

Original Article

Efficacy and prognosis evaluation of left colic artery preservation in laparoscopic NOSES for rectal cancer: retrospective survival analysis

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Abstract: This retrospective cohort study aimed to clarify the impact of preserving the left colic artery (LCA) during laparoscopic Natural Orifice Specimen Extraction Surgery (lapNOSES) for rectal cancer (RC) on perioperative outcomes and 3-year survival, and to examine treatment-by-covariate interactions on recurrence-free survival (RFS) and overall survival (OS). No significant interactions were identified for RFS, whereas significant interactions for OS were observed among patients with larger maximum tumor diameter and elevated CEA levels. RC patients who underwent lapNOSES between January 2018 and January 2022 were grouped according to LCA preservation status. Baseline clinicopathological features, perioperative indicators, and three-year follow-up data were collected. Kaplan-Meier and log-rank tests were employed for survival analysis, and prognostic factors were evaluated using Cox proportional hazard modeling. The baseline characteristics of the two groups were generally balanced. Perioperatively, surgical duration, splenic flexure mobilization, ileostomy creation, anastomotic leak (AL), urinary retention, and bowel perfusion status showed marked differences between groups ($P < 0.05$), while intraoperative hemorrhage volume and surgical site infection did not differ significantly ($P > 0.05$). Reduced 3-year recurrence/metastasis rates were observed in the LCA-preservation group (RFS: $P = 0.005$), although 3-year overall mortality showed no notable difference (OS: $P = 0.463$). In the multivariable Cox model, failure to preserve LCA independently predicted inferior RFS (HR=4.091, $P = 0.022$), along with advanced age, elevated preoperative CEA/CA19-9, advanced TNM staging, and poor differentiation; postoperative adjuvant chemotherapy was protective ($P = 0.045$). For OS (but not RFS), significant interactions were observed between the treatment plan and maximum tumor diameter as well as CEA elevation ($P < 0.001$ and $P = 0.007$, respectively). In conclusion, preserving the LCA in lapNOSES for RC is associated with lower 3-year recurrence/metastasis risks without compromising long-term survival, and individualized strategies should be considered based on tumor burden and CEA levels.

Keywords: Rectal cancer, NOSES, left colonic artery, recurrence-free survival, overall survival, Cox regression, interaction analysis

Introduction

With high morbidity and mortality, colorectal cancer is a common digestive tract malignant tumor globally [1]. As people's diet structures and lifestyles alter, the incidence of rectal cancer (RC) in China is constantly increasing, which has become a major public health problem that seriously threatens human health [2, 3]. RC treatment is mainly resorted to surgical resection. On this basis, continuous refinement of adjuvant radiotherapy, chemotherapy, and tar-

geted therapy has aided in extending overall survival (OS) [4]. Yet, on the premise of ensuring the radical treatment, minimizing surgical trauma, reducing complications, and boosting life quality is a key clinical challenge.

With the deepening of the concept of minimally invasive surgery, laparoscopic radical resection of RC has become the mainstream surgical method [5]. Natural orifice specimen extraction surgery (NOSES), a technique emerged in recent years, avoids the establishment of auxil-

ary incisions by using natural cavities such as the rectum or vagina to complete specimen extraction, significantly reducing surgical trauma, relieving postoperative pain, shortening recovery time, and possessing good aesthetic effects [6]. Many clinical studies have confirmed its non-inferiority to traditional laparoscopic surgery in terms of safety and feasibility [7, 8]. Nonetheless, its long-term efficacy and some technical disputes have not been completely resolved, one of which is whether to preserve the left colic artery (LCA) during the operation.

As an important branch of the inferior mesenteric artery (IMA), LCA mainly supplies the left colon and part of the sigmoid colon [9]. For a long time, it has been controversial whether it is necessary to ligate the IMA at a high position in radical resection of RC, that is, whether to sacrifice LCA. From a radical point of view, high ligation can achieve a D3 lymphadenectomy to the greatest extent, which is theoretically beneficial to reduce local recurrence and distant metastasis [10]. However, after cutting off the LCA, the blood supply of the intestine may depend on the compensation of marginal arteries. In some patients, especially those with arteriosclerosis or vascular anomalies, there will be insufficient blood supply in the anastomotic area, resulting in a significant increase in anastomotic leak (AL) risk [11]. As one of the most serious complications after RC surgery, AL often prolongs hospitalization time, increases reoperation rate, and even directly affects long-term survival [12]. Therefore, whether to preserve LCA in NOSES for RC has become an important issue that must be balanced between radical resection and safety.

In recent years, the research on LCA reservation at home and abroad has gradually increased. Preserving LCA has been indicated to improve anastomotic stoma perfusion, reduce AL incidence, accelerate recovery, and ensure oncological radicality (when a certain range of lymphadenectomy is ensured) [13]. However, conclusions vary across research, mainly due to the limited sample size, insufficient follow-up time, and fewer analyses dedicated to the new surgical mode of NOSES. Therefore, for RC treated by NOSES, the value and significance of LCA reservation are still lacking high-quality clinical evidence.

Based on this, this study selected RC patients undergoing NOSES in our hospital as the research subjects, and retrospectively analyzed the differences in perioperative indicators, complication rates, and long-term survival outcomes between the two surgical strategies of preserving and not preserving the LCA. By comparatively analyzing patients' clinical data, we focused on evaluating the two techniques' impacts on the three-year recurrence-free survival rate (RFS) and OS. Furthermore, combined with univariate, multivariate, and interaction analyses, we explored the indications and potential benefits of LCA preservation in different clinical pathological backgrounds. The research results are expected to provide evidence-based guidance for clinical formulation of more reasonable and individualized NOSES plans for RC, while also accumulating new practical experience for further optimizing minimally invasive surgical techniques and improving patient prognosis.

Methods and materials

Sample size estimation

Based on the $EPV \geq 10$ rule for retrospective studies, if the OS multivariable model plans to include 5 risk factors, at least 50 death events are required; referencing long-term outcomes reported by Zheng et al. [14] and Luo et al. [15], and conservatively assuming a 3-year mortality of 10% for design purposes, the total sample size needed is approximately $50/0.10=500$ to meet the EPV requirement (general formula: required sample size $\approx 10 \times$ number of covariates/event rate).

Research participants

This investigation was designed as a retrospective cohort study. We collected and analyzed clinical records of individuals who underwent laparoscopic radical RC resection via the NOSES procedure at our institution from January 2018 to January 2022. All operations were conducted by a consistent surgical team with more than 10 years of experience in laparoscopic colorectal surgery, each surgeon having performed over 200 laparoscopic RC resections. Lymphadenectomy quality was verified by routine postoperative pathological examination, with a minimum requirement of 12 lymph nodes harvested per specimen according to

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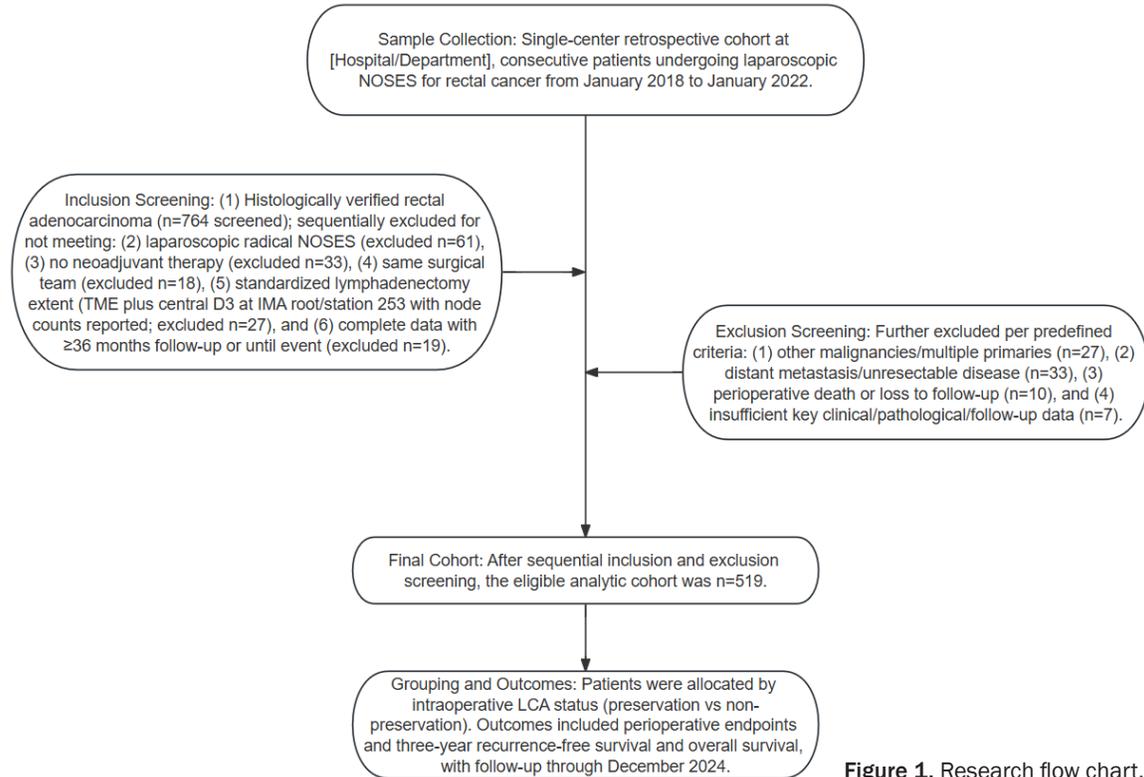


Figure 1. Research flow chart.

