 0.001**
ASA score n (%)				
≤2	70 (60.87)	32 (61.54)	38 (60.32)	1
>2	45 (39.13)	20 (38.46)	25 (39.68)	
Hospital admission within 3 months to surgery n (%)	33 (30.84)	9 (17.65)	24 (42.86)	**0.009**
Current smoking n (%)	15 (15.62)	6 (12.50)	9 (18.75)	0.574
BMI, n (%)				
<30 kg/m^2	70 (84.34)	42 (85.71)	28 (82.35)	0.915
≥30 kg/m^2	13 (15.66)	7 (14.29)	6 (17.65)	
Cardiovascular disease n (%)	19 (16.52)	10 (19.23)	9 (14.29)	0.685
Diabetes mellitus, n (%)	22 (19.13)	11 (21.15)	11 (17.46)	0.953
COPD n (%)	9 (7.83)	5 (9.61)	4 (6.35)	0.732
Previous abdominal surgery, n (%)	36 (31.30)	15 (28.85)	21 (33.33)	0.753
Site of previous abdominal surgery, n (%)				
Sub-mesocolic	26 (70.27)	11 (68.75)	15 (71.43)	1
Upper-mesocolic	3 (8.11)	1 (6.25)	2 (9.52)	
Both	8 (21.62)	4 (25.00)	4 (19.05)	
Diagnosis n (%)				
Neoplasia	70 (60.87)	41 (75.85)	29 (46.03)	**< 0.001**
Other[b]	45 (39.13)	11 (21.15)	34 (53.97)	
Neoplastic stage n (%)				
Early	42 (60.87)	23 (56.10)	19 (67.86)	0.464
Locally advanced	27 (39.13)	18 (43.90)	10 (32.14)	
Surgical procedure n (%)				
Colic splenic resection	30 (26.09)	17 (32.69)	13 (20.63)	0.309
Left colectomy[c]	75 (65.22)	30 (57.69)	45 (71.43)	
Transverse colon resection	10 (8.70)	5 (9.62)	5 (7.94)	
Operating time (minutes)	219 [166–275] (85–372)	239.5 [177.2–275.5] (114–372)	207 [160.5–268] (85–363)	**< 0.001**
First surgeon experience n (%)				
Junior	16 (13.91)	9 (17.31)	7 (11.11)	0.493
Senior	99 (86.09)	43 (82.69)	56 (88.89)	
Surgical approach, n (%)				
Laparoscopy	93 (80.87)	46 (88.46)	47 (74.60)	0.094
Laparotomy	22 (19.13)	6 (11.54)	16 (25.40)	
Converted to open, n (%)	18 (19.35)	3 (6.52)	15 (31.91)	**0.005**
Type of anastomosis n (%)				
Colocolic	54 (46.96)	29 (55.77)	25 (39.68)	0.125
Colorectal	61 (53.04)	23 (44.23)	39 (60.32)	
Anastomotic technique n (%)				
Hand-sewn	10 (8.70)	3 (5.77)	7 (11.11)	0.497
Mechanics	105 (91.30)	49 (94.23)	56 (88.89)	
Change in stapler line, n (%)	3 (2.61)	2 (3.85)	1 (1.59)	0.589
Anastomotic leak, n (%)	6 (5.22)	0 (0)	6 (9.52)	**0.031**
Postoperative length of stay (days)[a]	8 [6–11] (2–58)	7 [6–10] (2–29)	8 [7–11] (5–58)	**< 0.001**
Modality of discharge, n (%)				
Other hospital	13 (11.30)	7 (13.46)	6 (9.52)	0.713
At home	102 (88.70)	45 (86.54)	57 (90.48)	
Reintervention at 30 days, n (%)	13 (11.30)	7 (13.46)	6 (9.52)	0.713
Surgical morbidity within 30 days, n (%)	34 (29.57)	16 (30.77)	18 (28.57)	0.447
Medical morbidity within 30 days n (%)	24 (20.87)	13 (25.00)	11 (17.46)	0.362
Clavien–Dindo score ≥3, n (%)	21 (18.26)	10 (19.23)	11 (17.46)	0.998
Mortality within 30 days, n (%)	4 (3.48)	2 (3.85)	2 (3.17)	1

