Original Article

Risk Factors for Anastomotic Leakage in Patients with Rectal Tumors Undergoing Robot-assisted Low Anterior Resection without Protective Ostomy

Kevin A. Wang[1]
Yen-Cheng Chen[2,3]
Ching-Chun Li[2,4]
Po-Jung Chen[2,3]
Wei-Chih Su[2,3]
Tsung-Kun Chang[2,3,5]
Ching-Wen Huang[2,6]
Hsiang-Lin Tsai[2,6]
Jaw-Yuan Wang[2,3,6,7,8,9,10]
[1]*Division of General Surgery, Department of Surgery, Shin Kong Wu Ho Su Memorial Hospital, Taipei,*
[2]*Division of Colorectal Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University,*
[3]*Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University,*
[4]*Department of Surgery, Kaohsiung Municipal Hsiaokang Hospital,*
[5]*Department of Surgery, Faculty of Post-Baccalaureate Medicine,*
[6]*Department of Surgery, Faculty of Medicine,*
[7]*Graduate Institute of Medicine, College of Medicine,*
[8]*Center for Cancer Research,*
[9]*Center for Liquid Biopsy and Cohort Research, Kaohsiung Medical University, Kaohsiung,*
[10]*Pingtung Hospital, Ministry of Health and Welfare, Pingtung, Taiwan*

Purpose. To assess the risk factors for anastomotic leakage in patients undergoing robotic-assisted rectal surgery. Only a few studies have been conducted to assess the risk factors for anastomotic leakage after robotic colorectal surgery.

Methods. This study retrospectively evaluated patients who underwent robot-assisted rectal surgery without protective ostomy from May 2013 to February 2022 at our institution. Univariate and multivariate analyses were performed to determine the risk factors for anastomotic leakage.

Results. Anastomotic leakage was noted in 26 (9.2%) of 282 patients. Preoperative albumin level < 3.5 mg/dL (OR 9.34, CI 2.38-36.63, $p = 0.001$), operation time > 300 minutes (OR 3.66, CI 1.33-10.06, $p = 0.012$), and use of two or more linear staple firings (OR 4.45, 95% CI 1.31-15.10, $p = 0.017$) were independent risk factors for anastomotic leakage.

Conclusions. This study identified three risk factors associated with anastomotic leakage after robotic rectal surgery. Preoperative hypoalbuminemia should be corrected for patients undergoing rectal surgery; prolonged operative times and multiple linear staple firings should warrant the potential creation of a protective ostomy.

[*J Soc Colon Rectal Surgeon (Taiwan) 2022;33:202-211*]

Key Words
Anastomotic leakage;
Robotic surgery;
Rectal surgery;
Risk factor

Received: April 29, 2022. Accepted: July 22, 2022.

Correspondence to: Dr. Prof. Jaw-Yuan Wang, Division of Colorectal Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, No. 100, Tzyou 1st Road, Kaohsiung 80708, Taiwan. Tel: 886-7-312-2805; Fax: 886-7-311-4679; E-mail: cy614112@ms14.hinet.net; jawyuanwang@gmail.com

Anastomotic leakage (AL) after colorectal surgery is a severe complication encountered by every colorectal surgeon to varying degrees. Several preoperative, perioperative and postoperative factors have been identified. Despite this knowledge, postoperative AL is still a major problem, and leak rates have been reported from 1% to 20% in previous studies and reviews.[1-4] AL has devastating consequences including reoperation, stoma creation, enterocutaneous fistulas, increased mortality and increased length of hospital stay.[5] Oncological outcome can also be negatively affected if AL occurs after surgery for cancer.[3,6,7]

Previous studies have revealed certain patient-related factors are related to AL such as male sex, higher body mass index (BMI), higher American Society of Anesthesiologists (ASA) classification, preoperative nutritional status, neoadjuvant therapy, tumor size and stage.[2,4,8-10] Perioperative factors such as operative time, blood loss, number of linear staple firings have also been reported to be associated with higher rate of AL.[2] Additionally, a recent prospective study revealed that several modifiable perioperative factors were associated with AL, namely low preoperative hemoglobin, contamination of the operative field, hyperglycemia, duration of surgery of more than three hours, administration of vasopressors, inaccurate timing of preoperative antibiotic prophylaxis, and application of epidural analgesia.[4]

Earlier studies included open and laparoscopic surgeries in the evaluation of AL risk factors, but more recent studies focused on laparoscopic approaches.[2,11-16] Comparative studies of robotic and laparoscopic rectal surgery have shown benefits of lower conversion rates and lesser length of hospital stay, but with longer operation times. However, no significant decrease of post-operative leakage rate was demonstrated.[17-21] Furthermore, a PubMed search revealed that only a few studies have evaluated the risk factors for AL after robot-assisted low anterior resection (LAR). An observational study of 2956 patients in 2021 revealed a 4.4% leakage rate and out of 2956 patients receiving sphincter-preserving surgery in only primary resection, 130 (4.4%) patients had anastomotic leakage and that low anterior resection (middle and lower rectum) and intersphincteric resection were significant independent risk factors for AL. A study in Mandarin, conducted in 2020 indicated that male sex, shorter distance from anal verge and longer operative times were significantly associated with post-operative AL after robotic surgery.[22-25]

