

Risk factors for anastomotic leakage after anterior resection of rectal cancer with preservation of the left colic artery

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Abstract. Anastomotic leakage (AL) is a frequent and severe complication after anterior resection for rectal cancer. Most previous studies compared AL incidence between high and low ligation; however, the present study evaluated risk factors for AL in patients undergoing low ligation with preservation of the left colic artery, which has been associated with improved overall outcomes. Clinical data of patients with rectal cancer treated in the Second Department of General Surgery (Gastrointestinal Surgery) of The First Affiliated Hospital of Guangdong Pharmaceutical University (Guangzhou, China) between 2015 and 2024 were retrospectively reviewed, and patients meeting the inclusion and exclusion criteria were enrolled. Demographic characteristics and perioperative variables were collected. Differences between the AL group and the non-AL group were assessed using univariate analysis, and independent associations were identified using multivariate analysis to produce odds ratios (ORs). A total of 137 patients were included. Intergroup comparative tests showed significant differences in alcohol consumption, distance from the tumor to the anal verge and distance from the anastomosis to the anal verge between the AL group and the non-AL group ($P < 0.05$). Multivariate analysis identified alcohol consumption (OR=9.845; $P=0.0068$) and distance from the tumor to the anal verge (OR=0.485; $P=0.0368$) as independent factors associated with AL. In conclusion, alcohol consumption and distance from the tumor to the anal verge are independent risk factors for AL after anterior resection with preservation of the left colic artery. The risk of AL is 9.845-fold higher in patients with alcohol consumption. For each 1 cm decrease in distance

from the tumor to the anal verge, the risk of AL increases by 2.060-fold.

Introduction

Rectal cancer is the eighth most common cancer worldwide and the tenth leading cause of cancer-related mortality (1). Advances in surgical techniques and anastomotic devices have improved surgical outcomes. Abdominoperineal resection, previously regarded as the standard procedure, is no longer required for most patients; as a result, sphincter-preserving surgery has become feasible for a larger proportion of patients (2). Since Henri Hartmann introduced anterior resection in 1921, this approach has progressively replaced abdominoperineal resection and has become a notable surgical option for rectal cancer (3). Total mesorectal excision (TME) has subsequently evolved into a standardized technique for rectal cancer surgery (4). Despite these advances, postoperative complications remain common. Anastomotic leakage (AL) is of particular concern because it substantially worsens prognosis and quality of life (2,5,6). A meta-analysis including 9,735 patients who underwent anterior resection reported 941 cases of AL, corresponding to an overall incidence of 9.7% (range 0.0-36.3%); larger studies tended to report higher leakage rates (7).

Adequate blood supply to the anastomosis is widely recognized as essential (8). The level of vascular ligation has therefore received attention. High ligation refers to ligation at the origin of the inferior mesenteric artery. Low ligation refers to ligation distal to the origin of the left colic artery, with preservation of the left colic artery. Several studies have reported no clear association between ligation level and AL (9,10). By contrast, a previous meta-analysis found a notably higher leakage rate after high ligation than after low ligation (11). In addition, a review integrating tumor-related, anatomical and technical considerations supported advantages of low ligation over high ligation (8). However, most available evidence focuses on comparisons between high and low ligation, and to the best of our knowledge, detailed analyses restricted to low ligation remain limited.

The present study investigated risk factors for AL after anterior resection for rectal cancer with preservation of the left colic artery using a retrospective design. Identification of these

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factors may inform surgical strategy selection and postoperative management, with the aim of reducing AL incidence and improving clinical outcomes.

Patients and methods

Patient data selection. The present study used a retrospective design. Data were collected from patients with rectal cancer treated in the Department of Gastrointestinal Surgery, The First Affiliated Hospital of Guangdong Pharmaceutical University (Guangzhou, China), between 2015 and 2024. Strict inclusion and exclusion criteria were applied to improve the validity and reliability of the analysis.