AJCC guidelines. The adequacy of station 253 (IMA root) lymph node dissection was confirmed by intraoperative anatomical landmark identification and postoperative pathological documentation of separately labeled specimens. Patients were classified according to intraoperative LCA preservation status, resulting in an LCA-preservation group and a non-LCA-preservation group. Ethical approval was granted by the institutional Ethics Committee of Chongqing Hospital of Jiangsu Province Hospital (The People's Hospital of Qijiang District, Chongqing), and the study complied with the Declaration of Helsinki [16]. Due to the retrospective design and no involvement of private patient information, written informed consent was exempted by the Ethics Committee (Figure 1).

Eligibility requirements: (1) Histologically verified rectal adenocarcinoma (pre- or post-surgery); (2) Treatment with laparoscopic NOSES (lapNOSES) radical resection; (3) No prior exposure to radiotherapy, chemotherapy, or targeted therapy; (4) Complete clinical, pathological, and follow-up data; (5) Follow-up time ≥36 months or until an endpoint event; (6) Identical extent of lymphadenectomy: both groups

underwent TME plus central D3 with IMA-root (station 253) dissection; the only difference was LCA preservation; pathology reported total and station-253 node counts.

Exclusion grounds: (1) Additional malignancies or multiple primary cancers; (2) Distant metastasis or unresectable status; (3) Perioperative mortality or loss to follow-up; (4) Insufficient clinical data.

Clinicopathological information

Patient demographics, covering age, sex, body mass index (BMI), history of smoking/alcohol consumption, hypertension, and diabetes, were documented. The recorded tumor-related metrics were the tumor-anal verge distance (TAVD), maximum tumor diameter (MTD), preoperative serum carcinoembryonic antigen [CEA] and carbohydrate antigen 19-9 [CA19-9] levels, Tumor-Node-Metastasis (TNM) stage, T/N stage, histological grade, and tumor type. Surgical duration, intraoperative hemorrhage volume, splenic flexure mobilization, ileostomy creation status, AL, surgical site infection (SSI), urinary retention, and bowel perfusion were the perioperative parameters monitored. Post-

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operative recovery measures (time to first oral intake/flatus, hospitalization duration, and treatment expenses) and adjuvant therapy (postoperative chemotherapy and/or radiotherapy) were also documented.

Bowel perfusion evaluation criteria

Intraoperative intestinal perfusion evaluation was based on intestinal color, arterial pulsatility intensity, and submucosal vessel filling status. Well-perfused: The intestinal wall is pink or dark red, with obvious pulsation and submembranous vessel filling; Adequately perfused: the intestinal wall is slightly darker, the pulsation is weakened, and the submembrane vessels are moderately filled; Poorly perfused: the intestinal wall is dark purple or pale, without pulsations, and the submembranous vessels are poorly filled.

Laboratory testing methodology for biomarkers

Serum CEA and CA19-9 were all tested using electrochemiluminescence immunoassay (ECLIA) on a Beckman Coulter UniCel DXI 800 automatic immunoanalyzer within one week preoperatively. Morning fasting venous blood samples (5 mL) were collected and subjected to centrifugation (3000 rpm, 10 minutes) to separate the serum. The entire testing process strictly followed the manufacturer's operating procedures. According to the manufacturer's instructions, the normal reference ranges were: CEA < 5.0 ng/mL and CA19-9 < 37.0 U/mL. In this study, elevated CEA was defined as ≥ 5.0 ng/mL and elevated CA19-9 was defined as ≥ 37.0 U/mL.

Definition of recurrence and metastasis

Local recurrence was defined as tumor recurrence in the pelvic cavity or anastomotic site, confirmed by computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography-computed tomography (PET-CT), or colonoscopy with histopathological verification when feasible. Distant metastasis was defined as the presence of new lesions in distant organs (liver, lung, peritoneum, bone, brain, etc.) confirmed by imaging studies (CT, MRI, or PET-CT). All suspected recurrences or metastases were evaluated by a multidisciplinary team (MDT) comprising surgeons, radiologists, oncologists, and pathologists. Histo-

pathological confirmation was obtained whenever clinically feasible and safe.

Adjuvant therapy regimens

Postoperative adjuvant chemotherapy was recommended for patients with stage II (high-risk features) and stage III disease according to the Chinese Society of Clinical Oncology (CSCO) guidelines. The primary chemotherapy regimens included: (1) XELOX regimen: oxaliplatin 130 mg/m² intravenously on day 1, plus capecitabine 1000 mg/m² orally twice daily on days 1-14, repeated every 3 weeks for 8 cycles; (2) mFOLFOX6 regimen: oxaliplatin 85 mg/m² intravenously on day 1, leucovorin 400 mg/m² intravenously on day 1, fluorouracil 400 mg/m² intravenous bolus on day 1, then 2400 mg/m² continuous intravenous infusion over 46-48 hours, repeated every 2 weeks for 12 cycles; (3) Capecitabine monotherapy: 1250 mg/m² orally twice daily on days 1-14, repeated every 3 weeks for 8 cycles, reserved for patients intolerant to oxaliplatin-based regimens. Postoperative adjuvant radiotherapy (total dose 45-50.4 Gy in 25-28 fractions) was administered to selected patients with locally advanced disease (T3-4 or N+) who had not received neoadjuvant chemoradiotherapy, particularly those with positive circumferential resection margins or inadequate mesorectal excision quality.

Follow-up and outcome measures

Follow-ups, performed via outpatient re-examinations and telephone interviews, terminated till December 2024 or the patient's death. Assessments occurred quarterly during the initial two years after surgery and biannually thereafter until year three.

The primary endpoints were: (1) 3-year RFS, calculated from the surgical date to relapse or metastatic spread; (2) three-year overall survival (OS), representing the time from surgery to death from any cause.

Secondary endpoints included the rates of recurrence/metastasis, mortality, and perioperative complications.

Statistical methods

Statistical analysis: All analyses were performed in R version 4.3.3. Missing data handling:

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Table 1. Distribution of baseline clinicopathological features

Variable	LCA-preservation group (n=248)	Non-LCA-preservation group (n=281)	$\chi^2/t/Z$	P
Age	64.13±7.93	63.63±8.06	0.750	0.453
BMI	22.41 [20.30, 24.17]	22.06 [20.10, 24.42]	0.841	0.400
Tumor-anal verge distance (cm)	7.99±1.24	8.05±1.34	0.474	0.636
Maximum tumor diameter (cm)	7.97 [4.11, 9.91]	8.34 [3.84, 10.43]	0.917	0.359
Preoperative CEA (ng/mL)	3.85 [2.36, 5.62]	3.73 [1.79, 5.59]	1.111	0.267
Preoperative CA19-9 (ng/ml)	18.53 [7.90, 30.93]	15.66 [7.68, 28.37]	1.499	0.134
Sex			1.013	0.314
Male	161 (64.92%)	194 (69.04%)		
Female	87 (35.08%)	87 (30.96%)		
Hypertension history			0.286	0.593
Yes	62 (25.00%)	76 (27.05%)		
No	186 (75.00%)	205 (72.95%)		
Diabetes history			0.678	0.410
Yes	45 (18.15%)	59 (21.00%)		
No	203 (81.85%)	222 (79.00%)		
Smoking history			2.390	0.122
Yes	176 (70.97%)	216 (76.87%)		
No	72 (29.03%)	65 (23.13%)		
Alcohol consumption history			1.450	0.229
Yes	37 (14.92%)	53 (18.86%)		
No	211 (85.08%)	228 (81.14%)		
TNM staging			2.070	0.355
I	25 (10.08%)	37 (13.17%)		
II	124 (50.00%)	146 (51.96%)		
III	99 (39.92%)	98 (34.88%)		
T-staging			0.955	0.329
T1-T2	74 (29.84%)	95 (33.81%)		
T3-T4	174 (70.16%)	186 (66.19%)		
N-staging			1.434	0.231
N0	149 (60.08%)	183 (65.12%)		
N1-2	99 (39.92%)	98 (34.88%)		
Histological grade			0.000	0.999
Poor differentiation	15 (6.05%)	17 (6.05%)		
Moderate + well differentiation	233 (93.95%)	264 (93.95%)		
Tumor type			2.271	0.321
Infiltrating type	8 (3.23%)	14 (4.98%)		
Ulcerative type	151 (60.89%)	155 (55.16%)		
Protruded type	89 (35.89%)	112 (39.86%)		

Note: LCA, left colic artery; BMI, body mass index; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; TNM, Tumor-Node-Metastasis.

per eligibility criteria, cases with incomplete clinical, pathological, or follow-up information were excluded at screening; thus, variables entered into the models had no missing values. Time-to-event outcomes were right-censored at last contact. Continuous variables are

summarized as mean ± SD (normal) or median (IQR) (non-normal) and compared using t test or Wilcoxon rank-sum test; categorical variables as counts (%) and compared using χ^2 or Fisher's exact test. Survival was estimated by Kaplan-Meier and compared by log-rank test.