It has been well established that lower rectal surgeries are associated with higher AL rates, so most surgeons perform protective diverting ileostomies or transverse colostomies to minimize the detrimental consequences of AL. It is reasonable to assume that AL is under-diagnosed in the presence of a protective ostomy. Exclusion of these cases can potentially allow a more accurate evaluation of leakage rate. The purpose of this study was to evaluate the potential risk factors for AL after robotic middle to upper rectal surgeries without protective ostomies.

Materials and Methods

Study population and patient selection

A retrospective analysis was performed for patients between May 2013 and February 2022. Patients with lower rectal lesions (< 4 cm from anal verge) received robotic-assisted intersphincteric resection (ISR) and coloanal hand-sewn anastomosis with protective ostomy were excluded from this study. Patients who had surgeries involving the creation of a protective ileostomy or colostomy were also excluded.

Data collection and definitions

A patient was deemed to have an AL if bile or feces was noted from the drain or during laparotomy and abdominal computed tomography revealed fluid accumulation near the anastomosis or in the pelvic cavity. Data was collected mainly from a database of all robotic colorectal surgeries performed at our institution. Patient demographics (sex, age, BMI, ASA classification, diabetes mellitus (DM), smoking history, steroid use) were recorded from the database and confirmed through chart review. Disease characteristics (neoadjuvant concurrent chemoradiotherapy (CCRT), time of surgery from last radiation therapy

(RT) to surgery, tumor size, distance of tumor from anal verge, and pathological TNM staging) were also included in the database. Preoperative biochemical test results (glucose, hemoglobin, and albumin) were obtained by chart review. Data on perioperative factors (operation time, intra-operative blood loss, EndoGIA thickness, number of linear staplers at distal end, stapler type, diameter of circular EEA) were collected from the database and confirmed through a review of operation records.

Age, BMI and ASA classification cut-offs were set according to those of previous studies and the average BMI of Asian populations.[4] Cut-off values and definitions are presented in Table 1. Time to surgery after RT was set at 10-12 weeks according to our previous study.[26] Because lower rectal lesions were excluded from this study, we compared the results between middle and upper rectal lesions. Pre-operative cut-off values for glucose, hemoglobin and albumin were set according to normal value ranges. Operation time was defined as skin incision to skin closure, and the cut-off value was set around the median operation time of 300 minutes.

Surgical procedures and operative technique

The docking method used was the five to six-port technique described in our previous study.[27] The da Vinci® Si Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) was docked over the patient's left flank. We performed D3 lymph node dissection and low ligation of the inferior mesenteric artery with preservation of the left colic artery in all patients with malignant disease using a high dissection and low ligation technique. Total mesorectal excision (TME) was also performed in all patients with malignant disease. After the completion of mobilization of the sigmoid or descending colon, mesocolon, and the entire rectum and mesorectum, low anterior resection (LAR) with double-stapled technique was performed.[28,29] Ethicon manual or powered staplers (Ethicon, Johnson & Johnson, Bridgewater, New Jersey, USA) were used to perform distal transection of the rectum. The EEAs were performed using Ethicon CDH circular staplers (Ethicon, Johnson & Johnson, Bridgewater, NewJersey, USA). We routinely performed diverting colostomy when the remaining rectal stump was < 4 cm. If the rectal stump was ≥ 4 cm, a methylene blue leak test was performed to decide whether to perform diverting colostomy. Finally, a drain was placed posterior to the anastomosis in all patients.[30,31]

Statistical analysis

Data was analyzed using Statistical Package for the Social Sciences software (SPSS, Chicago, IL, USA). Categorical variables are expressed as proportions (%). Differences between patients with and without AL were tested using Pearson's χ^2 test. Continuous variables are presented as mean ± standard deviation or median (range) depending on skewness. Dif-

Table 1. Variable cut-off values and definitions

Variable	Cut-off/definition
Demographics	
Sex	Male/female
Age	> 70
Body mass index (kg/m^2)	> 24
ASA classification	≥ 3
Diabetes mellitus	Yes
Smoking history	Yes
Steroid use	Yes
Disease characteristics	
Neoadjuvant CCRT	Yes
Time of surgery from RT (days)	< 84
Tumor size (cm)	> 2.1
Distance of tumor from AV (cm)	Upper rectum (> 8) Middle rectum (4-8)
Pathological TNM stage	0-II III-IV
Preoperative blood tests	
Glucose (mg/dL)	≥ 110
Hemoglobin (mg/dL)	< 10
Albumin (mg/dL)	< 3.5
Perioperative factors	
Operation time (min)	> 300
Blood loss (mL)	> 100
EndoGIA thickness (mm)	3.8/4.8
No. of linear staplers at distal end	Single/multiple
Stapler type	Manual/powered
Diameter of circular EEA (mm)	25/29/33

