Research Square

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Multimodal Fluorescent Laparoscopy Improves Anastomosis Safety by Visualizing Left Colic Artery Preservation and Lymph Node Dissection in Ultra-low Rectal Cancer

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Abstract

Background

Anastomotic leakage (AL) remains a major complication after intersphincteric resection (ISR) for ultra-low rectal cancer. Multimodal fluorescence laparoscopy (MFL) integrates perfusion and lymphatic visualization and may provide additional intraoperative information.

Methods

We retrospectively analyzed patients undergoing ISR for ultra-low rectal adenocarcinoma between January 2012 and July 2023. Patients were grouped according to MFL use and compared using 1:2 propensity score matching (PSM). The primary endpoint was AL within 6 months. Secondary outcomes included left colic artery (LCA) preservation, lymph node (LN) retrieval, blood loss, and postoperative recovery.

Results

After PSM, 390 patients were analyzed (MFL, n = 130; non-MFL, n = 260). MFL was associated with lower blood loss (P = 0.004), greater LN retrieval, and faster postoperative recovery. The proportions of patients with ≥ 12 and ≥ 25 retrieved LNs were higher in the MFL group (87.7% vs. 77.3%, P = 0.014; 30.0% vs. 11.2%, P < 0.001). LCA preservation was comparable after matching (76.9% vs. 75.0%, P = 1.000). AL occurred in 3.1% and 10.4% of patients, respectively (P = 0.012), while grade A–B AL occurred in 2.3% and 7.3% (P = 0.045).

Conclusions

MFL use was associated with favorable perioperative, lymph node retrieval, and AL outcomes after ISR. These findings support further prospective evaluation. The present analysis shares part of its cohort with our previous study and should therefore be interpreted as complementary rather than an independent validation.

Introduction

Anastomotic leakage (AL) remains a major complication after intersphincteric resection (ISR) for ultra-low rectal cancer, with reported incidence rates of 5%–20% [1, 2]. AL is associated with increased postoperative morbidity, prolonged hospitalization, impaired anorectal function, and, in severe cases, life-threatening complications[2, 3]. Adequate blood supply to the anastomotic site is an important consideration in reducing ischemic complications, while preservation of the left colic artery (LCA) may be technically challenging because of anatomical variation and difficulties in intraoperative identification[4–7].. At the same time, adequate lymph node (LN) retrieval is essential for accurate oncologic staging and treatment planning. However, dissection around the mesenteric vessels requires a balance between adequate lymphadenectomy and preservation of critical vascular structures[8].

Fluorescence-guided laparoscopy using indocyanine green (ICG) has increasingly been applied to colorectal surgery to provide real-time visualization of vascular perfusion and lymphatic drainage[9, 10].. These applications may provide complementary information during ISR, where both vascular preservation and adequate lymph node retrieval are technically important. However, conventional fluorescence-guided approaches have often focused predominantly on a single imaging target, such as anastomotic perfusion or lymphatic mapping. A multimodal approach may therefore provide additional intraoperative information by integrating vascular and lymphatic visualization within the same surgical procedure.

Multimodal fluorescence laparoscopy (MFL) combines fluorescence-based visualization of vascular and lymphatic structures with conventional laparoscopic imaging. In the setting of ISR, MFL may facilitate identification of mesenteric vascular anatomy, assessment of perfusion, and visualization of lymphatic drainage pathways. These features may assist intraoperative decision-making regarding vascular preservation and lymph node dissection. Importantly, however, fluorescence visualization represents an imaging aid rather than a direct assessment of lymph node metastasis or oncologic completeness, and its clinical value should be evaluated based on patient-level surgical and postoperative outcomes.

Our group previously reported an association between fluorescence-guided surgery and a lower incidence of AL after ISR, including analyses stratified by body mass index[11]. The present study was developed to examine additional clinical outcomes associated with the broader application of MFL, particularly LCA preservation, LN retrieval, postoperative recovery, and AL. Because the present analysis was derived from a related institutional cohort and includes patients overlapping with our previous report, the findings should be interpreted as complementary rather than as an independent validation study.

Therefore, we conducted a propensity score-matched cohort study to evaluate the associations of MFL use with AL and perioperative outcomes in patients undergoing ISR for ultra-low rectal cancer. We specifically assessed LCA preservation, LN retrieval, blood loss, postoperative recovery, and AL, with additional analyses according to LCA preservation and body mass index.

Materials and Methods

Study Design and Patient Enrollment

This retrospective cohort study included consecutive patients with ultra-low rectal adenocarcinoma who underwent laparoscopic intersphincteric resection (ISR) between January 2012 and July 2023. Patients were eligible if the tumor was histologically confirmed as adenocarcinoma and located ≤ 5 cm from the anal verge. Patients with non-adenocarcinomatous malignancies, combined organ resection, or conversion to abdominoperineal resection were excluded. Decisions regarding neoadjuvant chemoradiotherapy (nCRT) were made by a multidisciplinary team according to institutional protocols. For patients receiving nCRT, long-course fluorouracil-based chemotherapy with 45–54 Gy radiotherapy was generally used, followed by restaging MRI approximately 8–12 weeks after treatment.

The study was approved by the institutional ethics committee (Ethics approval No. NCC2022C-790) and conducted in accordance with the Declaration of Helsinki and relevant regulations. Written informed consent was obtained from all participants.

Because the present analysis was derived from a cohort related to our previous study of fluorescence-guided surgery in ultra-low rectal cancer [11], overlapping patients may be present. The previous study primarily evaluated AL with BMI-stratified analyses, whereas the present analysis additionally examined LCA preservation, LN retrieval, perioperative recovery, and the association between MFL use and these outcomes.