Table 2. Comparison of perioperative outcomes

Variable	LCA-preservation group (n=248)	Non-LCA-preservation group (n=281)	χ^2/t	P
Surgical duration (min)	307.09±9.24	283.96±8.08	-30.713	<0.001
Intraoperative hemorrhage volume (mL)	84.36±11.61	86.01±13.07	1.524	0.128
Splenic flexure mobilization			10.875	<0.001
Yes	7 (2.82%)	28 (9.96%)		
No	241 (97.18%)	253 (90.04%)		
Ileostomy creation			5.045	0.025
Yes	10 (4.03%)	25 (8.90%)		
No	238 (95.97%)	256 (91.10%)		
Anastomotic leak			15.857	<0.001
Yes	7 (2.82%)	34 (12.10%)		
No	241 (97.18%)	247 (87.90%)		
Surgical site infection			0.274	0.600
Yes	10 (4.03%)	14 (4.98%)		
No	238 (95.97%)	267 (95.02%)		
Uroschisis			4.155	0.042
Yes	27 (10.89%)	48 (17.08%)		
No	221 (89.11%)	233 (82.92%)		
Bowel perfusion status			51.239	<0.001
Well-perfused	174 (70.16%)	110 (39.15%)		
Adequately perfused	64 (25.81%)	143 (50.89%)		
Poorly perfused	10 (4.03%)	28 (9.96%)		

Note: LCA, left colic artery.

Prognostic associations were evaluated using Cox proportional hazards models: variables were first screened in univariable analyses (clinical relevance and $P < 0.10$) and then entered into multivariable models; continuous predictors were modeled on their continuous scale with linearity assessed via restricted cubic splines. Proportional hazards were checked using Schoenfeld residuals, and multicollinearity was assessed by variance inflation factors (VIF). To explore effect modification, treatment-by-covariate interaction terms were added; interaction findings are exploratory without multiplicity adjustment. Results are reported as HRs with 95% CIs; two-sided $P < 0.05$ was considered statistically significant.

Results

Comparative analysis of baseline clinicopathological features

As shown in **Table 1**, both groups exhibited similar baseline clinicopathological features. None of the variables - including age ($P = 0.453$), BMI ($P = 0.400$), TAVD ($P = 0.636$), MTD

($P = 0.359$), preoperative CEA ($P = 0.267$), preoperative CA19-9 ($P = 0.134$), gender ($P = 0.314$), hypertension history ($P = 0.593$), diabetes ($P = 0.410$), smoking ($P = 0.122$), alcohol intake ($P = 0.229$), TNM staging ($P = 0.355$), T staging ($P = 0.329$), N staging ($P = 0.231$), histological grade ($P = 0.999$), and tumor type ($P = 0.321$) - demonstrated significant disparities.

Comparison of perioperative conditions

Surgical duration was greater in the LCA-preservation group ($P < 0.001$). Statistical between-group significance was also noted for splenic flexure mobilization ($P < 0.001$), ileostomy creation ($P = 0.025$), AL ($P < 0.001$), urinary retention ($P = 0.042$), and bowel perfusion status ($P = 0.042$). Intraoperative hemorrhage volume ($P = 0.128$) and SSI rates ($P = 0.600$) did not reach significance (**Table 2**).

Comparison of postoperative recovery and adjuvant therapy profiles

The two patient cohorts demonstrated parity across lymph node dissection counts (total:

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Table 3. Comparative analysis of postoperative recovery and adjuvant therapy

Variable	LCA-preservation group (n=248)	Non-LCA-preservation group (n=281)	$\chi^2/t/Z$	P
Lymph node yield	12.00 [9.00, 14.00]	12.00 [9.00, 14.00]	0.599	0.549
Number of harvested lymph nodes from station 253	4.00 [3.00, 6.00]	4.00 [3.00, 6.00]	0.291	0.771
Time to first oral intake (d)	3.00 [2.00, 4.00]	3.00 [2.00, 4.00]	1.396	0.163
Time to first flatus (d)	3.00 [2.00, 4.00]	3.00 [2.00, 4.00]	0.549	0.583
Hospitalization duration (d)	8.00 [7.00, 10.00]	8.00 [7.00, 10.00]	0.019	0.985
Treatment expense	41109.11±6210.33	40125.17±6434.60	-1.784	0.075
Postoperative adjuvant chemotherapy			1.579	0.209
Yes	62 (25.00%)	84 (29.89%)		
No	186 (75.00%)	197 (70.11%)		
Postoperative adjuvant radiotherapy			1.213	0.271
Yes	25 (10.08%)	37 (13.17%)		
No	223 (89.92%)	244 (86.83%)		

Note: LCA, left colic artery.

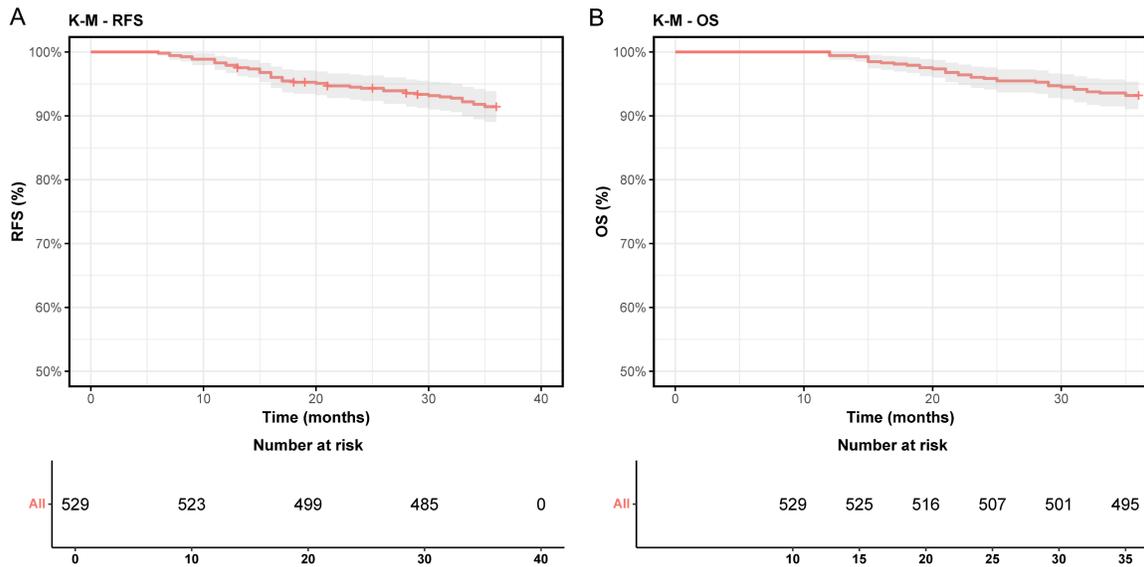


Figure 2. Comparative assessment of 3-year RFS and OS. A. Three-year RFS comparison. B. Three-year OS comparison. Note: K-M, Kaplan-Meier; RFS, recurrence-free survival; OS, overall survival.

P=0.549; station 253: P=0.771), recovery milestones (time to feeding: P=0.163; flatus: P=0.583), hospitalization duration (P=0.985), treatment expenses (P=0.075), and subsequent adjuvant chemotherapy (P=0.209) or radiotherapy (P=0.271) rates, all of which were devoid of statistical significance (**Table 3**).

Statistics of 3-year recurrence/metastasis, and mortality

The study cohort exhibited a RFS of 91.5% and an OS of 93.2% after 36 months of observation

(**Figure 2**). The subsequent between-group evaluation showed a superior outcome regarding recurrence/metastasis for the LCA-preservation strategy over the alternative (P=0.005). However, the difference in three-year all-cause mortality between the two groups did not reach statistical significance (P=0.463) (**Table 4**; **Figure 2**).