CCRT: concurrent chemoradiation therapy; RT: radiation therapy; AV: anal verge; EEA: end-to-end anastomosis; ASA: American Society of Anesthesiologists.

ferences between continuous variables were tested using Student's t test and p-values < 0.05 were considered statistically significant. In the univariate and multivariable logistic regression analysis, p-values < 0.05 were considered statistically significant. Both univariate and multivariate analyses were adjusted for sex, ASA score ≥ 3, diabetes mellitus and smoking history. Results are reported as odds ratios (OR) and 95% confidence intervals (CIs).

Results

A total of 546 patients were identified from our database, of which 464 patients had benign or malignant rectal lesions the 82 patients who received colon resections were excluded. Of these 464 patients, 136 patients underwent ISR and coloanal anastomoses with routine diverting distal transverse colostomies and were excluded from our study. An additional 46 patients from the middle and upper rectum groups received diverting distal transverse colostomies following the surgeon's decision, mostly because of positive methylene blue leak tests. These patients were also excluded, leaving 282 patients for our study population (Fig. 1). Of the 282 patients in our study, 26 (9.2%) patients were confirmed to have AL. The patients all received intervention with diverting transverse colostomies, and fortunately there were no patient mortalities.

The overall baseline characteristics, of the total population and separately as the "no anastomotic leakage" and "anastomotic leakage" groups are summarized in Table 2. Of the 282 patients, 151 (53.5%) were male and the mean age was 61.17 ± 11.74 years. There were no significant differences in the demographics between the leakage and no leakage groups. 183 (64.9%) patients received neoadjuvant CCRT and underwent elective robotic surgery carried out 80 days (range 29-356 days) after completion of RT. There were no significant differences between the leakage and no leakage groups in terms of neoadjuvant CCRT, time from last RT, tumor size, distance from anal verge, or pathological TNM staging. Differences in preoperative glucose and hemoglobin levels between the two groups were also not significant. In the leakage group there were significantly more patients with preoperative albumin level < 3.5 mg/dL than in the no leakage group (23.1% vs. 4.7%, $p = 0.004$). Significantly more patients in the leakage group had operative times > 5 hours (> 300 minutes) (53.8% vs. 27.0%, $p = 0.006$). There were no significant differences in blood loss, EndoGIA staple thickness, manual or powered stapler and the diameter of circular EEA stapler between the two groups. However, patients in the leakage group were significantly more likely to have received more than one linear stapler firing during transection of the distal end of the rectum compared with patients in the no leakage group (84.6% vs. 57.8%, $p = 0.010$).

In the univariate logistic regression analysis, preoperative albumin level less than 3.5 mg/dL (OR 7.5, 95% CI 2.36-23.90, $p = 0.001$), operative time greater than 300 minutes (OR 3.06, 95% CI 1.31-7.17, $p = 0.010$), and the use of multiple (2 or more) linear staple firings (OR 3.95, 95% CI 1.30-12.06, $p = 0.016$) were significantly associated with AL. Furthermore, multivariate analysis confirmed preoperative albumin

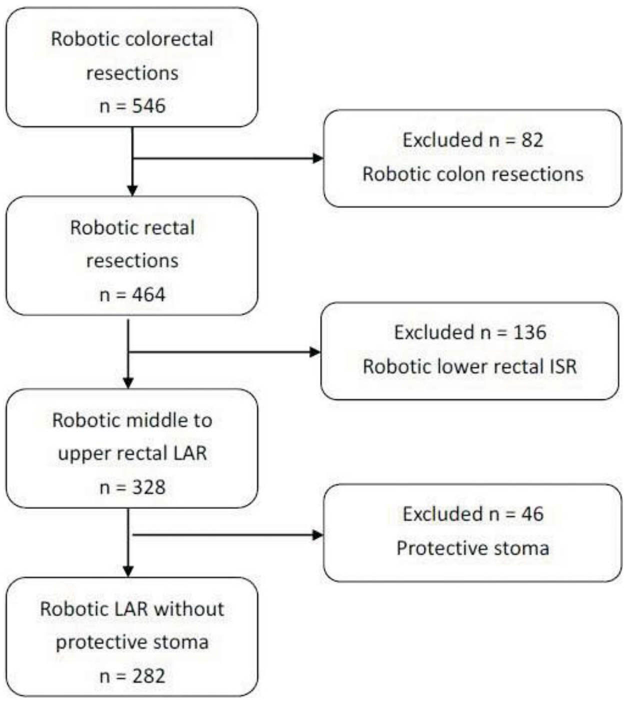

Fig. 1. Flow diagram of 282 enrolled patients. ISR: intersphincteric resection; LAR: low anterior resection.

