Identifying Important Predictors for Anastomotic Leak After Colon and Rectal Resection

Prospective Study on 616 Patients

Koianka Trencheva, MS, Kevin P. Morrissey, MD,* Martin Wells, PhD,‡ Carol A. Mancuso, MD,†§ Sang W. Lee, MD,* Toyooki Sonoda, MD,* Fabrizio Michelassi, MD,* Mary E. Charlson, MD,† and Jeffrey W. Milsom, MD**

Objective: The purpose of this study was to identify patient, clinical, and surgical factors that may predispose patients to anastomotic leak (AL) after large bowel surgery.

Background: Anastomotic leak is still one of the most devastating complications following colorectal surgery. Knowledge about factors predisposing patients to AL is vital to its early detection, decision making for surgical time, managing preoperative risk factors, and postoperative complications.

Methods: This was a prospective observational, quality improvement study in a cohort of 616 patients undergoing colorectal resection in a single institution with the main outcome being AL within 30 days postoperatively. Some of the predictor variables were age, sex, Charlson Comorbidity Index (CCI), radiation and chemotherapy, immunomodulator medications, albumin, preoperative diagnoses, surgical procedure(s), surgical technique (laparoscopic vs open), anastomotic technique (staple vs handsewn), number of major arteries ligated at surgery, surgeon's experience, presence of infectious condition at surgery, intraoperative adverse events, and functional status using 36-Item Short Form General Health Survey.

Results: Of the 616 patients, 53.4% were female. The median age of the patients was 63 years and the mean body mass index was 25.9 kg/m^2. Of them, 80.3% patients had laparoscopic surgery and 19.5% had open surgery. AL occurred in 5.7% (35) patients. In multivariate analysis, significant independent predictors for leak were anastomoses less than 10 cm from the anal verge, CCI of 3 or more, high inferior mesenteric artery ligation (above left colic artery), intraoperative complications, and being of the male sex.

Conclusions: Multiple risk factors exist that predispose patients to ALs. These risk factors should be considered before and during the surgical care of colorectal patients.

Keywords: anastomotic leak, leak after colorectal resection, prospective, risk factors for leak

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Despite many advances in surgery, the quest for uneventful healing of the intestinal anastomosis remains a challenge after colon and rectal resections. The prevalence of anastomotic leak (AL) has been reported to be between 0.5% and 21% after colon and rectal resections.[1–5] The incidence of clinically significant AL after colorectal surgeries is between 1% and 12% overall and up to 10% to 14% in low colorectal resections.[5–8] The rates of morbidity and mortality significantly increase after AL, with mortality reported between 12% and 27%.[8–12] The mean length of stay in the hospital for patients with AL has been described between 36 and 39 days, approximately 4 times longer than for patients without leak.[6,9] Multiple reoperations and stoma creation are often necessary to control the leak, which significantly increases health risks and health care costs up to 5 times that of patients with no leak.[13]

Limited quantitative knowledge about risk factors for AL is available today despite numerous studies reporting the rate of AL. Most of the AL risk factors described are derived from retrospective studies or from prospective studies designed to assess new surgical techniques, technology, or medical treatments. Although AL has been an outcome variable in such studies, identifying predictors for AL has not been the primary focus. The large spectrum of colorectal diseases, the variety of surgical and medical treatment modalities, different surgical anastomotic technologies, and not least of all, lack of a universal definition for AL contribute to the complexity of studying predisposing factors for AL. As a consequence, there is no established assessment of risk schema for AL before surgical treatment nor are there solidly established guidelines for its management. Knowledge about factors predisposing to AL is the key to its early detection and improving decision making for surgical treatment time, anticipating postoperative complications, and managing preoperative risk factors.

The primary aims of this prospective observational study were (1) to identify important predictors and/or risk factors contributing to AL after large bowel resection in both laparoscopic and open surgeries and (2) to develop a predictive model for AL based on the study findings. In this article, we present only the predictors and/or risk factors contributing to AL.