Near-Infrared Imaging and MFL

MFL was performed using a 4K near-infrared laparoscopic imaging system (DPM-ENDOCAM-03 and DPM-LIGHT-03; Dipu Medical Technology, Zhuhai, China), with an excitation wavelength of 785 ± 5 nm and fluorescence detection at 830–900 nm. The system allowed switching among white-light, monochrome fluorescence, and merged pseudo-color modes. Image-enhancement algorithms were incorporated into the imaging platform.

The principles of fluorescence-guided perfusion assessment and lymphatic visualization have been described previously [11]. In the present study, MFL was used intraoperatively to visualize mesenteric vascular structures, bowel perfusion, and lymphatic drainage during ISR.

Surgical Procedure

All procedures were performed or directly supervised by experienced colorectal surgeons with > 10 years of surgical experience and > 100 ISR procedures. Standard TME was performed with preservation of the pelvic autonomic nerves and neurovascular bundles. The intersphincteric plane was dissected according to the planned extent of ISR, followed by intracorporeal distal rectal transection and hand-sewn coloanal anastomosis. Frozen-section examination was performed when the distal margin was < 1 cm or when oncological uncertainty was present.

In the MFL group, ICG was administered intravenously according to the established institutional protocol. Fluorescence imaging was used to assess mesenteric perfusion and identify vascular structures, including the inferior mesenteric artery and LCA. Bowel transection was performed at a fluorescence-defined perfusion boundary when appropriate. After anastomosis, repeat ICG imaging was used to assess anastomotic perfusion. In the control group, bowel viability was assessed by conventional visual inspection. Intraoperative leak testing was performed using an underwater air-leak test; in the MFL group, fluorescence assessment was additionally available.

The detailed ICG administration and fluorescence imaging protocol has been described previously [11] and was applied consistently during the study period.

Data Collection and Outcomes

Demographic and clinical variables included age, sex, body mass index (BMI), diabetes, nCRT, tumor distance from the anal verge, tumor size, histological grade, pathological stage, hemoglobin, albumin, and CEA levels. Perioperative variables included operative time, estimated blood loss, LCA preservation, anastomotic level, diverting ileostomy, postoperative complications, lymph node (LN) retrieval, and length of hospital stay.

The primary endpoint was AL occurring within 6 months after surgery. Secondary outcomes included LCA preservation, LN retrieval, estimated blood loss, postoperative gastrointestinal recovery, postoperative complications, and length of hospital stay. AL was diagnosed according to clinical, radiological, endoscopic, or surgical findings during follow-up.

Patients were routinely followed every 3 months during the first 2 years, every 6 months during years 3–5, and annually thereafter.

Statistical Analysis

Categorical variables were compared using the chi-square or Fisher's exact test, and continuous variables were compared using the appropriate parametric or nonparametric tests. Propensity score matching (PSM) was performed at a 1:2 ratio using nearest-neighbor matching with a caliper of 0.2 standard deviations of the logit-transformed propensity score. The matching variables included age, sex, BMI, tumor size and location, pathological stage, preoperative therapy, anastomotic height, LCA preservation, and diverting ileostomy status, consistent with the prespecified analysis.

After matching, standardized mean differences (SMDs) were used to assess covariate balance. Logistic regression was used to evaluate factors associated with AL, with odds ratios (ORs) and 95% confidence intervals (CIs) reported. Variables with $P < 0.10$ in univariable analysis were considered for multivariable analysis, and backward stepwise elimination was applied. All analyses were performed using R version 4.3.3 and SPSS version 25.0. A two-sided $P < 0.05$ was considered statistically significant.

Results

Baseline Characteristics Before and After Propensity Score Matching

A total of 534 patients with ultra-low rectal cancer undergoing laparoscopic intersphincteric resection were included, comprising 404 patients in the non-MFL group and 130 in the MFL group. After 1:2 propensity score matching (PSM), 260 non-MFL patients were matched to the 130 MFL patients. Baseline characteristics before and after matching are presented in Table 1.

Table 1
Patient demographic characteristics and surgical procedures before and after the PSM