Univariate evaluation for RFS-associated predictors

Based on univariate Cox proportional hazards modeling, the following factors showed close

Table 4. Comparative outcomes of three-year recurrence/metastasis and mortality

Variable	LCA-preservation group (n=248)	Non-LCA-preservation group (n=281)	χ^2	P
Recurrence/metastasis			8.070	0.005
Yes	12 (4.84%)	33 (11.74%)		
No	236 (95.16%)	248 (88.26%)		
Mortality			0.539	0.463
Yes	19 (7.66%)	17 (6.05%)		
No	229 (92.34%)	264 (93.95%)		

Note: LCA, left colic artery.

associations with RFS: age (HR=1.084; P<0.001), TAVD (HR=0.651; P<0.001), preoperative CEA (HR=1.382; P<0.001) and CA19-9 (HR=1.029; P=0.001), surgical duration (HR=0.968; P=0.003), lymph node yield (HR=1.114; P=0.011), number of harvested lymph nodes from station 253 (HR=0.840; P=0.046), treatment regimen (LCA preservation vs. non-preservation: HR=2.462; P=0.008), TNM staging (HR=2.444; P=0.003), histological grade (poor vs. moderate/well: HR=6.254; P<0.001), and adjuvant chemotherapy (HR=0.241; P=0.007). In contrast, BMI (P=0.889), MTD (P=0.261), intraoperative hemorrhage volume (P=0.392), various postoperative recovery metrics (time to oral intake, time to first flatus, and hospitalization duration; all P>0.05), treatment expense (P=0.393), gender (P=0.197), comorbidities (hypertension, P=0.862; diabetes, P=0.223), lifestyle histories (smoking, P=0.416; drinking, P=0.900), tumor type (P>0.05), and the administration of postoperative adjuvant radiotherapy (P=0.867) lacked a statistically significant association with RFS. Moreover, a significantly lower 3-year RFS was observed in patients characterized by advanced age, tumors located closer to the anal verge, high preoperative CEA/CA19-9, shorter operative times, inadequate lymph node dissection, LCA non-preservation, advanced TNM stage, poor tumor differentiation, and lack of adjuvant chemotherapy, as evidenced by the K-M curves of significant variables (**Table 5; Figure 3**).

Multivariable analysis of RFS

The multivariate analysis, based on significant univariate predictors, indicated that several factors independently influenced RFS: age (HR=1.081, P<0.001), TAVD (HR=0.566, P<0.001), preoperative CEA (HR=1.342, P<0.001), preoperative CA19-9 (HR=1.027, P=

0.012), treatment regimen (non-LCA preservation vs. LCA preservation, HR=4.091, P=0.022), TNM stage (III vs. I-II, HR=2.443, P=0.007), and histological grade (poor vs. moderate/well, HR=4.333, P<0.001) were significant risk factors, while postoperative djuvant chemotherapy was protective (HR=0.342, P=0.045). Surgical duration, total lymph node yield, and the number of harvested lymph nodes from station 253 differed little (P>0.05) (**Table 6**).

Univariate Cox analysis of prognostic factors for OS

A univariate analysis screened factors influencing OS. According to Cox regression, significant predictors of OS included age (HR=1.044, P=0.031), TAVD (HR=0.725, P=0.012), MTD (HR=1.148, P=0.017), preoperative CEA (HR=1.538, P<0.001) and CA19-9 (HR=1.045, P<0.001), TNM staging (Stage II vs. I: HR=4.070, P<0.001), histological grade (moderate/well vs. poor: HR=8.385, P<0.001), and postoperative adjuvant chemotherapy (HR=0.071, P=0.009). No statistically significant correlations were detected for BMI (P=0.484), surgical duration (P=0.822), intraoperative hemorrhage volume (P=0.703), recovery parameters (time to first oral intake, first flatus, hospitalization duration; all P>0.05), treatment expenses (P=0.868), LCA preservation status (P=0.451), sex (P=0.294), hypertension (P=0.308), diabetes (P=0.087), smoking (P=0.291), alcohol consumption (P=0.337), tumor type (P>0.05), or adjuvant radiotherapy (P=0.357). K-M survival curves further indicated that patients who were older, had tumors located closer to the anal verge, larger tumor size, elevated preoperative CEA or CA19-9 levels, advanced TNM stage, poor tumor differentiation, or did not receive adjuvant chemotherapy experienced signifi-

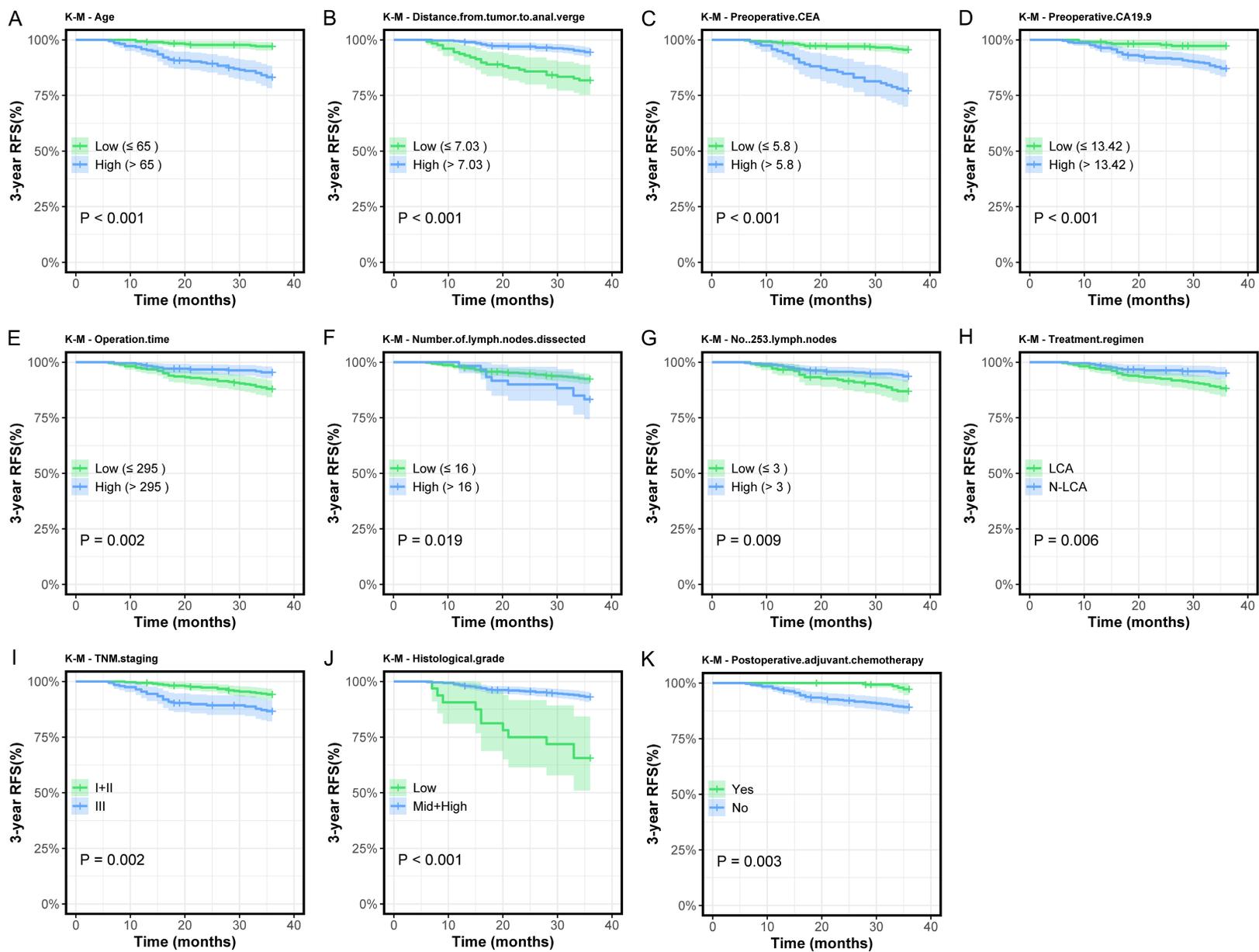
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Table 5. RFS-associated factors by univariate Cox analysis

Variable	Beta	SE	Wald	P	HR	Lower	Upper
Age	0.080	0.017	22.539	0.000	1.084	1.048	1.120
BMI	-0.007	0.049	0.020	0.889	0.993	0.902	1.094
Tumor-anal verge distance	-0.429	0.115	14.052	0.000	0.651	0.520	0.815
Maximum tumor diameter	0.053	0.047	1.266	0.261	1.054	0.962	1.155
Preoperative CEA	0.323	0.055	35.166	0.000	1.382	1.242	1.538
Preoperative CA19-9	0.028	0.009	10.363	0.001	1.029	1.011	1.047
Surgical duration	-0.033	0.011	8.554	0.003	0.968	0.947	0.989
Intraoperative hemorrhage volume (mL)	0.010	0.012	0.733	0.392	1.010	0.987	1.034
Lymph node yield	0.108	0.042	6.416	0.011	1.114	1.025	1.210
Number of harvested lymph nodes from station 253	-0.174	0.087	3.983	0.046	0.840	0.708	0.997
Time to first oral intake	-0.075	0.161	0.216	0.642	0.928	0.677	1.271
Time to first flatus	0.090	0.165	0.295	0.587	1.094	0.792	1.511
Hospitalization duration	-0.038	0.061	0.385	0.535	0.963	0.854	1.085
Treatment expense	0.000	0.000	0.731	0.393	1.000	1.000	1.000
Treatment regimen							
LCA-preservation							
Non-LCA-preservation	0.901	0.337	7.144	0.008	2.462	1.272	4.767
Sex							
Female							
Male	0.448	0.347	1.667	0.197	1.565	0.793	3.089
Hypertension history							
No							
Yes	0.059	0.337	0.030	0.862	1.060	0.548	2.053
Diabetes history							
No							
Yes	0.410	0.337	1.482	0.223	1.507	0.779	2.919
Smoking history							
No							
Yes	-0.262	0.322	0.663	0.416	0.769	0.409	1.446
Alcohol consumption history							
No							
Yes	0.049	0.390	0.016	0.900	1.050	0.489	2.256
TNM staging							
I+II							
III	0.894	0.302	8.765	0.003	2.444	1.353	4.416
Histological grade							
Moderate + well differentiation							
Poor differentiation	1.833	0.348	27.802	0.000	6.254	3.164	12.363
Tumor type							
Infiltrating type							
Ulcerative type	0.379	0.725	0.274	0.601	1.461	0.353	6.052
Protruded type	-1.524	0.866	3.096	0.078	0.218	0.040	1.190
Postoperative adjuvant chemotherapy							
No							
Yes	-1.422	0.524	7.372	0.007	0.241	0.086	0.673
Postoperative adjuvant radiotherapy							
No							
Yes	-0.080	0.474	0.028	0.867	0.923	0.364	2.340