METHODS

This was an institutional review board approved, prospective study of predictive factors contributing to AL. A cohort of 616 consecutive patients from the Colorectal Surgery practice at Weill Cornell Medical College–New York Presbyterian Hospital were studied from the first clinic visit and decision for surgery until 30 days after surgery. The study time period was 3 years, and patients from all 5 colorectal surgeons were included. Patients were eligible if they were 18 years of age or older and needed a laparoscopic or open large bowel resection with anastomosis as standard treatment for their medical conditions. Patients not requiring an anastomosis and special group subjects (pregnant women, prisoners, and cognitively impaired subjects) were excluded. Predictor and outcome variables were selected during the design of the study based on clinical expertise and literature review. The predictive variables collected are listed in Table 1. Variables that were outcomes or interventions were not evaluated for the prediction of AL. Outcome variables were postsurgical complications, gastrointestinal function restoration, pain management, and readmission and reoperation rates. The primary outcome was AL within 30 days postoperatively.

From the *Section of Colorectal Surgery, Department of Surgery; †Department of Medicine, Weill Cornell Medical College, New York, NY; ‡Department of Biostatistics, Cornell University, Ithaca, NY; and §Hospital for Special Surgery, New York, NY.

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Reprints: Koianka Trencheva, MS, Department of Surgery, Weill Cornell Medical College, New York, NY 10065. E-mail: kivanova@med.cornell.edu.

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TABLE 1. Risk Factors Evaluated

Preoperative Factors	Intraoperative Factors
Age	ASA
Sex	Oxygen saturation <90 />5 min
BMI, kg/m^2	
Smoking history	Intraoperative rectal wash
Current smoking	
Alcohol	
Weight lost > 5 kg/3 mo	State of UC and CD (inactive/active)
Albumin < 3.5	Surgical technique (laparoscopic/HALS/open)
ESR	Hepatic flexure takedown
C-reactive protein (for IBD patients only, n = 101)	Splenic flexure takedown
CCI score	Anastomotic technique (stapled/handsewn)
CCI score ≥ 3	Anastomotic fashion side-to-side
Hypertension	Side-to-end
Anemia	End-to-end
Diabetes	J-pouch
Insulin-dependent diabetes	Anastomotic anatomic location
Cardiovascular diseases	Ileocolic
Dialysis	Ileorectal
Anorectal diseases	Colocolonic
Allergies	Colorectal
Previous abdominal surgeries	Coloanal
	Ileoanal (j-pouch)
Number of previous abdominal surgeries	Anastomotic site (colon/rectal/anal)
Repeat rectal or pouch surgery	Rectal anastomosis level from anal verge
Radiation therapy	Upper rectal >10 cm
Chemotherapy	Middle rectal 7–10 cm
Neoadjuvant therapy	Low rectal 1–6 cm
Steroids use within 6 mo	Anastomosis ≤ 10 and ≥ 10 cm from anal verge
Immunosuppressant use within 6 mo	Major artery ligated during surgery
Blood transfusion within 72 hr before surgery	Ileocolic
Bacteremia within 48 hr	Right colic
Surgeon	Middle colic
Preoperative diagnosis (Neoplasm/IBD/DV/Other)	Left colic
Preoperative 36-Item Short Form Health Survey	Sigmoid arteries
Preoperative bowel preparation	Superior rectal arteries
	IMA
	IMA above left colic
	IMA below left colic
	Leak test
	Estimated blood loss, mL
	Blood transfusion in operating room
	Intraoperative complications
	Intraoperative surgical site contamination
	Presence of infectious condition at beginning surgery

BMI indicates body mass index; ASA, American Society of Anesthesiologists; HALS, hand-assisted laparoscopic surgery; IBD/DV, inflammatory bowel disease/diverticulitis; UC and CD, ulcerative colitis and Crohn Disease.

Anastomotic leak in this study was defined as (1) leakage of bowel content and/or gas from the surgical connection between the 2 bowel ends into the abdomen or pelvis with either spillage and/or fluid collection around the anastomotic site or extravasation through a wound, drain site, or anus; (2) clinical manifestation causing fever, abscess, septicemia, peritonitis, and/or organ failure; and (3) confirmation by imaging technique (eg, radiograph, endoscopy, computerized tomography scan, magnetic resonance imaging, sonography) or by digital rectal examination or anoscopy and/or proctoscopy for low rectal anastomoses. An AL detected by imaging study only but not clinically manifested was recorded as an "asymptomatic" AL.