Clinical variables	Before PSM				After PSM			
	Non-MFL group (n = 404)	MFL group (n = 404)	P	SMD	Non-MFL group (n = 260)	MFL group (n = 130)	P	SMD
Age, yr *	59.81(11.27)	60.71(9.90)	0.419	0.084	59.88(10.95)	60.71(9.90)	0.467	0.079
< 60	186 (46.0)	52 (40.0)	0.270	0.122	118 (45.4)	52 (40.0)	0.367	
≥ 60	218 (54.0)	78 (60.0)			142 (54.6)	78 (60.0)		0.109
Sex			0.093	0.179			0.203	0.148
Male	253 (62.6)	70 (53.8)			159 (61.2)	70 (53.8)		
Female	151 (37.4)	60 (46.2)			101 (38.8)	60 (46.2)		
BMI (kg/m^2) *	23.76 ± 3.15	23.87 ± 3.00	0.729	0.035	23.88(3.06)	23.87(3.00)	0.983	0.002
< 25	255 (63.1)	80 (61.5)	0.826	0.033	160 (61.5)	80 (61.5)	1.000	< 0.001
≥ 25	149 (36.9)	50 (38.5)			100 (38.5)	50 (38.5)		
Tumor status			0.101	0.178			0.484	0.088
T 1–2	178 (44.1)	46 (35.4)			103 (39.6)	46 (35.4)		
T 3–4	226 (55.9)	84 (64.6)			157 (60.4)	84 (64.6)		
Nodal stage			0.269	0.121			0.395	0.103
N0	263 (65.1)	77 (59.2)			167 (64.2)	77 (59.2)		
N+	141 (34.9)	53 (40.8)			93 (35.8)	53 (40.8)		
Smoking			0.077	0.207			0.107	0.182
No	347 (85.9)	120 (92.3)			224 (86.2)	120 (92.3)		
Yes	57 (14.1)	10 (7.7)			36 (13.8)	10 (7.7)		
Drinking			0.943	0.013			0.801	0.022
No	312 (77.2)	100 (76.9)			197 (75.8)	100 (76.9)		
Yes	92 (22.8)	30 (23.1)			63 (24.2)	30 (11.5)		
Diabetes			0.111	0.186			0.169	0.172
No	346 (85.6)	119 (91.5)			224 (86.2)	119 (91.5)		
Yes	58 (14.4)	11 (8.5)			36 (13.8)	11 (8.5)		
Preoperative Hb (g/L)			0.077	0.207			0.107	0.105
≥ 120	347 (85.9)	120 (92.3)			224 (86.2)	120 (92.3)		
<120	57 (14.1)	10 (7.7)			36 (13.8)	10 (7.7)		
Preoperative CEA (g/L)			0.538	0.065			0.456	0.088
≤ 5	285 (70.5)	88 (67.7)			187	88		
>5	119 (29.5)	42 (32.3)			73	42		
Preoperative CA199 (kU/L)			1.000	0.012			1.000	< 0.001
≤ 37	365 (90.3)	117 (90.0)			234 (90.0)	117 (90.0)		
>37	39 (9.7)	13 (10.0)			26 (10.0)	13 (10.0)		
Tumor lower margin to anus (cm) *	3.97(0.67)	3.79(0.77)	0.021	0.124	3.94(0.68)	3.79(0.77)	0.071	0.182
Anastomosis to anus (cm) *	2.23(0.63)	2.18(0.92)	0.597	0.059	2.29(0.68)	2.18(0.92)	0.245	0.124
Tumor size (mm) *	38.13(15.63)	39.11(15.51)	0.535	0.062	38.65(16.25)	39.11(15.51)	0.793	0.063
≤ 35	215 (53.2)	56 (43.1)	0.056	0.204	137 (52.7)	56 (43.1)	0.092	0.193

Clinical variables	Before PSM				After PSM			
	Non-MFL group (n = 404)	MFL group (n = 404)	P	SMD	Non-MFL group (n = 260)	MFL group (n = 130)	P	SMD
> 35	189 (46.8)	74 (56.9)			123 (47.3)	74 (56.9)		
LCA preservation			< 0.001	0.620			1.000	< 0.001
No	195 (48.3)	100 (76.9)			65 (25.0)	30 (23.1)		
Yes	209 (51.7)	30 (23.1)			195 (75.0)	100 (76.9)		
Diverting ileostomy			0.768	0.043			0.508	0.086
No	68 (16.8)	24 (18.5)			57 (21.9)	24 (18.5)		
Yes	336 (83.2)	106 (81.5)			203 (78.1)	106 (81.5)		
nCRT			0.103	0.172			0.396	0.106
No	357 (88.4)	107 (82.3)			224 (86.2)	107 (82.3)		
Yes	47 (11.6)	23 (17.7)			36 (13.8)	23 (17.7)		

Values in parentheses are percentages unless indicated otherwise; value in *mean (standard deviation)

SMD standardized mean differences; MFL Multimodal fuorescent laparoscopy, BMI body mass index; AL Anastomotic leak; LCA Left colic artery; nCRT neoadjuvant chemoradiotherapy.

Before matching, LCA preservation was more frequent in the MFL group than in the non-MFL group (76.9% vs. 51.7%, P < 0.001; SMD = 0.620). The groups also differed in the distribution of tumor size (≤ 35 mm: 53.2% vs. 43.1%, P = 0.056; SMD = 0.204) and T stage (T1–2: 44.1% vs. 35.4%, P = 0.101; SMD = 0.178).

After PSM, the measured baseline characteristics were substantially balanced. Age was 59.88 ± 10.95 years in the non-MFL group and 60.71 ± 9.90 years in the MFL group (P = 0.467; SMD = 0.079), and BMI was 23.88 ± 3.06 versus 23.87 ± 3.00 kg/m² (P = 0.983; SMD = 0.002). Tumor size was also comparable (38.65 ± 16.25 vs. 39.11 ± 15.51 mm, P = 0.793; SMD = 0.063), as were T stage (T3–4: 60.4% vs. 64.6%, P = 0.484; SMD = 0.088) and nodal positivity (35.8% vs. 40.8%, P = 0.395; SMD = 0.103).

LCA preservation was similar between the matched groups (76.9% vs. 75.0%, P = 1.000). Diverting ileostomy (81.5% vs. 78.1%, P = 0.508; SMD = 0.086) and nCRT (17.7% vs. 13.8%, P = 0.396; SMD = 0.106) were also comparable after matching.

Factors Associated With Anastomotic Leakage

Univariable and multivariable logistic regression analyses were performed to evaluate factors associated with AL (Table 2). In univariable analysis, male sex (P = 0.002), higher BMI (P = 0.034), nCRT (P < 0.001), lower tumor height (P = 0.040), and MFL use (P = 0.012) were associated with AL. Protective stoma formation showed a trend toward an association with lower AL risk (P = 0.080). LCA preservation was also associated with a lower incidence of AL in the univariable analysis (P = 0.089).