Inclusion criteria. Patients were eligible if rectal cancer was confirmed by preoperative colonoscopic biopsy or postoperative pathology; anterior resection was performed by either a laparoscopic or open approach; preservation of the left colic artery branch of the inferior mesenteric artery was achieved during surgery; and complete medical records were available, including a clear documentation of AL.

Exclusion criteria. Patients were excluded if synchronous primary colorectal cancer was diagnosed; if surgery involved simultaneous resection of metastatic lesions or other organs; or if abdominoperineal resection or the Hartmann procedure was performed.

Assessment of AL. The diagnosis of postoperative AL was determined using clinical findings, drainage characteristics and imaging results. Clinical evaluation included unexplained recurrent fever, tachycardia and signs of localized or diffuse peritonitis. These signs included marked abdominal pain, distension, abdominal rigidity and rebound tenderness on physical examination. Drainage assessment focused on the presence of feculent material, which was considered a key indicator of AL. For imaging evaluation, fistulography was routinely performed (Fig. 1) to determine whether contrast medium entered the intestinal lumen and to estimate the size of the leakage site. Leakage size was used to guide subsequent treatment planning.

Classification of the severity of AL. The International Study Group of Rectal Cancer grading system was used to classify AL severity (12). This system defines grades A-C according to the level of clinical management required. Grade A indicates AL detected on imaging without clinical symptoms and requires no active intervention. Grade B indicates symptomatic AL that does not require reoperation and is generally managed with conservative measures, including antibiotics, pelvic drainage and transanal irrigation. Grade C indicates severe AL requiring surgical intervention, most commonly Hartmann procedure or ileostomy.

Patient data. To evaluate potential risk factors for AL, baseline and perioperative variables were collected. Baseline variables included sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, smoking status, alcohol consumption and comorbidities, including hypertension, coronary heart disease (CHD) and diabetes. Perioperative variables included tumor characteristics and preoperative, intraoperative and postoperative data.

Tumor characteristics included distance from the tumor inferior margin to the anal verge, distance from the anastomosis to the anal verge, tumor size and postoperative pathological Tumor-Node-Metastasis (TNM) staging. Distance from the tumor to the anal verge was measured during preoperative colonoscopy by the endoscopist. Distance from the anastomosis to the anal verge was calculated intraoperatively by subtracting the length of the distal resected bowel segment. Preoperative variables included hemoglobin, albumin, carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), bowel obstruction, hematochezia (including a positive fecal occult blood test) and neoadjuvant therapy status (with or without radiotherapy). Intraoperative variables included surgical approach, operative time, estimated blood loss and intraoperative perfusion of lobaplatin (13). Postoperative variables included anal exhaust (time to first passage of flatus, including the first passage from a stoma) and hyperthermic intraperitoneal chemotherapy with lobaplatin or fluorouracil (14). For anastomosis construction, a disposable end-to-end stapler (Covidien; Meditronic) was used to perform end-to-end anastomosis between the transected bowel ends. Placement of a rectal tube and creation of a prophylactic ileostomy were determined by bowel edema severity and distance from the tumor to the anal verge. Because these decisions were not randomized, both variables were excluded from the analysis. In routine practice, a protective ileostomy was typically performed when any of the following conditions were met: i) History of neoadjuvant radiotherapy with marked tissue edema and fibrosis; ii) ultra-low rectal cancer, defined as tumor located ≤ 5 cm from the anal verge; and iii) presence of bowel obstruction with severe intestinal edema.

For patients who did not meet these criteria or who refused ileostomy, transanal decompression with a rectal tube was used as an alternative strategy.

Data analysis. RStudio (R version 4.3.1; RStudio, Inc.) was used for statistical analysis. Intergroup comparative tests were performed first. Continuous variables with a normal distribution are presented as mean \pm standard deviation and compared using the Student's *t*-test. Continuous variables with a skewed distribution were summarized as median (interquartile range) and compared using the rank-sum test. Categorical variables were summarized as number (percentage) and compared using the Fisher's exact test, as appropriate. Variables with statistical significance in univariate analyses were further evaluated using binary logistic regression. Before model fitting, linearity in the logit for continuous predictors was assessed using the Box-Tidwell test. Multicollinearity among independent variables was evaluated using variance inflation factors (VIF) to support the stability of regression estimates.