Significant P-values are shown in bold italics.
ASA: American Society of Anesthesiologists, COPD: chronic obstructive pulmonary disease, ICG: indocyanine green.
[a] median [interquartile range] (range).
[b] benign conditions.
[c] including left hemicolectomy with low-inferior mesenteric artery-ligation and sigmoidectomy.

test two laparoscope equipments were available and were used in every elective colorectal procedure unless in case of impossibility of indocyanine instrument as in the event of two consecutive surgery in the same day, concomitant indocyanine surgery or indocyanine malfunction.

ICG was supplied as a sterile water-soluble lyophilized powder (Diagnostic Green® GmbH). The ICG anastomosis angiography test is routinely used whenever available in daily practice according to the following protocol: after specimen resection, the two colon stumps or colon and rectum stumps are checked with 5 cc of ICG 25 mg diluted in 10 cc of sterile water before the anastomosis is fashioned. No preset distance of the laparoscope to the bowel stumps, no qualitative methods, and no ordinal scale of quality (i.e., poor, adequate, good) were used. The time to intravenous ICG injection and fluorescence onset is usually good within 29 s and satisfactory until 60 s, according to a qualitative study [21], but these data were not collected owing to poor reporting on the operating room form. The final decision to perform extra resection with change in stapler line of the bowel stump was left up to the judgment and experience of the operating surgeon.

2.3. Reporting and study BIAS detection

This study was reporting according to the STROBE statement checklist extension for cohort studies [22], available in Appendix 4.

We hypothesized that the risk of confounding bias for the presence of confounding factors would correlate with the primary outcome.

Selection bias may be present owing to the monocentric design, different indications of surgery (malignancy vs. benign pathology), various experience levels of the operating surgeon, and variations in time, technique, and reporting by the different surgeons involved in the study. To minimize the impact of missing data, we excluded from statistical analysis any variables with $\geq$ 20 % missing data.

2.4. Statistical analysis

Quantitative variables were described as medians and IQR (Interquartile Range), and qualitative variables were described by absolute and percentage frequencies. Normality was checked for all continuous variables. Comparisons of covariates were conducted using Pearson's X^2 test or Fisher's exact test for categorical variables and a *t*-test or Mann–Whitney test for continuous variables. Univariable analysis was conducted using logistic regression to examine the association of each predictive variable with the ALevent. Next, variables with $p < 0.05$ were considered for inclusion in a multivariable regression model. For each risk factor, Odds Ratios (OR) with associated Confidence Intervals (CI) are presented. All analyses were performed using RStudio version 3.6.0 statistical software with two-sided significance tests and a 5 % significance level.

Table 2
Univariate analysis.

Variable	OR (95 % CI)	p-value
Sex, male vs. female	1.11 (0.2, 6.36)	0.903
Age at surgery	1.01 (0.94, 1.0)	0.847
ASA score, <2 vs. ≤2	3.32 (0.58,18.92)	0.177
Hospital admission within 3 months of surgery, yes vs. no	0.74 (0.07,7.39)	0.797
BMI ≥30 vs. <30	0 (0, End)[a]	0.996
Cardiovascular disease. yes vs. no	3.33 (0.52, 21.49)	0.205
Diabetes mellitus, yes vs. no	4.1 (0.54) 30.91	0.171
COPD yes vs. no	0 (0, End)[a]	0.994
Previous abdominal surgery yes vs. no	1.1 (0.19, 6.32)	0.912
Diagnosis of neoplasia vs. other	1.3 (0.23, 7.42)	0.766
Surgical procedure		
Colo-splenic resection	Ref	
Sigmoidectomy	2.07 (0.23, 18.51)	0.515
Transverse colon resection	0 (0, End)[a]	0.994
Operating time	0.996 (0.983, 1.009)	0.543
First surgeon experience, senior vs. junior	0.8 (0.09, 7.31)	0.842
Surgical approach, laparoscopy vs. laparotomy	0.21 (0.04, 1.13)	0.069
Converted to open, yes vs. no	2.15 (0.18, 25.08)	0.542
Type of anastomosis, colorectal vs. colocolic	4.73 (0.54, 41.84)	0.162
Anastomotic technique, mechanical vs. hand-sewn	7009017 (0, End)[a]	0.994
Change in stapler line, yes vs. no	10.7 (0.83, 138.75)	0.070
ICG, yes vs. no	0 (0, End)[a]	0.994
Neoplastic stage, locally advanced vs. early	0.5 (0.05–5.07)	0.558