Table 2
Simple and multivariable linear regression analysis of anastomotic leakage

Variable	Univariate analysis		Multivariate analysis	
	Beta (95% CI)	***P* value**	**Beta (95% CI)**	***P* value**
Sex (Male vs. Female)	0.135 (0.029, 0.125)	0.002	0.110 (0.015, 0.109)	0.010
Age (years)	-0.031 (-0.003, 0.001)	0.474		
BMI (kg/m^2)	0.092 (0.001, 0.016)	0.034	0.081 (0.001, 0.015)	0.049
Diabetes (Yes vs. No)	0.044 (-0.034, 0.107)	0.311		
nCRT (Yes vs. No)	0.222 (0.114, 0.251)	< 0.001	0.230 (0.122, 0.257)	< 0.001
LCA retained (Yes vs. No)	-0.066 (– 0.084, 0.011)	0.089	-0.049 (-0.062, -0.003)	0.036
Protective stoma (Yes vs. No)	-0.076 (-0.118, 0.007)	0.080	-0.170 (-0.188, -0.062)	< 0.001
TNM stage	0.011 (-0.042, 0.055)	0.796		
Maximal tumor size (mm)	0.002 (-0.001, 0.002)	0.969		
Height of tumor from the anal verge (cm)	-0.089 (-0.069, -0.002)	0.040	-0.143 (-0.091, -0.023)	0.001
MFL (Yes vs. No)	-0.109 (-0.126, -0.016)	0.012	-0.119 (-0.131, -0.022)	0.006

In multivariable analysis, male sex (P = 0.010), higher BMI (P = 0.049), and nCRT (P < 0.001) remained associated with a higher likelihood of AL. Lower tumor height (P = 0.001), diverting stoma formation (P < 0.001), and MFL use (P = 0.006) were associated with a lower likelihood of AL. LCA preservation remained statistically associated with AL in the multivariable model (P = 0.036). The corresponding ORs and 95% CIs are presented in Table 2.

Anastomotic Leakage After Propensity Score Matching

After PSM, 390 patients were included, comprising 260 in the non-MFL group and 130 in the MFL group (Table 3). AL occurred in 3.1% of patients in the MFL group compared with 10.4% in the non-MFL group (P = 0.012). Grade A–B AL occurred in 2.3% and 7.3% of patients, respectively (P = 0.045), whereas grade C AL occurred in 0.8% and 3.1%, respectively (P = 0.283).

Table 3
Comparison of AL rate after the PSM

All Patients	All patients	Non-MFL group	MFL group	P value
Patients number	390	260	130	
AL (n, %)				0.012
No	359 (92.1)	233 (89.6)	126 (96.9)	
Yes	31 (7.9)	27 (10.4)	4 (3.1)	
AL grade (n, %)				
A-B	22 (5.6)	19 (7.3)	3 (2.3)	0.045
C	9 (2.3)	8 (3.1)	1 (0.8)	0.283
LCA resection				
Patients number	95	65	30	
AL (n, %)				0.173
No	84 (88.4)	55 (84.6)	29 (96.7)	
Yes	11 (11.6)	10 (15.4)	1 (3.3)	
AL grade (n, %)				
A-B	7 (7.4)	6 (9.2)	1 (3.3)	0.299
C	4 (4.2)	4 (6.2)	0 (0.0)	0.487
LCA preservation				
Patients number	295	195	100	
AL (n, %)				0.064
No	275 (93.2)	178 (91.3)	97 (97.0)	
Yes	20 (6.8)	17 (8.7)	3 (3.0)	
AL grade (n, %)				
A-B	15 (5.1)	13 (6.7)	2 (2.0)	0.429
C	5 (1.7)	4 (2.1)	1 (1.0)	0.391

Values in parentheses are percentages unless indicated otherwise;

Value in *mean (standard deviation)

MFL Multimodal fuorescent laparoscopy, LN lymph node, BMI body mass index; AL Anastomotic leak; SSAL Severe symptomatic anastomotic leaks; nCRT neoadjuvant chemoradiotherapy.

Among the 95 patients who underwent LCA resection, the overall AL rate was 11.6%. AL occurred in 3.3% of patients in the MFL group and 15.4% in the non-MFL group (P = 0.173). The differences in grade A–B and grade C AL were not statistically significant (P = 0.299 and P = 0.487, respectively).

Among the 295 patients with LCA preservation, AL occurred in 3.0% of patients in the MFL group and 8.7% in the non-MFL group (P = 0.064). Grade A–B AL occurred in 2.0% and 6.7%, respectively, while grade C AL occurred in 1.0% and 2.1%, respectively. Neither comparison reached statistical significance.

Operative Findings and Short-Term Outcomes

Operative findings and short-term outcomes after PSM are summarized in Table 4. Operative time did not differ significantly between the MFL and non-MFL groups in either the overall cohort or the LCA-specific subgroups (P > 0.05).