Note: RFS, recurrence-free survival; HR, hazard ratio; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; LCA, left colic artery; TNM, Tumor-Node-Metastasis.

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Figure 3. K-M curves of the impact of univariate analysis-identified significant variables on RFS. A. Age; B. Tumor-anal verge distance; C. Preoperative CEA level; D. Preoperative CA19-9 level; E. Surgical duration; F. Lymph node yield; G. Number of harvested lymph nodes from station 253; H. Treatment regimen (LCA preservation or not); I. TNM staging; J. Histological grade; K. Postoperative adjuvant chemotherapy. Note: K-M, Kaplan-Meier; RFS, recurrence-free survival; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; LCA, left colic artery; TNM, Tumor-Node-Metastasis.

Table 6. Multivariable Cox regression analysis of predictors for RFS

Variable	Beta	SE	Wald	P	HR	Lower	Upper
Age	0.078	0.019	16.274	0.000	1.081	1.041	1.123
Tumor-anal verge distance	-0.569	0.135	17.785	0.000	0.566	0.435	0.738
Preoperative CEA	0.294	0.059	24.987	0.000	1.342	1.196	1.506
Preoperative CA19-9	0.027	0.011	6.369	0.012	1.027	1.006	1.048
Surgical duration	-0.013	0.019	0.422	0.516	0.987	0.950	1.026
Lymph node yield	0.062	0.048	1.702	0.192	1.064	0.969	1.169
Number of harvested lymph nodes from station 253	-0.161	0.097	2.778	0.096	0.851	0.705	1.029
Treatment regimen							
LCA-preservation							
Non-LCA-preservation	1.409	0.617	5.222	0.022	4.091	1.222	13.698
TNM staging							
I+II							
III	0.893	0.332	7.247	0.007	2.443	1.275	4.680
Histological grade							
Moderate + well differentiation							
Poor differentiation	1.466	0.365	16.126	0.000	4.333	2.118	8.863
Postoperative adjuvant chemotherapy							
Yes							
No	-1.074	0.536	4.017	0.045	0.342	0.120	0.977

Note: RFS, recurrence-free survival; HR, hazard ratio; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; LCA, left colic artery; TNM, Tumor-Node-Metastasis.

cantly worse three-year OS (Table 7 and Figure 4).

Independent determinants of OS by multi-factor analysis

In the multivariable Cox regression model incorporating statistically significant variables from univariate analysis, TAVD (HR=0.726, P=0.011), MTD (HR=1.208, P=0.002), preoperative CEA (HR=1.325, P<0.001), CA19-9 (HR=1.026, P=0.015), TNM stage III (vs. I+II, HR=4.066, P<0.001), and poor differentiation (vs. moderate/well, HR=3.209, P=0.004) were independent predictors of poorer OS. Postoperative adjuvant chemotherapy was associated with improved OS (HR=0.126, P=0.042). Age lost its statistical significance in the multivariable model (P=0.173) (Table 8).

Interaction analysis of RFS

Subsequent interaction analysis examined how the associations between key prognostic factors and RFS were modified by the treatment approach (with or without LCA preservation). Analysis revealed an absence of significant interaction effects between the treatment regimen and most prognostic variables, such as age (P=0.577), TAVD (P=0.261), CA19-9 level (P=0.689), total lymph node yield (P=0.851), duration of surgery (P=0.275), number of harvested lymph nodes from station 253 (P=0.722), TNM stage (P=0.709), histologic differentiation (P=0.134), and postoperative adjuvant chemotherapy (P=0.179). This indicates a consistent treatment effect across patient subgroups. No significant interaction was detected between preoperative CEA and treatment strategy (P=0.074).

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Table 7. Univariate analysis of prognostic factors for OS

Variable	Beta	SE	Wald	P	HR	Lower	Upper
Age	0.043	0.020	4.653	0.031	1.044	1.004	1.086
BMI	-0.039	0.055	0.490	0.484	0.962	0.863	1.072
Tumor-anal verge distance	-0.322	0.129	6.249	0.012	0.725	0.563	0.933
Maximum tumor diameter	0.138	0.057	5.748	0.017	1.148	1.025	1.285
Preoperative CEA	0.431	0.060	51.139	0.000	1.538	1.367	1.731
Preoperative CA19-9	0.044	0.009	21.809	0.000	1.045	1.026	1.064
Surgical duration	0.003	0.012	0.051	0.822	1.003	0.980	1.025
Intraoperative hemorrhage volume (mL)	-0.005	0.013	0.145	0.703	0.995	0.969	1.021
Lymph node yield	0.077	0.048	2.604	0.107	1.080	0.984	1.186
Number of harvested lymph nodes from station 253	-0.167	0.098	2.907	0.088	0.846	0.699	1.025
Time to first oral intake	0.010	0.176	0.003	0.954	1.010	0.716	1.425
Time to first flatus	0.157	0.182	0.743	0.389	1.170	0.819	1.671
Hospitalization duration	0.047	0.067	0.484	0.487	1.048	0.919	1.194
Treatment expense	0.000	0.000	0.027	0.868	1.000	1.000	1.000
Treatment regimen							
LCA-preservation							
Non-LCA-preservation	-0.252	0.334	0.569	0.451	0.777	0.404	1.496
Sex							
Female							
Male	0.403	0.385	1.099	0.294	1.497	0.704	3.183
Hypertension history							
No							
Yes	0.360	0.354	1.039	0.308	1.434	0.717	2.867
Diabetes history							
No							
Yes	0.620	0.362	2.935	0.087	1.859	0.915	3.777
Smoking history							
No							
Yes	-0.373	0.354	1.113	0.291	0.689	0.344	1.377
Alcohol consumption history							
No							
Yes	-0.509	0.530	0.922	0.337	0.601	0.213	1.699
TNM staging							
I+II							
III	1.404	0.362	15.047	0.000	4.070	2.003	8.272
Histological grade							
Moderate + well differentiation	2.126	0.362	34.421	0.000	8.385	4.121	17.063
Poor differentiation							
Tumor type							
Infiltrating type	0.727	1.018	0.510	0.475	2.068	0.281	15.203
Ulcerative type	-0.261	1.069	0.059	0.807	0.771	0.095	6.263
Protruded type							
Postoperative adjuvant chemotherapy							
Yes	-2.638	1.014	6.767	0.009	0.071	0.010	0.522
No							
Postoperative adjuvant radiotherapy							
Yes	0.412	0.447	0.848	0.357	1.509	0.628	3.627
No	-0.252	0.334	0.569	0.451	0.777	0.404	1.496

Note: OS, overall survival; HR: hazard ratio; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; LCA, left colic artery; TNM, Tumor-Node-Metastasis.