ASA: American Society of Anesthesiologists, BMI: body mass index, CI: confidence interval at 95 %, COPD: chronic obstructive pulmonary disease, ICG: indocyanine green, OR: odds ratio, Ref: reference variable.

[a] Upper 95 % CI limit cannot not be calculated owing to the variable distribution.

3. Results

3.1. Patient characteristics

Following the screening of patients according to the inclusion and exclusion criteria, 115 patients were enrolled in the study. The ICG group included 52 patients, and the no-ICGgroup included 63 patients, as shown in the flow chart (Fig. 1).

On descriptive analysis, the two groups were nonhomogeneous for the following factors: age at surgery, hospital admission within 3 months of surgery, diagnosis, operating time, conversion to open approach, postoperative length of stay, and AL (Table 1). Notably, there was a greater statistically significant distribution regarding oncologic pathology diagnosis in the ICG group and a shorter median postoperative length of stay in the ICG group. Some of these statistical difference in distribution could reflect the low sample size of the study as regarding postoperative length of stay and age at surgery.

3.2. Anastomotic leakage

Regarding the distribution of AL at 30 days, no leaks occurred in the ICG group, and 6 leaks occurred in the no- ICG group, a statistically significant difference.

3.3. Intraoperative findings

The change in stapler line after colic resection is performed in three patients: 2 in ICGgroup (3.85 %) for revision of rectal stump for overlength with impossibility of stapler progression; in these patients good vascularization are achieved at subsequent ICG test.

3.4. Postoperative morbidity and mortality

Regarding postoperative morbidity (surgical morbidity, mortality, reintervention within 30 days, and Clavien-Dindo Score $\geq$ III), the distribution between the two groups was uniform. The results of univariate analysis for risk of AL showed no statistically significant risk factors related to the occurrence of AL (Table 2).

The ICG and no-ICG groups each had two cases of mortality within 30 days after surgery. One patient in the no-ICG group died because of multi-organ failure after AL, while the other died due to respiratory failure following the onset of postoperative pneumonia. In the ICG green group, both deaths were due to early postoperative anastomotic bleeding. One case was complicated by hemorrhagic shock requiring surgery and the by acute respiratory failure associated with SARS-CoV-2 infection in an 84-year-old multi-pathologic patient with postoperative episodes of acute kidney injury and congestive heart failure.

3.5. Anastomotic leakage management

Regarding patients with AL, five out of six patients underwent left hemicolectomy with lower mesenteric artery ligation, with only one case of AL after splenic flexure resection of the colon.

All diagnoses of ALwere based on abdominal Computed Tomography (CT) scans performed from 5 to 24 days postoperatively. Symptoms included abdominal pain with or without adynamic ileus and increased indices of inflammation, with or without enteric-like material from abdominal drainage.

Surgery was required in four of these patients with the need for laparotomic abdominal lavage; in one case, an open surgery had to be performed owing to the diffuse stercoraceous peritonitis and the patient's general condition. Two end colostomies were performed after anastomotic resection, and one protective ileostomy was performed after abdominal lavage without the need to resect the colorectal anastomosis. All cases of left hemicolectomy with lower mesenteric artery ligation with AL were end-to-end mechanical colorectal anastomoses (Table 3).