Table 2. Baseline characteristics of patient population (n = 282)

Variables	Total population (n = 282) No. (%)	No anastomotic leakage (n = 256) No. (%)	Anastomotic leakage (n = 26) No. (%)	*p*-value
Demographics				
Sex				0.222
Male	151 (53.5%)	134 (52.3%)	17 (65.4%)	
Female	131 (46.5%)	122 (47.7%)	9 (34.6%)	
Age	61.17 ± 11.74	61.20 ± 11.80	60.92 ± 11.18	0.911
≤ 70	227 (80.5%)	206 (80.5%)	21 (80.8%)	
> 70	55 (19.5%)	50 (19.5%)	5 (19.2%)	
Body mass index (kg/m^2)	24.3 ± 3.39			0.547
≤ 24	141 (50.0%)	125 (48.8%)	16 (61.5%)	
> 24	141 (50.0%)	131 (51.2%)	10 (38.5%)	
ASA classification				0.986
< 3	174 (61.7%)	158 (61.7%)	16 (61.5%)	
≥ 3	108 (38.3%)	98 (38.3%)	10 (38.5%)	
Diabetes mellitus	63 (22.3%)	55 (21.5%)	8 (30.8%)	0.322
Smoking history	42 (14.9%)	36 (14.1%)	6 (23.1%)	0.245
Steroid use	1 (0.4%)	1 (0.4%)	0 (0.0%)	0.75
Disease characteristics				
Neoadjuvant CCRT	183 (64.9%)	165 (64.5%)	18 (69.2%)	0.673
Time of surgery from RT (days)	80 (29-356)	91 (43)	105 (67)	0.285
≤ 84	125 (68.3%)	115 (69.7%)	10 (55.6%)	
> 84	58 (31.7%)	50 (30.3%)	8 (44.4%)	
Tumor size (cm)	2.29 ± 1.88	2.26 ± 1.92	2.59 ± 1.43	0.684
≤ 2.1	142 (50.5%)	130 (51.0%)	12 (46.2%)	
> 2.1	139 (49.5%)	125 (49.0%)	14 (53.8%)	
Distance of tumor from AV (cm)	8 (4-15)	8 (4-15)	8 (4-15)	0.539
Upper rectum (> 8)	127 (45.0%)	117 (45.7%)	10 (38.5%)	
Middle rectum (4-8)	155 (55.0%)	139 (54.3%)	16 (61.5%)	
Pathological TNM stage				0.288
Tis or benign	52 (19.5%)	44 (17.5%)	8 (32.0%)	
I (T1-2N0M0)	77 (27.3%)	69 (27.4%)	8 (32.0%)	
II (T3-4N0M0)	56 (19.8%)	54 (21.4%)	2 (8.0%)	
III (T1-4N1-2M0)	65 (23.0%)	60 (23.8%)	5 (20.0%)	
IV (T1-4N1-2M1)	27 (9.7%)	25 (9.9%)	2 (8.0%)	
Preoperative blood tests				
Glucose (mg/dL)	110 (69-364)	110 (69-364)	117.5 (77-306)	0.309
< 110	137 (48.6%)	127 (49.6%)	10 (38.5%)	
≥ 110	145 (51.4%)	129 (50.4%)	16 (61.5%)	
Hemoglobin (mg/dL)	12.3 (7.7-18.0)	12.35 (7.7-15.9)	11.70 (8.3-18.1)	0.705
≥ 10	262 (92.9%)	238 (93.0%)	24 (92.3%)	
< 10	20 (7.1%)	18 (7.0%)	2 (7.7%)	
Albumin (mg/dL)	4.41 (2.79-5.12)	4.46 (2.79-5.12)	4.10 (3.07-5.04)	**0.004**
≥ 3.5	263 (93.3%)	244 (95.3%)	20 (76.9%)	
< 3.5	19 (6.7%)	12 (4.7%)	6 (23.1%)	
Perioperative factors				
Operation time (min)	280 (180-795)	280 (180-795)	315 (210-595)	**0.006**
≤ 300	199 (70.6%)	187 (73.0%)	12 (46.2%)	
> 300	83 (29.4%)	69 (27.0%)	14 (53.8%)	
Blood loss (mL)	60 (10-550)	50 (10-550)	95 (20-300)	0.808
≤ 100	217 (77.0%)	196 (76.6%)	21 (80.8%)	
> 100	65 (23.0%)	60 (23.4%)	5 (19.2%)	