Results

Baseline clinical and pathological characteristics. After screening, 161 patients with rectal cancer underwent surgery with preservation of the left colic artery. Among these, 137 patients met the inclusion and exclusion criteria and were included in the analysis. The cohort included 96 males and 41 females, with a mean age of 63.84 years (range, 32-89 years).



Figure 1. Fistulography showing the contrast agent injected through the drainage tube entering the intestinal tract.

Low rectal cancer, defined as distance from the anal verge ≤ 7 cm, was identified in 35 patients (25.55%), including 3 cases of AL. Ultra-low rectal cancer, defined as distance from the anal verge ≤ 5 cm, was identified in 13 patients (9.49%), including one case of AL. The median distance from the anastomosis to the anal verge was 6 cm (range, 2-14 cm). All patients had negative proximal and distal resection margins.

Incidence and severity of postoperative AL. Postoperative AL occurred in 9 patients, yielding an incidence of 6.57%, and all patients with AL were symptomatic. AL severity was classified as grade B in 7 patients and grade C in 2 patients. Only 1 patient with a prophylactic ileostomy developed AL, which was grade B. Among patients who underwent surgical management for AL, the median interval from AL diagnosis to surgery was 7 days (range, 4-12 days) (data not shown).

Comparison of baseline characteristics between AL and non-AL groups. Baseline characteristics of the non-AL group and the AL group are presented in Table I. Among the eight baseline variables, alcohol consumption was the only factor that differed significantly between groups ($P=0.0216$). In the non-AL group, 113 patients were non-drinkers and 15 patients reported alcohol consumption. In the AL group, 5 patients were non-drinkers and 4 patients reported alcohol consumption. Among the 19 patients with alcohol consumption, 2 reported a frequency of 5-10 times per month, whereas the remaining patients reported daily consumption. All 4 patients with AL who reported alcohol consumption drank alcohol daily. All 19 patients reported an alcohol consumption history >10 years. Among the 4 patients with AL, alcohol consumption duration exceeded 30 years in 2 patients, exceeded 25 years in 1 patient and exceeded 20 years in 1 patient. No significant

Table I. Characteristics of participants enrolled in the present study.

Characteristic	Non-AL (n=128)	AL (n=9)	P-value
Age, years	63.7 (11.46)	65.89 (7.06)	0.5728
Sex			>0.9999
Female	38 (29.69)	3 (33.33)	
Male	90 (70.31)	6 (66.67)	
BMI, kg/m ²	22.89 (3.33)	21.99 (2.62)	0.4257
ASA			0.4007
I	17 (13.28)	2 (22.22)	
II	65 (50.78)	3 (33.33)	
III	46 (35.94)	4 (44.44)	
Smoke			0.115
No	95 (74.22)	4 (44.44)	
Yes	33 (25.78)	5 (55.56)	
Alcohol			0.0216
No	113 (88.28)	5 (55.56)	
Yes	15 (11.72)	4 (44.44)	
Hypertension			>0.9999
No	84 (65.62)	6 (66.67)	
Yes	44 (34.38)	3 (33.33)	
CHD			>0.9999
No	114 (89.06)	8 (88.89)	
Yes	14 (10.94)	1 (11.11)	
Diabetes			0.3648
No	106 (82.81)	6 (66.67)	
Yes	22 (17.19)	3 (33.33)	

Data are presented as n (%) or mean (SD). BMI, body mass index; ASA, America Society of Anesthesiologist; CHD, coronary heart disease; AL, anastomotic leakage.

between-group differences were observed for sex, age, BMI, ASA classification, smoking status, hypertension, CHD or diabetes.

Comparison of perioperative data between AL and non-AL groups. Perioperative characteristics of the non-AL group and the AL group are summarized in Table II. Distance from the tumor to the anal verge and distance from the anastomosis to the anal verge differed significantly between groups ($P=0.0058$ and $P=0.0395$, respectively). The median distance from the tumor to the anal verge was 10 cm in the non-AL group and 8 cm in the AL group. The median distance from the anastomosis to the anal verge was 6 cm in the non-AL group and 5 cm in the AL group.