The Charlson Comorbidity Index (CCI) was used to evaluate preoperative comorbidities. CCI is a validated index originally developed to measure the risk of 1-year mortality attributable to a comorbidity in a longitudinal study of general hospitalized patients. Patients were asked several questions about their comorbidities, using the CCI evaluation chart, and a CCI score was assigned prospectively before surgery (Fig. 1). Three ways of measuring CCI were calculated (1) the standard CCI, (2) the age-adjusted CCI, and (3) the CCI not accounting for the preoperative diagnosis.

The *36-Item Short Form Health Survey* is a validated scale with 8 domains used to provide information about the patient's functional status. The questionnaire was administered either at the clinic visit or in the hospital before surgery. These 8 domains were tested for prediction of AL.

Data were collected prospectively by 2 trained research nurses before, during, and after the surgery and entered into an electronic database created on Microsoft Access Version 3.3. After surgery, patients were followed up daily in the hospital until discharge, then at the first postoperative clinic visit within 2 to 3 weeks after hospital discharge and at 30 days after surgery. Patients with a diverting stoma as a part of the colorectal resection were followed up for several months until 30 days after the stoma was closed.

The study was powered to ensure there would be enough patients to evaluate multiple risk factors and conduct subgroup analysis (Table 1). This sample size was calculated using a 2-sample test of

Comorbidities: CCI

1

- ☐ Myocardial Infarction/heart attack
- ☐ Congestive heart failure
- ☐ Peripheral vascular disease
- ☐ Cerebrovascular disease/strock or TIA
- ☐ Dementia
- ☐ Chronic Pulmonary or lung disease
- ☐ Connective tissue disease
- ☐ Ulcer disease
- ☐ Diabetes

2

- ☐ Hemiplegia /cannot move one or more limbs
- ☐ Moderate or severe kidney disease
- ☐ Diabetes with end organ damage
- ☐ Any tumor
- ☐ Leukemia
- ☐ Lymphoma

3

- ☐ Moderate or severe liver disease

6

- ☐ Metastatic solid tumor/cancer
- ☐ AIDS

CCI Score ---------------------------------

FIGURE 1. CCI score evaluation chart.

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proportions with the 2 primary subgroups being AL patients with anastomoses less than 10 cm or greater than 10 cm from the anal verge. An initial sample size of 566 patients was calculated, assuming a significance level of $\alpha = 0.05$, to achieve a power of 80% to detect a difference of $\Delta = 0.06$ between the subgroups, assuming a 10% leak in the lower anastomoses group and 4% in the upper anastomoses group. When we added the consideration of multiple factors for AL prediction, a final sample of 631 patients was calculated to be needed. The risk factors were evaluated by performing univariate and multiple binary logistic regressions, using JMP 9.0 (Cornell University, Ithaca, NY).

RESULTS

The demographic characteristics of the 616 subjects are shown in Table 2. Body mass index was significantly different between male and female subjects, with males having a higher body mass index. Neoplasm was the leading preoperative diagnosis in 340 (55.2%) of the patients. Fifteen patients were excluded from analysis, 3 had cancelled the surgery, and in 12 patients, the surgical plan was changed. The group "Other" includes patients with preoperative diagnoses of appendicitis, small bowel obstruction, bowel perforation, and constipation. Surgical procedure details are presented in Table 3. The most common operations were left colectomy in 213 (34.5%), right colectomy in 212 (34%), and low anterior resection in 74 (12%). Our study found clinically evident AL in 5.7% (35/616 patients) overall, with a 3% leak rate in upper anastomoses (> 10 cm from anal verge) and 13.9% leak rate in lower anastomoses (<10 cm from the anal verge), $P < 0.0001$. Mortality rate was 0.9% (6/616 patients) overall, whereas that of the AL group was 2/35 (5.7%), and it was significantly higher than that of the No Leak group, 4/565 (0.7%), $P = 0.0428$. Only in 1 patient did the AL seem to be a contributing factor for death, and this patient had a very low anastomosis with a diverting ileostomy created at the time of surgery. In this study, anastomoses 10 cm or less from the anal verge had a significantly higher leak rate [13.9% (21/151)] than those 10 cm from the anal verge [3% (14/465)]. More than half (19/35 or 51%) of all leaks were from low rectal anastomoses 6 cm or less from the anal verge.