Table 4
Operative findings and short-term outcomes after PSM

Characteristics	All patients (n = 390)			LCA resection (n = 95)			LCA preservation (n = 295)		
	Non-MFL (n = 260)	MFL (n = 130)	P	Non-MFL (n = 65)	MFL (n = 30)	P	Non-MFL (n = 195)	MFL (n = 100)	P
Operative Findings									
Operation time (min) *	181.71(64.09)	189.62(65.35)	0.258	185.81(74.15)	195.34(86.83)	0.588	180.36(60.58)	187.93(57.95)	0.307
Blood loss (ml)*	65.21(73.02)	45.04(59.16)	0.004	69.54(73.39)	60.50(92.91)	0.610	63.77(73.02)	40.40(44.01)	0.001
Total LNs*	16.47(7.37)	21.25(11.45)	< 0.001	18.52(8.75)	17.47(8.69)	0.585	15.78(6.74)	22.39(11.96)	< 0.001
Retrieved LNs ≥ 12	201(77.3%)	114(87.7)	0.014	51(78.5%)	23(76.7%)	< 0.001	150(76.9%)	91(91.0%)	0.003
Retrieved LNs ≥ 25	29(11.2%)	39(30.0)	< 0.001	11(16.9%)	7(23.3%)	0.459	18(9.2%)	32(32.0%)	< 0.001
Complications (Excluding AL)									
Intraoperative bleeding	8 (3.1%)	3 (2.3%)	0.672	2 (3.1%)	1 (3.3%)	0.963	6 (3.1%)	2 (2.0%)	0.552
Ileus incisional	11 (4.2%)	5 (3.8%)	0.887	3 (4.6%)	1 (3.3%)	0.800	8 (4.1%)	4 (4.0%)	0.978
Infection	14 (5.3%)	5 (3.8%)	0.487	4 (6.2%)	2 (6.7%)	0.936	10 (5.1%)	3 (3.0%)	0.438
Postoperative Recovery									
Gas passing (days)*	2.9 (0.8)	2.6 (0.7)	0.008	3.0 (0.9)	2.8 (0.8)	0.368	2.9 (0.8)	2.5 (0.6)	0.004
Soft diet (days)*	4.2 (1.3)	3.8 (1.2)	0.002	4.5 (1.4)	4.1 (1.3)	0.163	4.1 (1.2)	3.7 (1.1)	0.007
Hospital stay (days)*	10.7 (3.8)	9.5 (3.1)	0.012	11.4 (4.0)	10.3 (3.6)	0.253	10.5 (3.7)	9.1 (2.9)	0.006

Values in parentheses are percentages unless indicated otherwise; value is *mean (standard deviation); AL Anastomotic leak

MFL Multimodal fuorescent laparoscopy; BMI body mass index; AL Anastomotic leak; nCRT neoadjuvant chemoradiotherapy.

Estimated blood loss was lower in the MFL group than in the non-MFL group in the overall cohort (P = 0.004) and among patients with LCA preservation (P = 0.001). No significant differences were observed in other reported postoperative complications, including ileus and infection. In the overall matched cohort, intraoperative bleeding occurred in 8 (3.1%) non-MFL patients and 3 (2.3%) MFL patients (P = 0.672), ileus occurred in 11 (4.2%) and 5 (3.8%) patients (P = 0.887), and infection occurred in 14 (5.3%) and 5 (3.8%) patients (P = 0.487).

The MFL group had earlier passage of gas than the non-MFL group (P = 0.008), as well as earlier initiation of a soft diet (P = 0.002) and a shorter postoperative hospital stay (P = 0.012). Similar differences were observed among patients with LCA preservation, with earlier passage of gas (P = 0.004), earlier soft-diet initiation (P = 0.007), and shorter hospitalization (P = 0.006).

Lymph Node Retrieval

The number of retrieved LNs was higher in the MFL group than in the non-MFL group in the overall matched cohort and in the LCA-preservation subgroup (P < 0.001 for both comparisons). In the overall cohort, 87.7% of patients in the MFL group and 77.3% in the non-MFL group had ≥ 12 retrieved LNs (P = 0.014), while 30.0% and 11.2%, respectively, had ≥ 25 retrieved LNs (P < 0.001).

Discussion

In this propensity score-matched cohort study, MFL use was associated with several favorable perioperative outcomes in patients undergoing ISR for ultra-low rectal cancer. After matching, patients in the MFL group had lower estimated blood loss, greater LN retrieval, earlier postoperative gastrointestinal recovery, and a lower incidence of AL than those in the non-MFL group. LCA preservation was comparable between groups after matching. These findings suggest that MFL may provide complementary intraoperative information for vascular and lymphatic assessment during ISR, although the retrospective design does not permit causal inference.

AL remains a clinically important complication after rectal cancer surgery. Adequate perfusion of the anastomotic bowel segment is considered an important factor in anastomotic healing, and ICG fluorescence angiography has been increasingly used to provide real-time information on tissue perfusion [12–15]. LCA preservation may contribute to maintaining colonic blood supply, although its relationship with AL is influenced by multiple anatomical,

technical, and patient-related factors [16, 17]. In the present cohort, LCA preservation was substantially more frequent in the MFL group before matching. After matching, however, LCA preservation was similar between groups (76.9% vs. 75.0%, P = 1.000). Therefore, the present data do not establish that MFL increases the likelihood of LCA preservation. Rather, they suggest that the use of fluorescence imaging can provide additional visualization of mesenteric vascular anatomy during surgical dissection.

The association between MFL and AL remained evident after matching, with AL occurring in 3.1% of MFL patients compared with 10.4% of non-MFL patients (P = 0.012). The difference was also observed for grade A–B AL. Among patients with LCA preservation, AL was numerically lower in the MFL group (3.0% vs. 8.7%), although the difference did not reach statistical significance (P = 0.064). Among patients undergoing LCA resection, AL was also numerically lower with MFL (3.3% vs. 15.4%), but the sample size and number of events were limited. These subgroup findings should therefore be interpreted as exploratory. Possible explanations include the additional information provided by fluorescence-based perfusion assessment, but residual confounding and selection effects cannot be excluded.

The present findings are consistent with previous studies reporting an association between fluorescence-guided perfusion assessment and postoperative anastomotic outcomes[18, 19]. ICG fluorescence can provide visual information that is complementary to conventional assessment of bowel color and may help surgeons identify areas with relatively inadequate perfusion. However, fluorescence intensity is affected by multiple technical and physiological factors, and visual interpretation remains partly subjective. Quantitative fluorescence analysis and standardized perfusion thresholds may therefore improve reproducibility in future clinical applications.