No significant between-group difference was observed for ultra-low rectal cancer ($P>0.999$). Among 13 patients with ultra-low rectal cancer, 9 patients (69.23%) underwent prophylactic ileostomy, whereas the remaining patients without ileostomy received rectal tube placement. Among 124 patients without ultra-low rectal cancer, 18 patients (14.52%) underwent

Table II. Factors of participants enrolled in the present study.

Factor	Non-AL (n=128)	AL (n=9)	P-value
Tumor distance, cm	10 (7.75,14)	8 (7,8)	0.0058
Ultra-low site			>0.9999
No	116 (90.62)	8 (88.89)	
Yes	12 (9.38)	1 (11.11)	
Anastomotic distance, cm	6 (5,9)	5 (4,6)	0.0395
Preoperative hemoglobin, g/l	122.1 (18.03)	117.11 (21.83)	0.4300
Preoperative albumin, g/l	38.68 (4.16)	40.14 (4.67)	0.3120
CEA	3.47 (1.95,7.16)	5.77 (3.22,27.07)	0.1042
CA199	10.93 (6.43,19.98)	15.43 (13.96,20.43)	0.2495
Bowel obstruction			0.3854
No	122 (95.31)	8 (88.89)	
Yes	6 (4.69)	1 (11.11)	
Hematochezia			>0.9999
No	10 (7.81)	0 (0)	
Yes	118 (92.19)	9 (100)	
Neoadjuvant therapy			>0.9999
No	103 (80.47)	7 (77.78)	
Yes	25 (19.53)	2 (22.22)	
Operation type			>0.9999
Open surgery	8 (6.25)	0 (0)	
Laparoscopic surgery	120 (93.75)	9 (100)	
Intraoperative lavage			0.3542
No	107 (83.59)	9 (100)	
Yes	21 (16.41)	0 (0)	
Time, min	274 (235,325)	295 (260,389)	0.2046
Blood loss, ml	30 (20,50)	30 (10,100)	0.9218
Tumor size, cm	4 (3,5.5)	5 (4,6)	0.2051
TNM			0.6499
I	27 (21.09)	1 (11.11)	
II	42 (32.81)	5 (55.56)	
III	45 (35.16)	2 (22.22)	
IV	14 (10.94)	1 (11.11)	
Hot perfusion			0.3015
No	72 (56.25)	7 (77.78)	
Yes	56 (43.75)	2 (22.22)	
Anal exhaust, day	2 (1,2)	2 (1,2)	0.9007

Continuous variables are shown as mean (SD) or median (IQR) and categorical data as n (%). Intraoperative perfusion, intraoperative perfusion of lobaplatin; postoperative perfusion, postoperative hyperthermic intraperitoneal chemotherapy; AL, anastomotic leakage; CEA, carcinoembryonic antigen; CA19-9 carbohydrate antigen 19-9; TNM, Tumor-Node-Metastasis.

prophylactic ileostomy. Preoperative hemoglobin, albumin, CEA and CA19-9 levels did not differ significantly between groups.

Preoperative bowel obstruction did not differ significantly between groups ($P=0.3854$); only 1 patient in the AL group had bowel obstruction. Among 6 patients with bowel obstruction in the non-AL group, 3 underwent prophylactic ileostomy. Preoperative hematochezia also showed no between-group difference ($P>0.999$); however, all 9 patients in the AL group had positive findings. Neoadjuvant therapy did not differ

significantly between groups ($P>0.999$). Among 27 patients who received neoadjuvant therapy, 17 received neoadjuvant radiotherapy, and no AL occurred; 11 of these 17 patients (64.71%) underwent prophylactic ileostomy. Among the 27 patients who received neoadjuvant therapy, 4 achieved complete pathological response, and no AL occurred.