Table 4 shows only the significant findings from univariate analysis of the evaluated potential risk factors. There was no significant difference between the leak and nonleak patients in terms of age, preoperative diagnosis, laparoscopic procedure, type of surgical exposure techniques, and stapled or handsewn anastomoses. On multivariate analysis, the following were found to be independent risk factors for AL: anastomoses less than 10 cm from the anal verge; CCI of 3 or more; high ligation of inferior mesenteric artery; being of the male sex; and intraoperative complications/adverse events.

TABLE 2. Demographics

Parameter	ALL (N = 616)	Female	Male	P*
Sex F/M	329/287	329 (53.4%)	287 (46.6%)	NS
Age, median (range), yr	63 (19–92)	60 (19–92)	63 (19–91)	NS
BMI, kg/m^2	25.9 ± 5.8	25.1 ± 6.1	26.9 ± 5.1	0.0001
ASA, median (range)	2 (1–4)	2 (1–4)	2 (1–4)	NS
CCI, mean (SD)	2.3 ± 2	2.3 ± 1.9	2.3 ± 2.2	NS
Follow-up 30 d	616			
Mortality, n (%)	6 (0.9)	2 (0.6)	4 (1.4)	NS

*Chi-square test, Fisher exact test, and *t* test, Wilcoxon test- $P < 0.05$.

BMI indicates body mass index; ASA, The American Society of Anesthesiologists (ASA) Physical Status classification; NS- not significant.

TABLE 3. Preoperative Diagnosis and Surgical Procedures

Parameter	Total (N = 616)
Preoperative diagnoses, n (%)	
Neoplasm	340 (55.2)
Inflammatory bowel diseases	101 (16.4)
Diverticulitis	86 (14)
Other	89 (14.4)
Surgical procedures, n (%)	
Right colectomy	208 (33.8)
Right colectomy + ileostomy	3 (0.5)
Transverse colectomy	6 (1.0)
Left colectomy	209 (33.9)
Left colectomy + ileostomy	3 (0.5)
Left colectomy + colostomy	2 (0.3)
Proctectomy, LAR	42 (6.8)
Proctectomy, LAR+ ileostomy	53 (8.6)
Subtotal colectomy IRA	4 (0.6)
Total colectomy IRA	4 (0.6)
Total colectomy IRA + ileostomy	2 (0.3)
Total proctocolectomy IPAA	3 (0.5)
Total proctocolectomy IPAA + ileostomy	21 (3.4)
Completion proctectomy IPAA	4 (0.6)
Completion proctectomy IPAA + ileostomy	24 (4.0)
J-pouch redo + ileostomy	1 (0.2)
Colostomy takedown	2 (0.3)
Colostomy takedown + ileostomy	3 (0.5)
Hartman takedown	6 (1.0)
Hartman takedown + ileostomy	1 (0.2)
Other	15 (2.4)
State of procedure, n (%)	
Elective	593 (96.3)
Emergent	23 (3.7)
Surgical technique, n (%)	
Lap	252 (40.9)
HALS	243 (39.4)
Open Surgery	120 (19.5)
Other	1 (0.2)
Converted, n (%)	23 (3.7)
Lap to HALS	1 (0.2)
Lap to open	18 (2.9)
HALS to open	4 (0.6)
Diverting stoma, n (%)	113 (18.3)
Ileostomy	111 (18)
Colostomy	2 (0.3)
Reversed diverting stoma	103/113 (91.1)
Intraoperative leak test, n (%)	292 (47.4)
Drain placement, n (%)	88 (14.2)
Intraoperative blood transfusion, n (%)	24 (3.9)
Preoperative antibiotics, n (%)	606 (98.3)
Bowel prep, n (%)	575 (93.4)
Rectal wash before surgery, n (%)	245 (39.7)
Wound classification, n (%)	
Clean contaminated	603 (97.9)
Contaminated	7 (1.1)
Dirty infected	6 (1.0)

IRA indicates ileorectal anastomosis; IPAA-ileal pouch anal anastomosis; Lap-laparoscopic surgery; HALS-hand-assisted laparoscopic surgery.

The area under the curve for these variables collectively was 0.807 (Table 5). None of the domains of the 36-Item Short Form Health Survey Questionnaire were found to be associated with AL.