MFL may also provide information relevant to lymphatic dissection. In the matched cohort, the MFL group had a higher number of retrieved LNs, including a greater proportion of patients with ≥ 12 and ≥ 25 retrieved LNs. These findings suggest an association between MFL use and LN retrieval, but they should not be interpreted as evidence that MFL improves oncologic clearance or lymph node metastasis detection. ICG fluorescence primarily visualizes lymphatic drainage pathways and does not directly determine whether an individual LN contains metastatic disease. The higher LN yield may reflect improved visualization of lymphatic pathways, differences in surgical dissection, or other unmeasured factors. Whether fluorescence-guided lymphatic visualization translates into improved staging accuracy or long-term oncologic outcomes requires prospective evaluation.

Our findings should also be considered in the context of our previous study published in *Updates in Surgery*[11]. That study evaluated fluorescence-guided surgery in a related cohort of patients with ultra-low rectal cancer and primarily focused on AL and BMI-stratified outcomes. The present analysis was conducted in a related institutional cohort during an overlapping study period, and some patients may therefore overlap between the two studies. The current study should not be regarded as an independent replication. Instead, it provides a complementary analysis addressing additional outcomes, particularly LCA preservation, LN retrieval, blood loss, and postoperative recovery. We have revised the manuscript to make this relationship explicit and to minimize unnecessary textual overlap with the previous publication.

Several limitations should be acknowledged. First, the retrospective design introduces the possibility of selection bias and residual confounding despite PSM[20, 21]. Second, the study was conducted within a related institutional cohort, and overlap with the previously published cohort limits its interpretation as an independent validation study. Third, subgroup analyses according to LCA preservation were limited by sample size and the small number of AL events. Fourth, fluorescence assessment was based largely on intraoperative visual interpretation, which may introduce interobserver variability. Finally, the present study focused primarily on perioperative and short-term outcomes; further studies are required to determine whether MFL is associated with long-term oncologic outcomes, anorectal function, quality of life, and other patient-reported outcomes.

Conclusions

In patients undergoing ISR for ultra-low rectal cancer, MFL use was associated with lower blood loss, greater LN retrieval, faster postoperative recovery, and a lower incidence of AL after propensity score matching. LCA preservation was comparable between groups after matching. These findings suggest that MFL may provide complementary information for intraoperative vascular, perfusion, and lymphatic assessment. Given the retrospective design and overlap with a previous cohort, these results should be interpreted cautiously and require confirmation in prospective, independently evaluated studies.

Abbreviations

AL
anastomotic leakage
BMI
body mass index
CEA
carcinoembryonic antigen
CI
confidence interval
ICG
indocyanine green
IMA
inferior mesenteric artery
ISR

intersphincteric resection
LCA
left colic artery
LN
lymph node
LND
lymph node dissection
MFL
multimodal fluorescence laparoscopy
NIR
near-infrared
nCRT
neoadjuvant chemoradiotherapy
OR
odds ratio
PSM
propensity score matching
SMD
standardized mean difference
TME
total mesorectal excision.

Declarations

Ethics approval and consent to participate

This study was approved by the National GCP Center for Anticancer Drugs,The Independent Ethics Committee (Ethics approval No. NCC2022C-790). The study was conducted in accordance with the principles of the Declaration of Helsinki and relevant institutional and national ethical guidelines and regulations. Written informed consent to participate was obtained from all participants.

Consent for publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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Author Contribution

Wenlong Qiu: Conceptualization, Methodology, Formal analysis, investigation, Writing - original draft. Gang Hu: Resources, Methodology, Data curation, Writing - review & editing, Project administration. Jianqiang Tang: Conceptualization, Methodology, Writing - review & editing, Supervision, Project administration.# Wenlong Qiu and Gang Hu contributed equally to this work.All authors have approved the final version of the article.

Acknowledgements

Not applicable.

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available because of confidentiality requirements and restrictions related to participant privacy, but are available from the corresponding author on reasonable request.