Surgical approach (laparoscopic or open) did not differ between groups ($P>0.999$). Intraoperative perfusion of lobaplatin, operative time, blood loss, tumor size, tumor deposits,

Univariate and multivariate logistic regression analysis

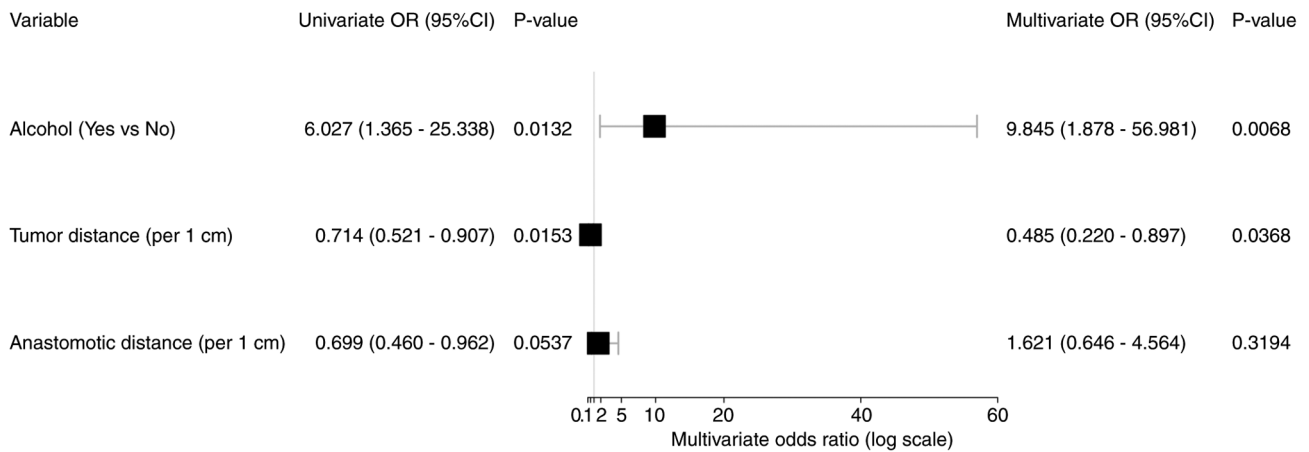


Figure 2. Forest plot of binary logistic regression analysis for anastomotic leakage risk factors. OR, odds ratio; Tumor distance: distance from the tumor to the anal verge (per 1 cm increase); Anastomotic distance: distance from the anastomosis to the anal verge (per 1 cm increase, not statistically significant).

TNM staging, postoperative hyperthermic intraperitoneal chemotherapy and time to first postoperative passage of flatus also showed no significant between-group differences.

Risk factors for AL by binary logistic regression analysis. Binary logistic regression results are shown in Fig. 2. In the univariate analysis, alcohol consumption was significantly associated with AL, with an odds ratio (OR) of 6.027 [95% confidence interval (CI), 1.365-25.338; P=0.0132]. The distance from the tumor to the anal verge was also significantly associated with AL, with an OR of 0.714 (95% CI, 0.521-0.907; P=0.0153). The distance from the anastomosis to the anal verge showed a non-significant trend with AL (OR, 0.699; 95% CI, 0.460-0.962; P=0.0537). In the multivariate analysis, alcohol consumption (OR, 9.845; 95% CI, 1.879-51.580; P=0.0068) and distance from the tumor to the anal verge (OR, 0.485; 95% CI, 0.246-0.957; P=0.0368) were significantly associated with AL. Distance from the anastomosis to the anal verge was not significantly associated with AL (P=0.3194).

Before model fitting, linearity in the logit for continuous predictors was assessed using the Box-Tidwell test, and no violations were identified (all P>0.05). Multicollinearity was evaluated using VIF, and all VIF values were <5, indicating no substantial multicollinearity among the independent variables.

Discussion

AL is a common and serious complication after anterior resection for rectal cancer and can adversely affect prognosis and quality of life (2,5). AL may lead to intra-abdominal abscess, wound infection, diffuse peritonitis and sepsis. These complications are associated with prolonged hospital stay, reoperation, increased mortality, and reduced survival (12).