DISCUSSION

The uncomplicated healing of an intestinal anastomosis even after attentive technical performance from an experienced surgeon is still a challenge because the healing process is dependent on multiple physiological, biochemical, and morphological factors. In

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TABLE 4. Univariate Analysis AL Versus No Leak (N = 616)

Variables	Patients With AL n	%	P*
Sex			0.0085
Male	24/287	8.4	
Female	11/329	3.3	
CCI Score, mean (SD)			
Leak yes	3 ± 2.3		0.0413
Leak no	2.3 ± 2		
CCI Score ≥ 3	20/228	8.8	0.0178
CCI Score < 3	15/388	3.9	
Neoadjuvant therapy for patients with rectal cancer			
Yes	7/40	17.5	0.0049
No	28/576	4.9	
Anastomotic fashion			
side-to-side	8/203	3.9	0.0092
Side-to-end	8/207	3.9	
End-to-end	11/152	7.3	
J-pouch	8/54	14.8	
Type of anastomosis			
ileocolic	8/221	3.6	0.0037
Ileorectal	0/11	0	
Colocolonic	1/45	2.2	
Colorectal	13/252	5.2	
Coloanal	5/33	15.1	
Ileoanal (j-pouch)	8/54	14.8	
Anastomosis level			
Anastomosis >10 cm from anal verge	14/465	3	<0.0001
Anastomosis ≤10 cm from anal verge	21/151	13.9	
Major artery ligated during surgery on left side			
Left colic			
yes	13/127	10.2	0.0281
No	6/176	3.4	
No	1/57	1.7	
Sigmoid arteries			
yes	18/269	6.7	0.7066
No	1/34	2.9	
Superior rectal arteries			
Yes	18/246	7.3	0.2194
No	1/57	1.7	
IMA ligated above left colic artery	13/127	10.2	0.0281
IMA ligated below left colic artery	6/176	3.4	
Diverting stoma			
Yes	20/130	17.7	<0.0001
No	15/503	3	
Intraoperative complications			
Yes	7/41	17	0.0057
No	28/575	4.9	
Type of intraoperative complications number of events			
Intraoperative blood transfusion	4/24	16.7	0.0350
Medical/Anesthetic	1/7	14.3	
Surgical	2/12	16.7	
No complication	28/575	4.9	

*Chi-square, Fisher exact test, *t* test, Univariate analysis- $P < 0.05$.
SD indicates standard deviation; IMA- inferior mesenteric artery.

this prospective study, we described some new risk factors that have not been described before.

The impact of preoperative comorbidities on AL after colorectal resection has not been studied extensively and prospectively. Some recent colorectal studies have used CCI to measure the influence of various preoperative comorbidities on some postsurgical outcomes, but the impact of CCI on AL rate has yet to be studied.[14, 15] In this study, the overall CCI score was significantly higher in patients with leak, and patients with CCI of 3 or more were 3.5 times more likely to develop a leak than those with CCI of less than 3 (Fig. 2). This new finding may bring further understanding of the influence of various comorbidities on AL rate. Interestingly, when comorbidities were compared as single entities, no significant differences were detected between the leak and nonleak patients. However, when comorbidities were evaluated together as a total comorbidity burden, a significant difference between groups became obvious. This phenomenon may be explained within the nature of the index, which considers both the number and the severity level of comorbidities.[16] Another study in 2003 identified the presence of 2 or more underlying comorbidities to be an independent risk factor for AL and supports our study's concept of a cumulative effect of preoperative comorbidities.[17]

The effect of comorbidities, such as diabetes and atherosclerosis on local blood flow and AL, has been described in the literature. Two studies reported diabetes as an independent predictor for AL.[5,18] Other studies, including our own, do not find diabetes to be a significant factor for AL. This may be due to the fact that only 1.6% (10/616) of the patients in our study had insulin-dependent diabetes and no patient had diabetes with end-stage organ damage. In this sense, CCI allows for better evaluation of diabetes by appreciating its range of severity and not evaluating it only as a static binary outcome (Fig. 1). Use of a global index such as CCI may be a better tool for evaluation of the patient's comorbidity status before surgery and of facilitating salutary decisions for perioperative management.