Table 2. Continued

Variables	Total population (n = 282) No. (%)	No anastomotic leakage (n = 256) No. (%)	Anastomotic leakage (n = 26) No. (%)	*p*-value
EndoGIA thickness (mm)				0.359
3.8	206 (73.0%)	189 (73.8%)	17 (65.4%)	
4.8	76 (27.0%)	67 (26.2%)	9 (34.6%)	
No. of linear staplers at distal end				**0.010**
Single	112 (39.7%)	108 (42.2%)	4 (15.4%)	
Multiple (2-4)	170 (60.3%)	148 (57.8%)	22 (84.6%)	
Stapler type				0.974
Manual	32 (11.3%)	29 (11.3%)	3 (11.5%)	
Powered	250 (88.7%)	227 (88.7%)	23 (88.5%)	
Diameter of circular EEA (mm)				0.766
25	12 (4.3%)	11 (4.2%)	1 (3.8%)	
29	265 (94.0%)	240 (93.8%)	25 (96.2%)	
33	5 (1.7%)	5 (2.0%)	0 (0.0%)	

Data presented as number (%), mean ± standard deviation or median (range).
Overall anastomosis leakage rate: 9.2%.
Blood loss includes tissue fluid.
CCRT: concurrent chemoradiation therapy; RT: radiation therapy; AV: anal verge; EEA: end-to-end anastomosis; ASA: American Society of Anesthesiologists score.
Statistically significant *p*-values ($p < 0.05$) are in bold.

less than 3.5 mg/dL (OR 9.34, 95% CI 2.38-36.63, $p = 0.001$), operation time greater than 300 minutes (OR 3.66, 95% CI 1.33-10.06, $p = 0.012$), and use of two or more linear staple firings (OR 4.45, 95% CI 1.31-15.10, $p = 0.017$) as independent risk factors for AL (Table 3).

Discussion

Several studies have evaluated risk factors for AL after colorectal surgery. Sciuto et al. conducted a meta-analysis of studies from 2008 to 2018 on predictive factors for AL after laparoscopic colorectal surgery. Numerous factors have been reported to be associated with increased AL rate including male sex, higher BMI, low tumor location, larger tumor size, higher TNM staging, preoperative CCRT, multiple linear staple firings, longer operation times, greater intraoperative blood loss, and more recently factors such as lack of transanal tube placement and low gut microbiota diversity.[2]

Robotic surgery has been gaining popularity in colorectal surgery in recent years because of its ability to operate in deep and narrow spaces, 3-D and magnified views and articulated instruments. Understanding the risk factors associated with AL after robotic rectal surgery will provide surgeons more information to identify patients at high-risk of leakage, so that protective ostomies may be created to prevent clinical consequences of AL. To date, only a few studies have evaluated risk factors for AL after robotic rectal surgery. Most of the studies conducted included patients with protective ostomies. Park et al. reasoned that protective ostomies can mask subclinical AL, resulting in underestimation of leakage rates.[16] In this current study, all patients with protective ostomies were excluded for a better estimation of actual leakage rate. Furthermore, pelvic drainage tubes were placed routinely in all of our patients, so AL could be detected earlier and more accurately. In our study the leakage rate was 9.2% (26 out of 282), which is higher than the leakage rate (5.4%) of our previous study that included patients with protective ostomies.[32]

In our study, patients with preoperative serum albumin below 3.5 mg/dL has a significantly higher risk of AL. Poor preoperative nutritional status is a well-known factor that impairs anastomotic healing by af-

Table 3. Logistic regression analyses for anastomotic leakage

Variable	No. (%)	Univariate analysis		Multivariate analysis	
		OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Disease characteristics					
Neoadjuvant CCRT					
No	99 (35.1%)	1		1	
Yes	183 (64.9%)	1.11 (0.46-2.70)	0.821	1.111 (0.36-3.44)	0.855
Time of surgery from RT (days)					
≤ 84	125 (68.3%)	1		1	
> 84	58 (31.7%)	1.75 (0.64-4.77)	0.275	1.883 (0.55-6.42)	0.312
Tumor size (cm)					
≤ 2.1	142 (50.5%)	1		1	
> 2.1	139 (49.5%)	1.13 (0.50-2.58)	0.770	0.88 (0.34-2.30)	0.801
Distance of tumor from AV (cm)					
Upper rectum (> 8)	154 (54.6%)	1		1	
Middle rectum (4-8)	128 (45.4%)	1.30 (0.55-3.04)	0.549	0.72 (0.25-2.05)	0.537
Pathological TNM stage					
0-II	185 (66.8%)	1		1	
III-IV	92 (33.2%)	.776 (0.31-1.96)	0.591	1.22 (0.43-3.44)	0.708
Preoperative blood tests					
Glucose (mg/dL)					
< 110	137 (48.6%)	1		1	
≥ 110	145 (51.4%)	1.40 (0.58-3.36)	0.452	2.53 (0.89-7.19)	0.082
Hemoglobin (mg/dL)					
≥ 10	262 (92.9%)	1		1	
< 10	20 (7.1%)	1.13 (0.23-5.51)	0.885	1.01 (0.17-5.93)	0.989
Albumin (mg/dL)					
≥ 3.5	263 (93.3%)	1		1	
< 3.5	19 (6.7%)	7.50 (2.36-23.90)	**0.001**	9.34 (2.38-36.63)	**0.001**
Perioperative factors					
Operation time (min)					
≤ 300	199 (70.6%)	1		1	
> 300	83 (29.4%)	3.06 (1.31-7.17)	**0.010**	3.66 (1.33-10.06)	**0.012**
Blood loss (mL)					
≤ 100	217 (77.0%)	1		1	
> 100	65 (23.0%)	0.73 (0.26-2.03)	0.545	0.26 (0.07-1.02)	0.053
EndoGIA thickness (mm)					
3.8	206 (73.1%)	1		1	
4.8	76 (26.9%)	1.53 (0.65-3.65)	0.334	1.059 (0.37-3.01)	0.914
No. of linear staplers at distal end					
Single	112 (39.7%)	1		1	
Multiple (2-4)	170 (60.3%)	3.95 (1.30-12.06)	**0.016**	4.45 (1.31-15.10)	**0.017**