Adequate blood supply to the anastomosis is widely recognized as essential (8). Low ligation preserves vascular inflow to the proximal colon adjacent to the anastomosis. By contrast, after high ligation, perfusion of the distal colon and sigmoid colon relies mainly on the middle colic artery and marginal arteries (8,15,16). High ligation has been reported to reduce

perfusion to the proximal bowel, particularly in patients with atherosclerosis (8,17,18). Intraoperative assessment of anastomotic perfusion was performed using visual indicators: Bowel wall color (bright red or pink indicates adequate perfusion; pallor or cyanosis suggests reduced perfusion), subserosal vessel pulsation (visible pulsation indicates adequate flow) and capillary bleeding after gentle serosal scratching (fresh oozing indicates adequate perfusion). These assessments allow real-time evaluation of anastomotic blood supply and support intraoperative decision-making. In the present cohort, the AL incidence was 6.57%, which is lower than the 9.7% reported in a meta-analysis including 9,735 patients (7).

In addition to blood supply, the management of tension at the anastomosis is also crucial. Intraoperatively, anastomotic tension is assessed using different methods in clinical practice. First, the active traction test, prior to anastomosis the proximal bowel is gently pulled to determine if it can naturally reach the distal stump without excessive tension. If the tension is high or mobilization is insufficient, further dissection of the proximal colon and splenic flexure is performed. In most cases, adequate mobilization after splenic flexure release ensures satisfactory tension, and high ligation of the inferior mesenteric artery (IMA) is not necessary. Second, the mesenteric laxity assessment, whether the proximal bowel can reach the anastomotic site without tension on the mesentery is evaluated. If the mesentery is tight or short, further root dissection or high IMA ligation may be considered to improve mobility, although this is rarely required in our experience. Finally, post-anastomosis bowel positioning, after the anastomosis is completed, the bowel is repositioned in the pelvis to assess natural alignment and rule out tension, recoil or twisting. If these issues persist, further mobilization is performed. In summary, with adequate mobilization of the proximal bowel and splenic flexure, preserving the left colic artery does not appear to increase anastomotic tension.

Since the introduction of TME, a marked concern with low ligation has been the potential retention of apical lymph nodes (group 253) around the inferior mesenteric artery, which could impact survival outcomes (10,19). However, previous

meta-analyses have shown no significant differences in survival outcomes between high and low ligation, with a similar number of lymph nodes harvested in both approaches (11,20). In fact, in the present institution, during the dissection of the left colic artery from the root of the inferior mesenteric artery, the apical lymph nodes are routinely clear, making it unlikely that low ligation would have a substantial effect on oncological outcomes.

Given that previous studies have primarily focused on comparing high and low ligation, there is a lack of detailed summaries on low ligation. Therefore, the present retrospective study aimed to analyze the influence of baseline demographic data and perioperative factors on the incidence of AL following rectal cancer anterior resection with preservation of the left colic artery. The results of the present univariate analysis of baseline data revealed that most baseline characteristics between the non-AL and AL groups did not differ significantly, with the only statistically significant difference being alcohol consumption. A higher proportion of non-drinkers was found in the non-AL group, suggesting that alcohol consumption may increase the risk of AL, consistent with previous studies (21-24). A total of four patients in the AL group, who were alcoholics, had consumed alcohol daily for >20 years. A study has indicated that consuming >35 drinks per week is associated with an increased risk of AL (23). Subclinical cardiac dysfunction, immunosuppression, impaired hemostasis and vitamin deficiencies, commonly observed in long-term heavy drinkers, may contribute to the increased risk of AL (23). Mechanistically, ethanol has been shown to reduce hypoxia-inducible factor 1- α and vascular endothelial growth factor signaling, leading to reduced capillary formation in the anastomosis, which is essential for healing (25). Therefore, for patients with heavy alcohol consumption, enhanced prevention of AL may be necessary, such as the use of an indwelling anal tube. Furthermore, the Enhanced Recovery After Surgery Society recommends that patients cease alcohol consumption for 4 weeks prior to surgery as a preventive measure (26,27). In the present study, other characteristics, such as sex, age, BMI, smoking status, hypertension, coronary artery disease and diabetes, showed no statistically significant differences between the two groups. However, other literature has suggested that male sex and smoking may increase the risk of AL (24,28). A prospective study also indicated that a BMI >30 may elevate the risk of AL in patients with colorectal cancer (29).