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Figures

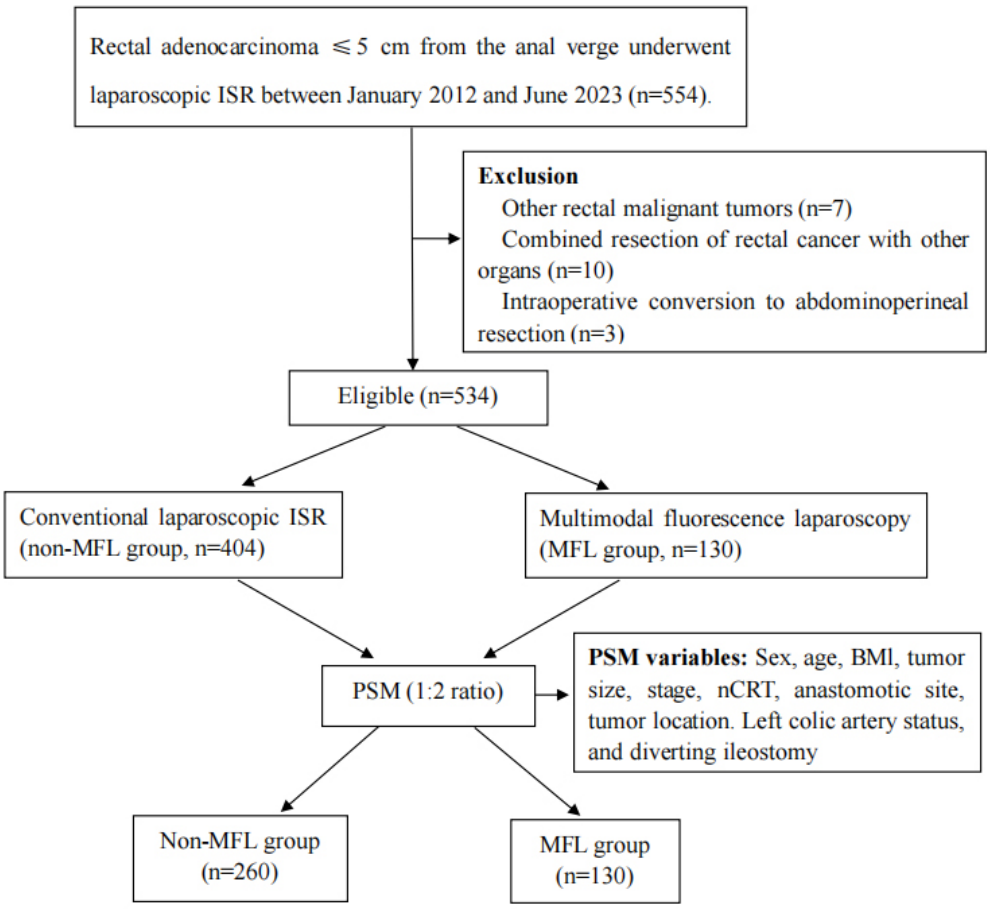


Figure 1

Flowchart of this study.

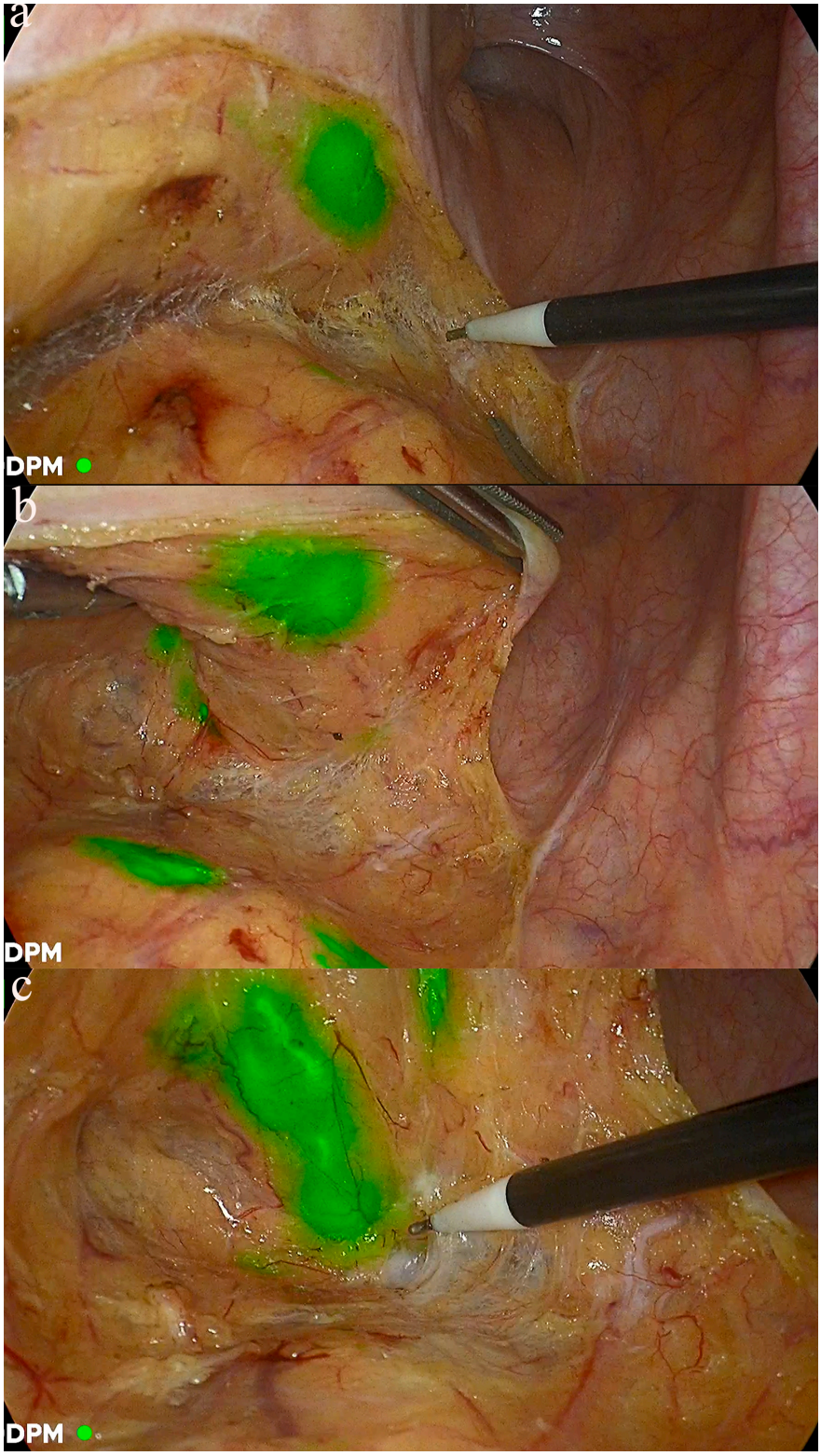


Figure 2

Fluorescence-guided lymphadenectomy demonstrating clear visualization of lymph node locations across different anatomical layers.