Univariate and multivariate analyses adjusted for: Sex, ASA score ≥ 3, diabetes mellitus and smoking history.
OR: odds ratio; CI: confidence interval.
Statistically significant *p*-values ($p < 0.05$) are in bold.

fecting collagen synthesis and fibroblast proliferation. The median operative time in our study is about 300 minutes or five hours. Operative times longer than this is significantly associated with AL. Longer operation times is indicative of intraoperative difficulties such as adhesions, bleeding, and excessive mesocolic and mesorectal fat, narrow pelvic cavity, larger bulky tumors and difficult transection of the rectum with linear staplers.

There have been several studies that focused solely on the effect of the number of linear staple firings on AL.[15,33,34] Our present study found that more than one staple firing significantly increased the risk of AL. Of our 282 patients, rectal transection with a single firing was achieved in 112 (39.7%) patients, which is higher than other studies that recorded single firings (31.0%).[15] Improved automated staplers with greater angulation such as SureForm™ (Intuitive Surgical, Inc., Sunnyvale, CA, USA), which are already available for the da Vinci® Xi Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA), may help increase the chance of single staple firings. Further studies are warranted to evaluate the impact of these improved linear staples on AL rate. Previous studies have identified neoadjuvant CCRT as independent risk factors for AL by multivariate analysis.[2] Interestingly, 183 (64.9%) patients received neoadjuvant CCRT in our study, but there was no significant increase in AL.

The major limitation of this study is that it was performed retrospectively. Without randomization, selection bias cannot be eliminated. Furthermore, the patients' medical histories could only be obtained by medical records, hence details of smoking history and steroid use could not be completely determined.

Conclusion

This study identified three risk factors associated with AL after robotic rectal surgery. Although the robotic system facilitates surgeons in several technical aspects of rectal surgery, there was still a 9.2% leakage rate in our robotic rectal resections without protective ostomies, which indicates that there are several patient-, disease- and operative-factors associated with AL that are independent to surgical method. Awareness of these factors should allow the surgeon to correct any modifiable factors preoperatively to minimize AL. This awareness can also enable surgeons to recognize perioperative factors other than leak tests that identify patients as high-risk for leakage so that protective ostomies may be created to lessen the severe clinical consequences of AL.

Acknowledgments

This work was supported by grants through funding from the Ministry of Science and Technology (MOST 109-2314-B-037-035, MOST 109-2314-B-037-040, MOST 109-2314-B-037-046-MY3, MOST 110-2314-B-037-097) and the Ministry of Health and Welfare (MOHW109-TDU-B-212-134026, MOHW 109-TDU-B-212-114006, MOHW110-TDU-B-212-1140026) and funded by the health and welfare surcharge of on tobacco products, and the Kaohsiung Medical University Hospital (KMUH110-0R37, KMUH 110-0R38, KMUH110-0M34, KMUH110-0M35, KMUH 110-0M36, KMUHSA11013, KMUH-DK(C) 110010, KMUH-DK(B)110004-3) and KMU Center for Cancer Research (KMU-TC111A04-1) and KMU Center for Liquid Biopsy and Cohort Research Center Grant (KMU-TC109B05) and KMU Office for Industry-Academic Collaboration (S109036), Kaohsiung Medical University. In addition, this study was supported by the Grant of Taiwan Precision Medicine Initiative and Taiwan Biobank, Academia Sinica, Taiwan, R.O.C.