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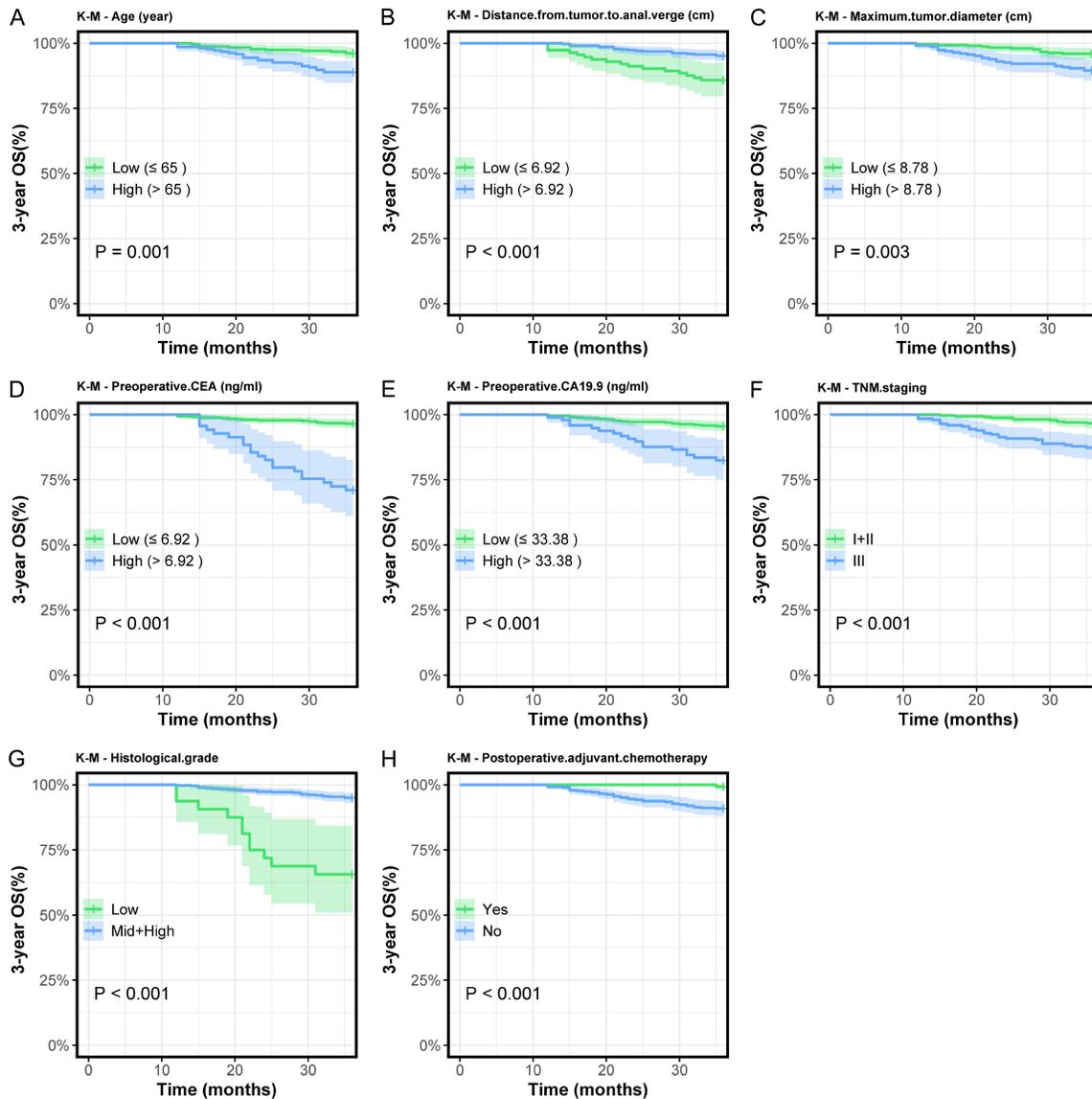


Figure 4. K-M analysis of OS stratified by clinicopathological characteristics with significant univariate associations. A. Age; B. Tumor-anal verge distance; C. Maximum tumor diameter; D. Preoperative CEA level; E. Preoperative CA19-9 level; F. TNM staging; G. Histological grade; H. Postoperative adjuvant chemotherapy. Note: K-M, Kaplan-Meier; OS, overall survival; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; TNM, Tumor-Node-Metastasis.

Overall, the treatment effect was stable across all subgroups, and common clinicopathological factors did not significantly influence the association between treatment strategy and RFS (**Figure 5**).

Interaction analysis of OS

In the OS-associated interaction analysis, we found no noticeable main effect for the treatment regimen in the primary analysis (i.e., LCA preservation). Yet, notable findings emerged within certain patient subgroups. First of all, a

significant treatment-by-tumor-size interaction was detected ($P < 0.001$). LCA non-preservation resulted in a markedly higher risk of death in patients with larger tumors (≥ 8.78 cm in diameter), whereas its effect on OS was minimal in those with smaller tumors. Second, preoperative CEA was a significant effect modifier of the treatment strategy ($P = 0.007$). Failure to preserve the LCA significantly elevated mortality risk in patients with high CEA levels, whereas the treatment strategy was not a major determinant of OS in patients with low CEA levels. In

Table 8. Independent predictors of OS identified by multivariate Cox analysis

Variable	Beta	SE	Wald	P	HR	Lower	Upper
Age	0.024	0.018	1.856	0.173	1.024	0.990	1.060
Tumor-anal verge distance	-0.320	0.125	6.541	0.011	0.726	0.568	0.928
Maximum tumor diameter	0.189	0.062	9.451	0.002	1.208	1.071	1.364
Preoperative CEA	0.281	0.062	20.690	0.000	1.325	1.174	1.496
Preoperative CA19-9	0.026	0.011	5.879	0.015	1.026	1.005	1.048
TNM staging							
I+II							
III	1.403	0.400	12.280	0.000	4.066	1.856	8.912
Histological grade							
Moderate + well differentiation							
Poor differentiation	1.166	0.402	8.394	0.004	3.209	1.458	7.063
Postoperative adjuvant chemotherapy							
Yes							
No	-2.072	1.021	4.117	0.042	0.126	0.017	0.932

Note: OS, overall survival; HR: hazard ratio; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; LCA, left colic artery; TNM, Tumor-Node-Metastasis.

addition, the interaction of histological differentiation with treatment regimen showed a trend toward statistical significance (P=0.066). This suggests that whether to preserve the LCA may have a more significant impact on OS in poorly differentiated tumors, but further verification is needed. Age (P=0.163), TAVD (P=0.942), CA19-9 (P=0.315), TNM stage (P=0.300), and postoperative adjuvant chemotherapy (P=0.997) did not show statistically significant interactions with the treatment plan. Overall, the interaction analysis of OS indicates that tumor burden (max diameter), biological behavior (CEA), and differentiation degree may have differential effects on patient prognosis under different treatment plans, while most clinicopathological features did not significantly modify the relationship between the treatment plan and OS (Figure 6).

Discussion

Clinical implications of the key findings

Through a retrospective cohort analysis, this study found that preserving the left colon artery in lapNOSES for RC has significant perioperative safety advantages and long-term oncology benefits. During the perioperative period, we noted a markedly lower AL incidence in the LCA preservation group compared to non-LCA preservation counterparts, which was basically consistent with the AL incidence range report-

ed internationally. Literature [12] shows that preserving the LCA and superior rectal artery in laparoscopic sigmoid colon cancer surgery significantly reduces AL occurrences, further verifying the positive effect of vascular preservation on anastomotic healing. In the large-scale meta-analysis by Wang et al. [17], which included 5,054 patients across 15 studies, preserving LCA contributed to reduced AL risk in radical sigmoid and RC surgery while being clinically safe and feasible. Zeng et al. [18] meta-analyzed 18 studies (n=5,917), which clearly showed that IMA high ligation notably increased AL development possibilities (OR=1.33, P=0.004), providing strong evidence-based support for the safety of LCA retention. More importantly, preserving LCA significantly improved intestinal perfusion, evidenced by a larger proportion of patients with good blood supply in the LCA preservation group compared to the non-LCA preservation group. This improvement of blood supply is directly translated into clinical benefits, which is manifested in the significant reduction of ileostomy rate and uroscheisis rate, effectively reducing the postoperative pain and medical burden of patients.

In terms of long-term oncology outcomes, preserving LCA exhibited an intimate connection with recurrence and metastasis rates in three years, with the LCA-preservation group showing evidently lower recurrence and metastasis rates than the non-LCA-preservation group.