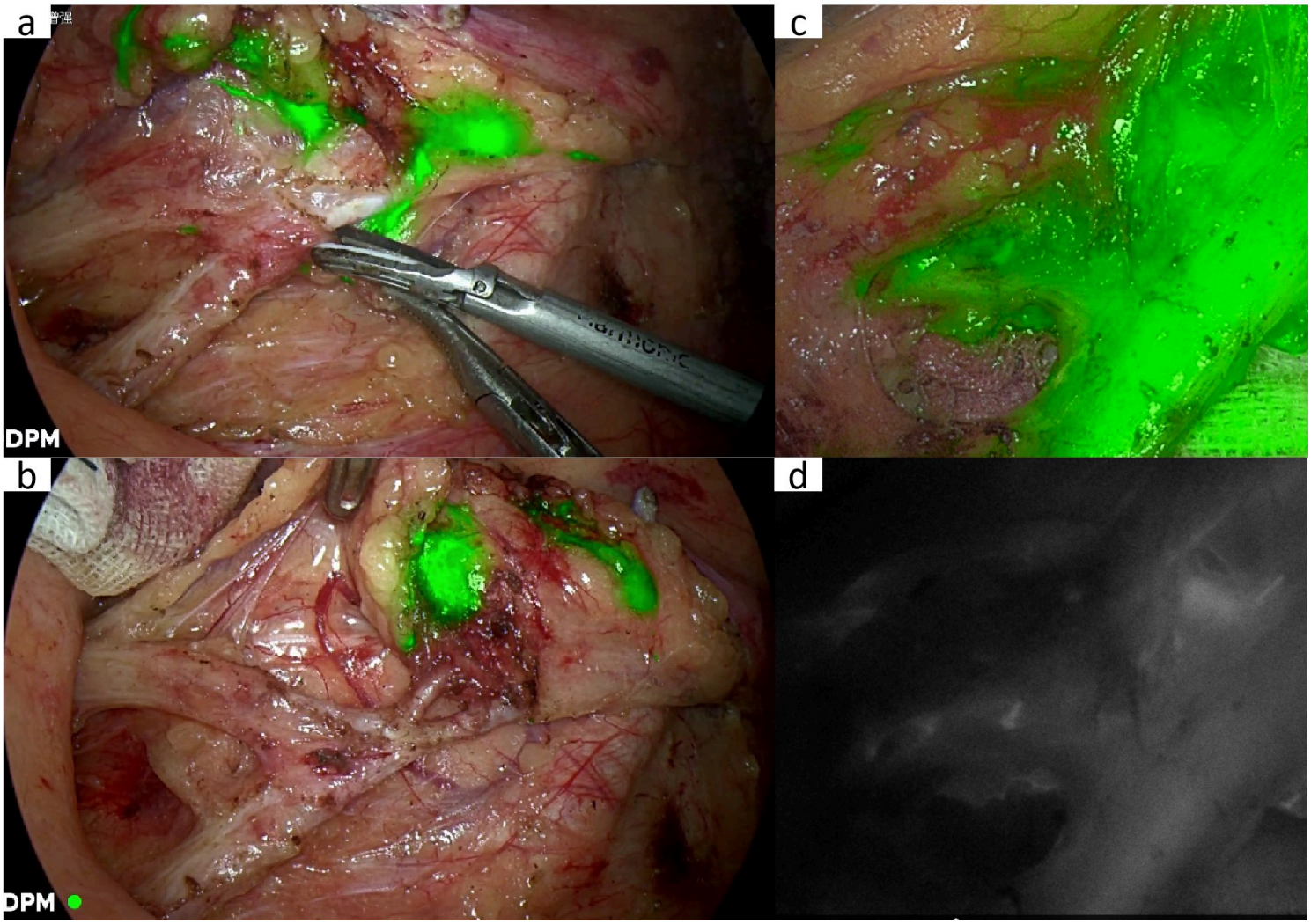


Figure 3

Anatomical dissection and branching of the IMA visualized using fluorescence angiography for enhanced vascular delineation.

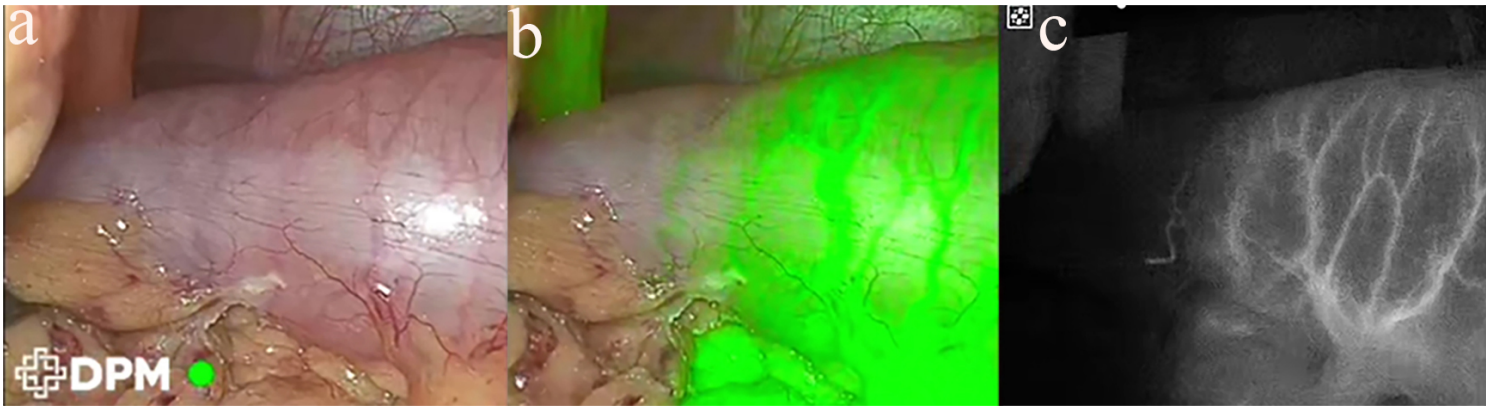


Figure 4

Bowel perfusion visualized under white color (a), pseudo-color merged modes (b), and monochrome fluorescence (c).