References

1. van Rooijen SJ, Huisman D, Stuijvenberg M, et al. Intraoperative modifiable risk factors of colorectal anastomotic leakage: why surgeons and anesthesiologists should act together. *Int J Surg* 2016;36(PtA):183-200.
2. Sciuto A, Merola G, De Palma GD, et al. Predictive factors for anastomotic leakage after laparoscopic colorectal surgery. *World J Gastroenterol* 2018;24(21):2247-60.
3. Saur NM, Paulson EC. Operative management of anastomotic leaks after colorectal surgery. *Clin Colon Rectal Surg* 2019;32(3):190-5.
4. Huisman DE, Reudink M, van Rooijen SJ, et al. LekCheck: a prospective study to identify perioperative modifiable risk factors for anastomotic leakage in colorectal surgery. *Ann Surg* 2022;275(1):e189-97.
5. Chiu HC, Hsieh HM, Wan CL, et al. Cost-effectiveness of mini-laparotomy in patients with colorectal cancers: a propensity scoring matching approach. *PLoS One* 2019;14:e0209970.
6. Thomas MS, Margolin DA. Management of colorectal anastomotic leak. *Clin Colon Rectal Surg* 2016;29(2):138-44.
7. Karim A, Cubas V, Zaman S, et al. Anastomotic leak and cancer-specific outcomes after curative rectal cancer surgery: a systematic review and meta-analysis. *Tech Coloproctol* 2020;24(6):513-25.
8. Favuzza J. Risk factors for anastomotic leak, consideration for proximal diversion, and appropriate use of drains. *Clin*

Colon Rectal Surg 2021;34(6):366-70.

9. Ghuman A, Ganga R, Parisi Severino N, et al. Clinical factors contributing to anastomotic leak after mid-to-high colorectal anastomosis. *Am Surg* 2021:31348211041555.
10. Zarnescu EC, Zarnescu NO, Costea R. Updates of risk factors for anastomotic leakage after colorectal surgery. *Diagnostics (Basel)* 2021;11(12).
11. Alberts JC, Parvaiz A, Moran BJ. Predicting risk and diminishing the consequences of anastomotic dehiscence following rectal resection. *Colorectal Dis* 2003;5(5):478-82.
12. Peeters KC, Tollenaar RA, Marijnen CA, et al. Risk factors for anastomotic failure after total mesorectal excision of rectal cancer. *Br J Surg* 2005;92(2):211-6.
13. Silva-Velazco J, Stocchi L, Costedio M, et al. Is there anything we can modify among factors associated with morbidity following elective laparoscopic sigmoidectomy for diverticulitis? *Surg Endosc* 2016;30(8):3541-51.
14. Tanaka K, Okuda J, Yamamoto S, et al. Risk factors for anastomotic leakage after laparoscopic surgery with the double stapling technique for stage 0/I rectal carcinoma: a subgroup analysis of a multicenter, single-arm phase II trial. *Surg Today* 2017;47(10):1215-22.
15. Lee S, Ahn B, Lee S. The relationship between the number of intersections of staple lines and anastomotic leakage after the use of a double stapling technique in laparoscopic colorectal surgery. *Surg Laparosc Endosc Percutan Tech* 2017;27(4): 273-81.
16. Park JS, Choi GS, Kim SH, et al. Multicenter analysis of risk factors for anastomotic leakage after laparoscopic rectal cancer excision: the Korean laparoscopic colorectal surgery study group. *Ann Surg* 2013;257(4):665-71.
17. Prete FP, Pezzolla A, Prete F, et al. Robotic versus laparoscopic minimally invasive surgery for rectal cancer: a systematic review and meta-analysis of randomized controlled trials. *Ann Surg* 2018;267(6):1034-46.
18. Hoshino N, Sakamoto T, Hida K, et al. Robotic versus laparoscopic surgery for rectal cancer: an overview of systematic reviews with quality assessment of current evidence. *Surg Today* 2019;49(7):556-70.
19. Phan K, Kahlaee HR, Kim SH, et al. Laparoscopic vs. robotic rectal cancer surgery and the effect on conversion rates: a meta-analysis of randomized controlled trials and propensity-score-matched studies. *Tech Coloproctol* 2019;23(3): 221-30.
20. Wang X, Cao G, Mao W, et al. Robot-assisted versus laparoscopic surgery for rectal cancer: a systematic review and meta-analysis. *J Cancer Res Ther* 2020;16(5):979-89.
21. Safiejko K, Tarkowski R, Koselak M, et al. Robotic-assisted vs. standard laparoscopic surgery for rectal cancer resection: a systematic review and meta-analysis of 19,731 patients. *Cancers (Basel)* 2021;14(1).
22. Chen JW, Chang WJ, Zhang ZY, et al. Risk factors of anastomotic leakage after robotic surgery for low and mid rectal cancer. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020;23(4): 364-9.
23. Chen K, Shiomi A, Kagawa H, et al. Efficacy of a robotic stapler on symptomatic anastomotic leakage in robotic low anterior resection for rectal cancer. *Surg Today* 2022;52(1):120-8.
24. Ose I, Perdawood SK. A nationwide comparison of short-term outcomes after transanal, open, laparoscopic, and robot-assisted total mesorectal excision. *Colorectal Dis* 2021; 23(10):2671-80.
25. Xu J, Tang B, Li T, et al. Robotic colorectal cancer surgery in China: a nationwide retrospective observational study. *Surg Endosc* 2021;35(12):6591-603.
26. Huang CW, Su WC, Yin TC, et al. Time interval between the completion of radiotherapy and robotic-assisted surgery among patients with stage I-III rectal cancer undergoing preoperative chemoradiotherapy. *PLoS One* 2020;15(10):e0240742.
27. Huang CW, Yeh YS, Ma CJ, et al. Robotic colorectal surgery for laparoscopic surgeons with limited experience: preliminary experiences for 40 consecutive cases at a single medical center. *BMC Surg* 2015;15:73.
28. Huang CW, Yeh YS, Su WC, et al. Robotic surgery with high dissection and low ligation technique for consecutive patients with rectal cancer following preoperative concurrent chemoradiotherapy. *Int J Colorectal Dis* 2016;31(6):1169-77.
29. Yin TC, Su WC, Chen PJ, et al. Oncological outcomes of robotic-assisted surgery with high dissection and selective ligation technique for sigmoid colon and rectal cancer. *Front Oncol* 2020;10:570376.
30. Chen CW, Chen MJ, Yeh YS, et al. Intraoperative anastomotic dye test significantly decreases incidence of anastomotic leaks in patients undergoing resection for rectal cancer. *Tech Coloproctol* 2013;17(5):579-83.
31. Chen PJ, Su WC, Chang TK, et al. Oncological outcomes of robotic-assisted total mesorectal excision after neoadjuvant concurrent chemoradiotherapy in patients with rectal cancer. *Asian J Surg* 2021;44(7):957-63.
32. Huang CW, Tsai HL, Yeh YS, et al. Robotic-assisted total mesorectal excision with the single-docking technique for patients with rectal cancer. *BMC Surg* 2017;17(1):126.
33. Ito M, Sugito M, Kobayashi A, et al. Relationship between multiple numbers of stapler firings during rectal division and anastomotic leakage after laparoscopic rectal resection. *Int J Colorectal Dis* 2008;23(7):703-7.
34. Balciscueta Z, Uribe N, Caubet L, et al. Impact of the number of stapler firings on anastomotic leakage in laparoscopic rectal surgery: a systematic review and meta-analysis. *Tech Coloproctol* 2020;24(9):919-25.