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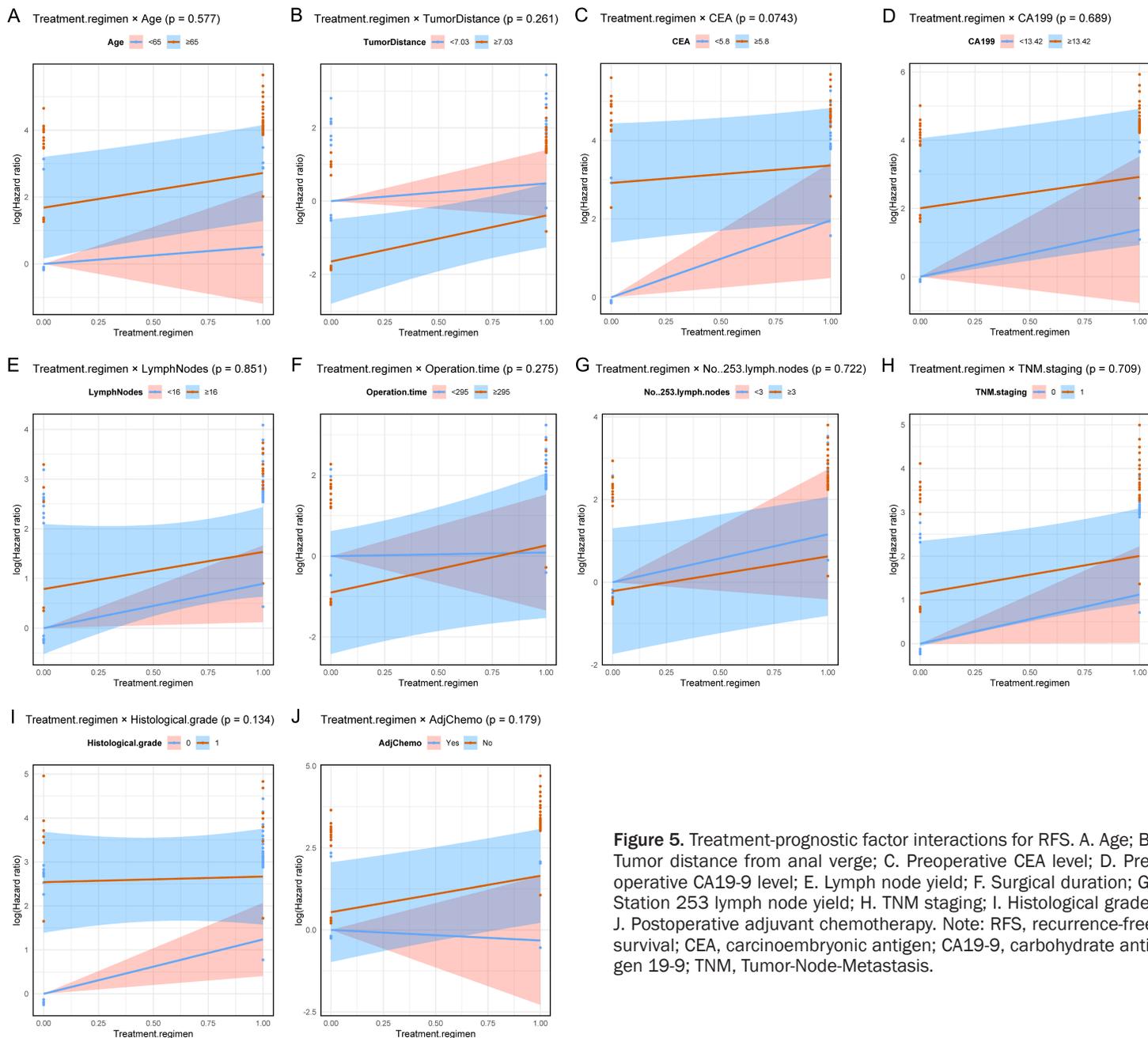


Figure 5. Treatment-prognostic factor interactions for RFS. A. Age; B. Tumor distance from anal verge; C. Preoperative CEA level; D. Preoperative CA19-9 level; E. Lymph node yield; F. Surgical duration; G. Station 253 lymph node yield; H. TNM staging; I. Histological grade; J. Postoperative adjuvant chemotherapy. Note: RFS, recurrence-free survival; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; TNM, Tumor-Node-Metastasis.

Impact of left colic artery preservation on prognosis following noses for rectal cancer

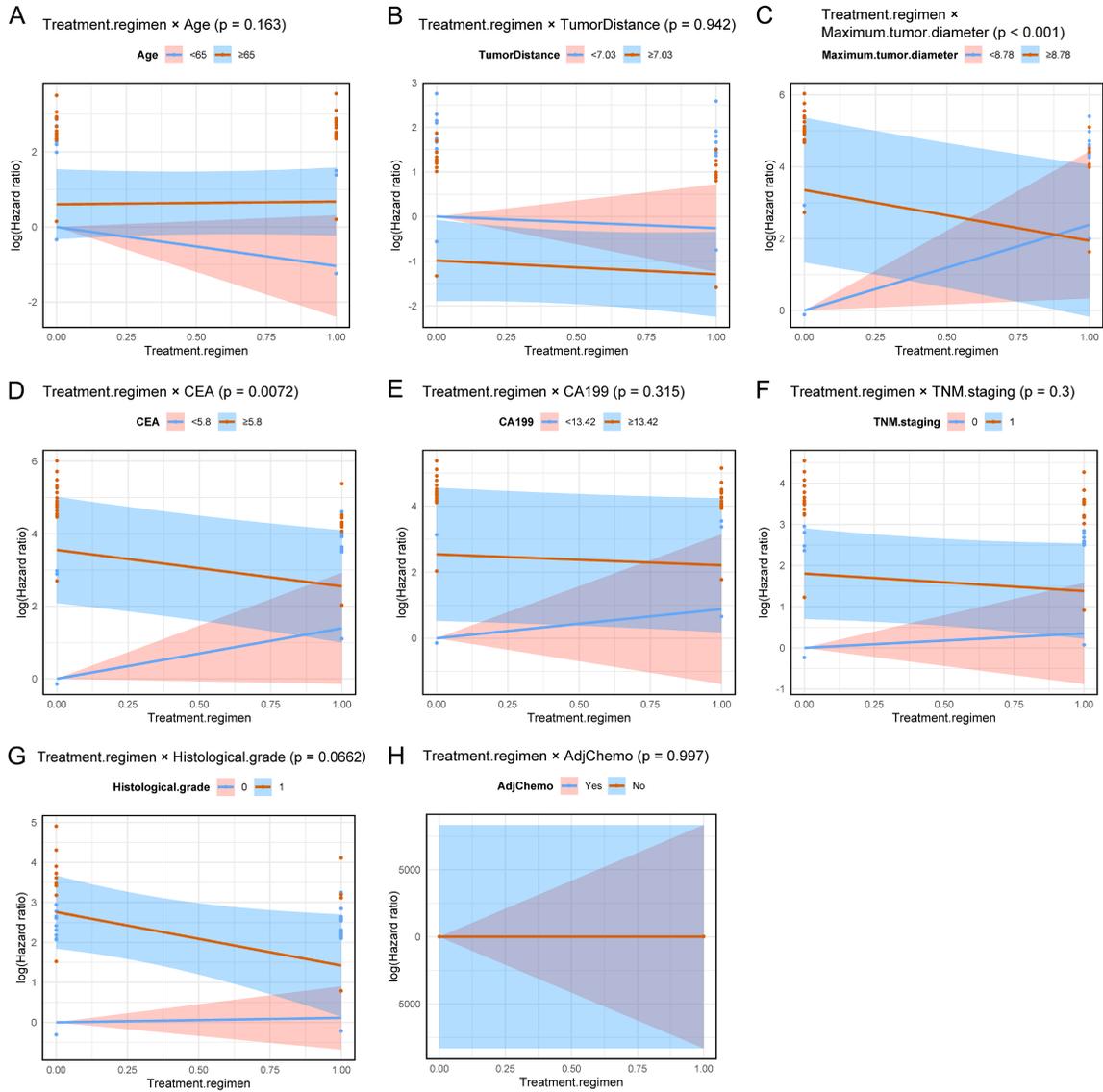


Figure 6. Treatment-Prognostic Factor Interactions for OS. A. Age; B. Tumor distance from anal verge; C. Maximum tumor diameter; D. Preoperative CEA level; E. Preoperative CA19-9 level; F. TNM staging; G. Histological grade; H. Postoperative adjuvant chemotherapy. Note: OS, overall survival; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; TNM, Tumor-Node-Metastasis.

Multivariate analysis showed that not preserving LCA independently elevated the risk of reduced RFS. It is worth noting that despite the presence of statistical significance in recurrence and metastasis, the three-year OS rate differed insignificantly. This phenomenon may reflect that under the modern comprehensive treatment model, early detection of recurrence and metastasis can still lead to better survival outcomes through timely intervention. It also suggests the safety of preserving the LCA in maintaining radicality.

Comparative analysis with previous studies

In recent years, the research on LCA preservation in RC surgery has gradually increased, but the conclusions vary. Zheng et al. [14] demonstrate that retaining LCA is effective in reducing AL incidence, reporting an incidence of 3.3% in the LCA-preservation group and 13.3% in the non-preservation group, which is consistent with the trend observed herein. However, they fail to comprehensively evaluate long-term survival differences due to a limited sample

size and follow-up duration. In the large-scale meta-analysis (6,247 patients in 17 studies) by Fan et al. [19], preserving LCA is clearly indicated to reduce AL rates (OR=0.78, P=0.03), while showing no notable differences in 5-year mortality, lymph node yield, and postoperative complications. Literature [13] shows that in laparoscopic anterior resection of low RC, LCA retention reduced AL risk without affecting surgical or oncological outcomes, which further supports the safety of LCA preservation. Other studies [10, 20] reported that in robotic-assisted and laparoscopic radical resection of RC, preserving LCA not only reduces intraoperative blood loss but also significantly shortens the time for removing the urinary catheter, lowers the incidence of urinary retention, and improves postoperative urinary and reproductive functions. This is completely consistent with the findings of this study regarding the perioperative benefits. In laparoscopic total mesorectal excision, LCA preservation also led to markedly reduced AL (OR=0.44, P<0.0001) and postoperative urogenital dysfunction incidences, with a shorter time to intestinal function restoration [21].