4. Discussion

The primary objective of our study was to investigate how the use of ICG can reduce the incidence of ALin patients undergoing segmental colon resection. We found the AL rate to be significantly lower in the ICG group than in the no-ICG group. Although our data appear strongly indicative of superior performance in the ICG group, it did not reach significance in univariate analysis (Table 2). The reduced rate of AL had direct clinical benefit, with a corresponding reduction in postoperative morbidity and mortality [6] but in our study despite the advantage in the low rate of AL in ICGgroup no benefit was found in postoperative morbidity between two groups and could be an interesting item in order to assess other important factor for morbidity as postoperative, anesthesiologists and medical management. Moreover, in cases of oncological pathology, no leakage allows antiblastic therapies to be performed sooner, whereas a septic state and consequent immunosuppression could worsen the oncological outcomes and increase local recurrence rates [23].

Regarding the financial impact of AL, a health economics study estimated the average adjusted patient cost to be 108 % higher for patients with ALversus those without [24].

In this context, a predictive test that helps clinicians to discriminate, stratify, and potentially correct the AL takes on primary importance. Currently, this is possible with two different tools: a preoperative angio-CT study of the vascular tree, marginal artery, and artery calcification score to identify the blood supply and help plan the type of intervention [25] and with intraoperative methods such

Table 3
Characteristics of patients with anastomotic leak.

SEX	AGE AT SURGERY (years)	GROUP	DIAGNOSIS (AND STAGING[a])	SURGICAL PROCEDURE - TECHNIQUES	FIRST SURGEON EXPERIENCE	ANASTOMOSIS	CDS°; CCI[c]	AL METHOD OF DIAGNOSIS; AL POD	AL TREATMENT	POSTOPERATIVE STAY (days)	MORTALITY
M	82	NO-ICG	DIVERTICULAR DISEASE	SIGMOIDECTOMY-LAPAROTOMY	SENIOR	MECHANICAL; COLORECTAL; E-E	IIIb; 33.7	TRANS ANAL SOLUBLE ENEMA; 17	RE-INTERVENTION: ANASTOMOSIS RESECTION AND END COLOSTOMY	10	NO
M	77	NO-ICG	SIGMOID CANCER (T3N0)	SIGMOIDECTOMY-LAPAROSCOPY[b]	SENIOR	MECHANICAL; COLO-COLIC; E-E	V; 100	ABDOMEN CT SCAN; 5	RE-INTERVENTION: ANASTOMOSIS RESECTION AND OPEN ABDOMEN	14	YES[d]
M	48	NO-ICG	SIGMOID CANCER (T1N1)	SIGMOIDECTOMY-LAPAROSCOPY	SENIOR	MECHANICAL; COLO-COLIC; E-E	IIIb &II[e]; 39.7	ABDOMEN CT SCAN; 10	CONSERVATIVE THERAPY ANTIBIOTICS	19	NO
M	46	NO-ICG	DIVERTICULAR DISEASE	SIGMOIDECTOMY-LAPAROSCOPY	JUNIOR	MECHANICAL; COLORECTAL; E-E	IIIb; 33.7	ABDOMEN CT SCAN WITH SOLUBLE RECTAL ENEMA; 24	RE-INTERVENTION: ABDOMINAL TOILETTE AND PROTECTION ILEOSTOMY	9	NO
F	76	NO-ICG	SPLENIC FLEXURE CANCER (T3N0)	SPLENIC FLEXURE RESECTION-LAPAROTOMY	SENIOR	MECHANICAL; COLO-COLIC; S-E	IIIb; 42.7	ABDOMEN CT SCAN; 9	RE-INTERVENTION: ANASTOMOSIS RESECTION AND END COLOSTOMY.	58	NO
F	82	NO-ICG	SIGMOID CANCER (T3N1b)	SIGMOIDECTOMY-LAPAROTOMY	SENIOR	MECHANICAL; COLORECTAL; E-E	I & IIIa[e]; 27.6	ABDOMEN CT SCAN;	ANTIBIOTICS THERAPY AND PERCUTANEUS DRAINAGE	33	NO

AL: anastomotic leak, CCI: comprehensive complication index, CDS: Clavien-Dindo score, E-E: end-to-end anastomosis, E-S: end-to-side anastomosis, F: female, M: male, NA: not available, POD: post-operative days, S-E: side-to-end anastomosis, S-S: side-to-side anastomosis.

[a] Staging for neoplastic disease according to TNM-AJCC 8th edition; °Reported only for surgical morbidity within 30 days.