The results of the present univariate analysis of perioperative data revealed significant differences in the distance from the tumor to the anal verge and the distance from the anastomosis to the anal verge between the non-AL and AL groups, with the AL group having tumors and anastomoses located closer to the anal verge. Similar findings have been reported in other studies; one study indicated a notable association between tumor location (high, middle, low) and AL, with lower tumor locations associating with higher leakage rates (28). However, when patients were categorized based on the presence of ultra-low rectal cancer, no significant association with the occurrence of AL was found. This may be due to the fact that 69.23% of patients with ultra-low rectal cancer underwent preventive ileostomy, whereas the remaining patients had a rectal tube retained.

The binary logistic regression analysis performed in the present study, revealed that alcohol consumption and the distance between the tumor and the anal verge significantly affected the occurrence of AL, and were independent influencing factors. Specifically, the risk of AL in alcohol drinkers was 9.845 times higher than that in non-drinkers. In addition, for every 1 cm increase in the distance between the tumor and the anal verge, the risk of AL decreased by ~48.5%; conversely, for every 1 cm decrease, the risk increased by ~2.060 times. The reason why the distance from the anastomosis to the anal verge is not an independent factor may be related to the influence of the distance between the tumor and the anal verge.

Although the relationship between stomas and the risk of AL remains controversial, some studies suggest that stomas may reduce the occurrence of AL, whereas others have found no significant association (22,30-33). However, there is a general consensus that stomas can mitigate the adverse consequences of AL, such as fecal peritonitis and septic complications, and that when AL occurs, patients typically do not require reoperation (28,34-36). In the present study, only one patient with a stoma experienced AL, classified as grade B. The literature also indicates that selectively using stomas in high-risk patients with low anastomoses, who are at an increased risk of leakage, is most beneficial (22). In clinical practice, whether to perform preventive stoma formation or indwelling rectal tube placement is determined based on the degree of bowel edema and the distance from the anastomosis to the anal verge, a clinical decision strongly associated with tumor location (such as ultra-low rectal cancer, ≤ 5 cm from the anal verge). Some studies have suggested that leaving an anal stent in place after rectal cancer resection can substitute for preventive stoma formation to ensure the safety of the anastomosis (37,38). Therefore, either a prophylactic enterostomy or an indwelling anal tube are chosen, but it is rare to use both.

Notably, the non-random assignment of these prophylactic interventions may introduce a mild selection bias and influence the observed associations between tumor location and AL. Specifically, these interventions were targeted at high-risk patients with low/ultra-low rectal cancer (a subgroup closely associated with the short distance from the tumor to the anal verge, the key independent risk factor identified in the present study), and 69.23% of patients with ultra-low rectal cancer received prophylactic ileostomy in the present cohort. This uniform clinical intervention according to pre-defined indications likely attenuated the actual AL risk in this high-risk subgroup, which may have slightly reduced the effect size of tumor distance to the anal verge on AL occurrence in the regression analysis and explained why ultra-low rectal cancer was not a statistically significant factor for AL in our univariate analysis. Since these interventions were excluded from statistical analysis due to non-randomization, their confounding effect on the tumor location-AL association cannot be fully adjusted for in the model, but the bias is considered minimal given the standardized clinical decision-making process with no arbitrary assignment of interventions.