In the latest meta-analysis, including 17 studies by Reyaz et al. [22], low ligation (preserving LCA) was related to a reduced AL risk and shortened time to initial flatus, providing updated evidence-based support for the perioperative advantages of LCA. Si et al.'s large-scale systematic review [23] included 30 studies, validating the ability of low ligation to lower AL development possibilities and significantly reduce urinary dysfunction occurrences, which is highly consistent with the reduction of uroschesis observed in this study.

The uniqueness of this study lies in the analysis of lapNOSES, a field that has been rarely explored in previous research. NOSES, as an emerging minimally invasive surgical method, removes specimens through natural body orifices, eliminating the need for additional incisions and further reducing surgical trauma. In this context, preserving LCA not only conforms to the minimal invasiveness concept but also plays an important role in protecting the blood supply and preventing complications. Compared with traditional open surgery or conventional laparoscopic surgery, the technique of preserving LCA in NOSES is more feasible and

enables a better surgical field of vision, which provides favorable conditions for fine anatomy and vascular protection.

The traditional view holds that performing high ligation of the IMA is a necessary condition for achieving D3 lymph node dissection. However, the data from this study show that, while ensuring adequate lymph node dissection, preserving the LCA does not affect the oncological radicality of the treatment. Instead, it leads to a reduction in the risk of recurrence and metastasis. A meta-analysis by Yin et al. [24] further confirmed that compared with high ligation, low ligation combined with high dissection (LL+HD) significantly reduced the AL incidence while ensuring equivalent IMA root lymph node dissection and comparable long-term oncology outcomes. Another study also supports the decreased AL incidence by low ligation versus the high ligation technique (5.6% vs. 14.9%, P=0.041) [25], offering an important reference for the selection of treatment strategies for specific anatomical sites. This suggests that we need to re-examine the traditional surgical concept and formulate more individualized treatment strategies under the guidance of evidence-based medicine.

Exploration of underlying biological mechanisms

As an important branch of the IMA, LCA mainly supplies the left colon and part of the sigmoid colon. The vascular anatomy study by Wang et al. [8] revealed that there are three main types of anatomical variations in the branches of the IMA. Understanding these variations is crucial for performing vascular resection and lymph node dissection while preserving the LCA during laparoscopic radical surgery. Cirocchi et al. [26] conducted a systematic review and meta-analysis that included 19 studies involving 2,040 patients. They detailed the anatomical variations of the LCA: the overall LCA absence prevalence was 1.2%, the Type I and Type II variation incidence was approximately 50% each, and the distance from the IMA origin to the LCA origin averaged 40.41 mm. These anatomical data provide important references for surgical strategy formulation. In particular, the absence of the LCA may lead to insufficient vascularization of the proximal colon, thereby increasing the risk of AL.

Anatomical studies have shown that the LCA and the left branch of the middle colic artery, as well as the sigmoid colon artery, form a rich collateral circulation through marginal arteries. However, this compensatory ability shows significant individual differences, especially in elderly patients, diabetic patients, or those with arteriosclerosis, where the compensatory function of the marginal arteries may be insufficient. In this study, the significant improvement of intestinal perfusion in LCA-preserved patients is the direct embodiment of this anatomical advantage. Kimura et al. [27] objectively evaluated the influence of IMA ligation level on anastomotic perfusion by indocyanine green angiography, revealing greater blood perfusion abnormalities as well as a higher poor perfusion rate in the high versus low ligation group (2.8% vs. 1.5%), though not reaching statistical significance. Feng et al.'s prospective randomized study [28] further confirmed that 2 patients in the high ligation group needed extended intestinal segment resection and splenic flexure mobilization ranges due to anastomotic ischemia, compared to zero cases in the low ligation group showing intestinal segment ischemia, which intuitively verified the important value of LCA preservation in blood supply protection.

From an oncological perspective, the safety of preserving the LCA is based on the following aspects: First, RC lymphatics primarily drain upward via the rectal and inferior mesenteric vessels, and the lymph nodes around the LCA are not the main route of metastasis. Second, modern imaging technology and preoperative evaluation can accurately judge lymph node metastasis and provide basis for surgical strategy selection. Third, this study shows no significant inter-group difference in the lymph node yield from station 253, which shows that adequate lymphadenectomy can be achieved while preserving LCA.

It is noteworthy that the reduction in recurrence and metastasis rate in the LCA-preservation group may be related to many mechanisms. Besides avoiding AL-induced local immunosuppression and inflammation, good perfusion is also beneficial to the tolerance and effectiveness of postoperative adjuvant therapy. Postoperative adjuvant chemotherapy was identified in this research to independently protect RFS and OS, while preserving LCA creates

favorable conditions for timely adjuvant therapy initiation by reducing complications and shortening recovery time.

Clinical value of interaction analysis for informing decision-making

Our interaction analysis for OS provides an important basis for treatment strategy individualization, identifying a robust MTD-treatment plan interaction. Not preserving LCA significantly increases the death risk in those detected with larger tumor diameters, suggesting possible greater survival benefits brought by preserving LCA for patients with a larger tumor burden. This may be due to greater surgical trauma and relatively poorer tissue healing associated with larger tumors. By maintaining a good perfusion status, preserving LCA reduces postoperative complications and thus enhances overall prognosis.

In neoadjuvant therapy-treated RC patients, keeping LCA ensures radical lymphadenectomy and effectively reduces postoperative AL without an obvious increase in operation duration and bleeding volume, further supporting its implications for high-risk populations [29]. Zhong et al. [30] specifically meta-analyzed IMA treatment strategies in laparoscopic RC surgery, noting a lowered AL risk, shortened first postoperative exhaust time, and reduced hospitalization time in those keeping LCA, which reflected the advantages of keeping LCA in promoting postoperative rehabilitation.

The preoperative CEA-treatment plan interaction also attracts our attention. CEA (a critical biomarker for colorectal cancer) implies a stronger tumor invasive nature when its expression is increased. In cases of elevated CEA, preserving LCA may exert protective actions by reducing perioperative stress and maintaining immunity. More active adjuvant treatment is often indicated for patients exhibiting CEA elevation. The reduction in complications caused by keeping LCA further helps improve compliance.

Although we found no significant interaction between most prognostic factors and treatment schemes, these analyses provide valuable information for clinical decision-making. In preoperative evaluation, comprehensive consideration of tumor size, CEA expression,

and tumour differentiation is helpful for precision surgical strategy development. For high-risk cases, retaining LCA may bring greater clinical benefits; while the difference between the two strategies is relatively small for low-risk individuals, with the specific choice contingent upon the surgeon's experience and specific situation.

Research limitations and prospects

As a retrospective cohort study, this investigation inevitably has several limitations. First, the retrospective design may introduce selection bias. Despite well-balanced baseline characteristics, some unmeasured confounding factors may still affect the results. The decision to preserve or not preserve the LCA was made at the surgeon's discretion based on intraoperative findings, which could introduce confounding by indication. Second, although all operations were performed by the same surgical team, differences in learning curves over the 4-year study period cannot be entirely excluded. Third, the generalizability of results may be limited, as all samples were sourced from a single center. Fourth, although the follow-up time is sufficient to evaluate early recurrence and metastasis, long-term survival differences may not be fully captured. Additionally, certain factors such as preoperative performance status (ECOG score) and comorbidity indices were not systematically collected. Importantly, the interaction analyses presented here are exploratory in nature, conducted without pre-specified hypotheses and without adjustment for multiple comparisons. Therefore, these findings should be interpreted as hypothesis-generating rather than confirmatory, and require validation in independent cohorts.

Regarding current evidence, while most data on LCA preservation derives from observational studies, recent RCTs have provided higher-level evidence. Kimura et al. [27] using indocyanine green angiography found greater perfusion abnormalities in the high ligation group, and Feng et al. [28] reported anastomotic ischemia cases exclusively in the high ligation group. However, most RCTs have focused on short-term outcomes, and large-scale trials with extended follow-up are still needed to establish long-term oncological safety. Future research should focus on: multicenter prospec-

tive RCTs to eliminate selection bias; extended follow-up to 5 years or longer; individualized strategies based on biomarkers and molecular typing; standardized surgical quality control systems; and incorporation of objective perfusion assessment tools such as indocyanine green angiography.

Conclusion

Based on the results of this study, preserving the left colonic artery in lapNOSES for RC shows significant clinical benefits. Preserving LCA effectively reduces serious complications (e.g., AL) and improves perioperative safety. More importantly, it is related to a lower risk of recurrence and metastasis in three years, without affecting patient OS. Our interaction analysis on overall survival further revealed the importance of treatment strategy individualization, especially in cases of heavy tumor loads and CEA elevation, where preserving the LCA may confer greater benefits. These findings provide an important evidence-based medical basis for the technical optimization of NOSES for RC, support the surgical strategy of giving priority to preserving LCA on the premise of ensuring adequate lymphadenectomy, and truly realize the organic unity of radicality and safety.

Disclosure of conflict of interest

None.

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