[b] Not reported reason of conversion.

[c] Overall morbidity within 30 days including surgical site infection and medical morbidity.

[d] Death due multiorgan failure.

[e] In addition to AL, surgical site infection CDS grade I and reintervention due hemoperitoneum CDS grade IIIb occurred.

as the ICGanastomosis angiography test [26]. Many studies' [10,27] have shown great variability in the vascularity of the left colon, with a possible increase in the risk of AL in cases of segmental colon resection.

ALin segmental colon resection has not been exhaustively studied. A previous meta-analysis reported an increase in the secondary outcome of the rate of AL in transverse colon resection (OR: 0.62, 95 % CI: 0.40–0.97, $p = 0.04$) [28]. Similarly, inconclusive results were reported for AL in left hemicolectomy with high-inferior mesenteric and lower mesenteric artery ligation' [29,30] and in splenic flexure resection compared to right extended colectomy, or sub-total colectomy [31,32].

None of these studies investigated the role of the ICG anastomosis angiography test to identify AL; moreover, no study has exclusively investigated the association between the ICG anastomosis angiography test and AL in segmental colon resection only. Literature research identified eight retrospective studies including segmental colon resection and the ICGanastomosis angiography test [33–40]. These studies had a limited sample size and included a small number of patients with segmental colon resection. The cases were mixed and included patients who underwent colon and anterior rectal resection. Four of these studies identified a significant reduction in AL in the descriptive analysis [33–35] or after propensity score matching [36].

Most reports of significantly decreased leakage involved patients who underwent anterior rectal resection, [33,35,36]. However, Impelizzeri et al. [34] reported that four of six cases of AL occurred in patients who had undergone sigmoidectomy without ICG; however, the surgical technique was poorly described, and the vascular level was not reported. The same sigmoidectomy procedure was reported by Yanagita et al. [36], but this report also described the surgical technique poorly and did not report the AL rate in colon surgery.

Furthermore Tsang et al. [41] in 2020 in a prospective study compared 62 patients in ICG group vs 69 in no-ICG group evaluating the protective role of ICG perfusion on AL failed to reach statistical meaning. Despite the similarity of sample size the study included different type of surgical procedure with different AL risk low anterior resection, right hemicolectomy and left hemicolectomy. In addition no segmental resection were reported and no extended definition of techniques were reported but the authors emphasize the possible misunderstanding in the identification of perfused area due the absence of quantification.

Watanabe et al. (2021) demonstrated that the use of near-infrared observation with indocyanine green (ICG) can significantly reduce the risk of anastomotic leakage in stapled side-to-side colonic anastomoses. In a multicenter study on patients with colon cancer, the leakage rate was reduced to 0.8 % in the ICG group compared to 3.5 % in the no-ICG group, emphasizing the importance of ICG in intraoperative perfusion assessment [42]. Similarly, Somashekhar et al. (2021) explored the use of ICG during sigmoidectomies, where a high inferior mesenteric artery ligation technique was employed [43]. In contrast, our study utilized a low inferior mesenteric artery ligation technique, which could influence the perfusion outcomes and anastomotic integrity. Despite the difference in ligation techniques, both studies highlight the potential benefits of ICG in reducing anastomotic leakage and improving clinical outcomes.

ALin our study (Table 3) occurred in five patients who underwent left colectomy with lower mesenteric artery ligation and one patient who underwent splenic flexure resection, all in the no-ICG group. These data agree with the reports of AL in patients who underwent segmental colic artery resection and indicate that preserving the left colic artery may not ensure sufficient vascularization [10,29,44]. The ICGanastomosis angiography test could ensure effective vascularization and lead to a better understanding of the vasculature. As mentioned previously, a comparison of high-inferior mesenteric artery ligation vs. lower mesenteric artery ligation did not show either technique to be more favorable, but the ICG-anastomosis angiography test was not used [29].

Meta-analyses have shown reduced AL with the use of the ICG anastomosis angiography test in oncologic pathology [45]and colorectal pathology in general [46], with more reliable results reported for anterior rectal resection [8]. However, these meta-analyses have limitations, as RCTs for colon surgery are not performed, and the primary studies included mixed samples of colon surgery and anterior rectal resection, with benign and oncological indications [45].