Although no significant differences were observed in other parameters, the literature reports inconsistent findings. The association between preoperative chemoradiotherapy and AL remains controversial, and published studies have yielded conflicting results (22,39-41). In a subgroup analysis of patients

without stoma formation, preoperative chemoradiotherapy was reported to increase the risk of AL (42). By contrast, no significant association between preoperative chemoradiotherapy and AL was identified in the present study. Notably, among patients who received preoperative radiotherapy, no cases of AL occurred, and 64.71% of these patients underwent preventive stoma formation. Previous studies have also suggested that complete pathological response after neoadjuvant therapy may be associated with a higher risk of AL than incomplete response (43,44). However, in the present study, none of the four patients with complete pathological response developed AL.

Prolonged operative duration can increase bacterial exposure and tissue injury, thereby increasing the risk of AL (45). A prospective study reported that an operative time >4 h was associated with a higher risk of AL in patients with colorectal cancer (46). A meta-analysis including 4,580 patients with rectal cancer showed that blood loss >100 ml increased the risk of AL (39). Intraoperative blood loss can cause hypovolemia, which may result in tissue ischemia and impaired anastomotic healing, which increases the risk of AL (47). In addition, transfusion administered for bleeding has also been associated with an increased risk of AL (39).

Overall, the present findings differ partly from previous studies. Differences in population characteristics and sample size may contribute to this discrepancy. Preservation of the left colic artery may also be protective because it improves blood supply to the anastomotic site. This mechanism may explain why several variables traditionally regarded as risk factors for anastomotic leakage were not significant in this cohort.

To the best of our knowledge, the present study is the first to specifically evaluate the association between left colic artery preservation and AL after anterior resection for rectal cancer. Several limitations should be acknowledged. First, the present study has a retrospective, single-institutional design and only evaluates the low ligation technique with left colic artery preservation; these factors collectively limit the broader applicability of the present results to other medical institutions, diverse patient populations and different surgical practices for rectal cancer. Second, the sample size was relatively small, with only 9 cases of AL as the primary outcome event, which raises the potential risk of model overfitting in the binary logistic regression analysis. In accordance with the classic events-per-variable (EPV) criterion, a minimum EPV of 10 is recommended for stable regression models (48). A total of three variables with significant differences in univariate analysis were initially included in the preliminary logistic regression model (EPV=3.0, 9 events/3 variables) and distance from the anastomosis to the anal verge was excluded from the final model due to lack of independent statistical significance. This optimization yielded a final model with two independent variables (EPV=4.5, 9 events/2 variables), which minimized overfitting risk to the greatest extent possible under the current sample size. Third, alcohol consumption was not consistently documented in medical records (such as specific intake volume), precluding further subgroup analyses based on drinking quantity; this finding was also partly driven by the imbalance in drinking status between the AL and non-AL groups, and its clinical significance needs confirmation in larger cohorts. Prospective, multi-institutional studies with

larger sample sizes and adequate AL events are urgently needed to validate our findings and provide more robust evidence for clinical practice.

In conclusion, the present study evaluated the association between left colic artery preservation and the occurrence of AL after rectal cancer resection. The results indicated that alcohol consumption and shorter distances from the tumor and anastomosis to the anal margin were associated with a higher risk of AL. Alcohol consumption and the distance from the tumor to the anal verge were identified as independent influencing factors. The risk of AL in patients with alcohol intake was ~9.845 times that in patients without alcohol intake. In addition, the risk of AL increased by ~2.060 times for each 1 cm decrease in the distance from the tumor to the anal verge. Given the limited sample size, prospective studies with larger cohorts are warranted to validate these findings.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ST, FZ, ZC and HC collected the data. ST wrote the manuscript. WZ, ST and DC analyzed and interpreted the data and revised the manuscript. ST and DC confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present retrospective study was approved by the Ethics Committee of the First Affiliated Hospital of Guangdong Pharmaceutical University (approval no. 2025-IIT-28). All patients signed a general informed consent form at the time of hospital admission, which authorized the anonymous use of their de-identified clinical data for scientific research purposes. In view of the retrospective nature of the study and the use of anonymized clinical data without any identification of individual patients, the Ethics Committee granted a waiver of specific informed consent for this study. All research procedures were conducted in accordance with the Declaration of Helsinki.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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