原　著

直腸腫瘤的病人接受達文西機械輔助性低前位切除手術且無保護性造口術後腸吻合滲漏之危險因子

王凱緯[1]　陳彥成[2,3]　李京錞[2,4]　陳柏榕[2,3]　蘇偉智[2,3]　張琮琨[2,3,5]
黃敬文[2,6]　蔡祥麟[2,6]　王照元[2,3,6,7,8,9,10]

[1]新光吳火獅紀念醫院　外科部　一般外科
[2]高雄醫學大學附設醫院　外科部　大腸直腸外科
[3]高雄醫學大學　醫學院　臨床醫學研究所
[4]高雄市立小港醫院　外科部
[5]高雄醫學大學　醫學院　學士後醫學系　外科學科
[6]高雄醫學大學　醫學院　醫學系　外科學科
[7]高雄醫學大學　醫學院　醫學研究所
[8]高雄醫學大學　癌症研究中心
[9]高雄醫學大學　液態生物檢體暨世代研究中心
[10]衛生福利部　屏東醫院

目的　評估接受達文西機械直腸輔助手術患者術後腸吻合滲漏的危險因子。很少有評估達文西機械結直腸輔助手術後發生腸吻合滲漏危險因子的研究發表。

方法　本研究是回顧性分析。針對本機構從 2013 年 5 月至 2022 年 2 月接受機械輔助直腸手術，且無施行保護性腸造口的患者，進行單變異數和多變異數分析找尋出腸吻合滲漏的危險因子。

結果　282 名患者中有 26 名 (9.2%) 出現吻合滲漏。術前白蛋白低於 3.5 mg/dL (OR 9.34, CI 2.38-36.63, $p = 0.001$)，手術時間超過 300 分鐘 (OR 3.66, CI 1.33-10.06, $p = 0.012$) 和使用多次 linear staples (OR 4.45, CI 1.31-15.10, $p = 0.017$) 是腸吻合滲漏的獨立危險因子。

結論　本研究找尋出三個在機械輔助直腸手術後腸吻合滲漏的危險因子。要接受直腸手術的患者，如果白蛋白過低，術前應該先補充營養。另外，手術時間過長或在截斷直腸時使用二次以上的 linear staples 時，術中應可能需要加做保護性造口。

關鍵詞　腸吻合滲漏、機械輔助手術、直腸手術、危險因子。