Finally, the low statistical significance of the studies could be explained by factors intrinsic to the ICG method. A two-round-consensus using the Delphi method among experts from the International Society for Fluorescence Guided Surgery'[47,48] identified critical points regarding the use of ICGin colorectal surgery. These included the optimal dose, concentration, ICG quantification of anastomotic stump perfusion, timing of drug administration, and exact timing of indocyanine green repetition after further resection. Further research is needed in this area, as the current literature shows wide variability on these points.

Postoperative morbidity and mortality rates were analyzed as secondary outcomes; however, no significant differences between the two groups were found, in agreement with available meta-analyses,[8,45,46]. The only item that showed a different distribution favoring the ICG anastomosis angiography test group was the shorter postoperative length of stay, a finding that suggests control with ICGfavors earlier discharge, as the clinician has more confidence at discharge. This finding must be contextualized with the absence of enhanced recovery after surgery in our center; moreover, our colon surgery protocol remains unchanged. Specifically, this protocol provides for discharge starting from day 6 based on the patient's clinical condition. The effect of the ICG anastomosis angiography test on postoperative hospitalization days has been poorly investigated in the literature. Different statistically significant distributions of postoperative stay were reported in two prior studies [34,40], with p values of <0.001 and 0.004, respectively. The only study that aimed to investigate theICG anastomosis angiography test as an item within the enhanced recovery after surgery protocol did not document statistically significant differences in postoperative hospitalization [35].

ICG fluorescence imaging has demonstrated considerable potential advantages in colorectal surgery by enhancing the precision of surgical procedures, particularly in lymphadenectomy for left-sided colorectal cancer. Although the results are preliminary, they provide promising evidence that ICG-guided techniques could improve surgical outcomes and reduce complications, warranting further investigation in larger, more comprehensive studies [49].

4.1. Study limitations

Our study has several limitations, including its observational, single-center design and small sample size. To increase the sample size, the inclusion criteria were extended to several types of colon resection surgeries sharing the same anatomical region with wide variability in the marginal vascularization arcade, encompassing both benign and malignant pathologies. This could have created a selection bias related to different risks of leakage according to surgery and indication [1,4]. Another potential bias results from fewer benign indications owing to the SARS-CoV-2 pandemic in 2020 and limited operating room space due to restrictions by the anesthesiology team.

Despite these limitations, our study is the first to investigate the effect of the ICGanastomosis angiography test in preventing ALin left segmental colon resection using a homogeneous patient sample. Univariate regression found no association with decreasedAL. We did identify an absence of ALin the ICG anastomosis angiography test group in segmental colon resection, a procedure carries a risk of inadequate anastomotic blood due to high vascular artery variability [25].

Our findings provide useful information for developing multicenter observational studies on ICG. An adequate sample size should be used, and the study should assess individual intervention type, indications, and setting to establish evidence of an association between ALand the ICG anastomosis angiography test. Future research could also investigate the heterogeneity between indocyanine green tools in order to clarify quantitative confounding factors and the fluorescence threshold to establish good control of the anastomosis blood supply.

In conclusion although there is no significant evidence on univariate analysis, the encouraging statistically significant difference in the distribution of AL in favor of the ICG anastomosis angiography test group can direct future well-designed studies to clarify the true implications of the indocyanine green anastomosis angiography test on AL.

CRediT authorship contribution statement

Andrea Romboli: Writing – review & editing, Writing – original draft, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Elena Orlandi:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **Chiara Citterio:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation. **Filippo Banchini:** Writing – review & editing, Writing – original draft, Conceptualization. **Marta Ribolla:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Gerardo Palmieri:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Mario Giuffrida:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Enrico Luzietti:** Writing – review & editing, Writing – original draft, Methodology. **Patrizio Capelli:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Data curation.

Consensus statement and institutional review board

All participants have given informed consent to participate in the study after that our local ethics committee have authorized the research protocol.

Meeting presentation

None.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e39730.

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