Another interesting finding in this study is the effect of blood vessel ligation. At the time of surgery, we prospectively recorded the ligation of each major arterial pedicle (ileocolic, right colic, middle colic, left colic, sigmoid, and superior rectal arteries) and whether the inferior mesenteric artery was ligated above (high ligation) or below the left colic artery (low ligation) or not ligated in cases of left-sided procedures. In this study, patients with high ligation of the inferior mesenteric artery had a 3.8 times higher chance of leaking than those with low ligation. This finding most likely represents the extent of the surgical procedure in patients with left-sided surgery and with neoplasm where the dissection protocol demands more extensive lymphovascular dissection. Creating a tension-free low rectal or coloanal anastomosis with a good blood supply is often not possible without performing a high ligation of the inferior mesenteric artery and inferior mesenteric vein. Therefore, the choice of high ligation of the inferior mesenteric artery may be influenced by a variety of factors including: level of anastomosis (how much reach is needed to the rectum), degree of atherosclerosis in the mesentery, or whether or not there are intact marginal vessels in colon mesentery. In this study, we did not record inferior mesenteric vein ligation separately because it is always done when the inferior mesenteric artery is tied off. In our practice, the inferior mesenteric vein is usually ligated separately from the inferior mesenteric artery, just below the inferior boarder of the pancreas, to provide maximum reach without tension for low rectal or coloanal anastomosis. With complete devascularization of the inferior mesenteric artery (high ligation), the proximal portion of the anastomosis relies only on marginal blood flow coming from the middle colic vessels. A recent study by Nash et al[19] reported that the number of the vascular pedicles resected during colon cancer surgery is an independent factor for lymph node yield. In the same study, the authors also reported that resection of an additional pedicle had a diminishing return of lymph nodes. The current recommendation for the minimum number of lymph nodes harvested during colorectal cancer surgery, to adequately predict nodal metastases, is 12 to 15.[20–22] Our data merely suggest that extensive vascular ligation on

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TABLE 5. Significant Independent Predictors From Multivariate Analysis (N = 616)

Variables in Model	Estimate	P*	Odds Ratio	95% CI	AU ROC
Sex	− 0.424	0.0294	2.336	1.110–5.192	
Neoadjuvant therapy	0.236	0.406	1.602	0.502–4.770	
CCI ≥ 3	− 0.559	0.0034	3.061	1.461–6.588	
Anastomosis level < 10 cm	− 0.629	0.0067	3.522	1.448–9.046	
IMA ligation and level of ligation	− 0.712	0.0165	3.824	1.385–12.454	
Intraoperative complications	− 0.707	0.0256	4.112	1.053–13.372	
					0.807

*$P < 0.005$ significant multiple logistic regression with outcome AL.
AU ROC indicates area under receiver operating characteristic; IMA- inferior mesenteric artery.

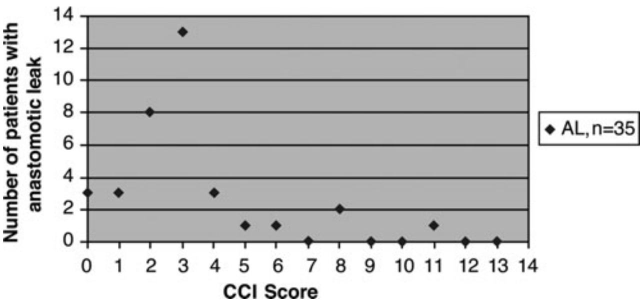

FIGURE 2. Distribution of CCI score in AL patients.

the left side of the colon should be considered carefully in patients with risk factors for poor mesenteric blood flow in the postoperative period. Other reports have tried to quantify reduction of blood flow and colonic ischemia as factors increasing the AL rate.[23,24] In addition, anatomical variations of the major mesenteric blood vessels and collaterals, if not appreciated at surgery, may further increase the risk of ischemia. In 5% of the population, the marginal artery of Drummond (through which the superior and inferior mesenteric arteries communicate) may be absent, and in up to 43% the connection at Griffith's point in the marginal artery of Drummond may be absent or diminutive, thus leaving the splenic flexure area at significant risk of ischemia.[25]

Knowledge about anastomotic level and leak rate is important for surgical planning. The level of the anastomoses has been related to clinical and physiological outcomes especially in patients undergoing low rectal resection for rectal cancer, for example, total mesorectal excision. Frequency of bowel movements and control of continence were found to be associated with sphincter preservation and level of anastomoses during low anterior resection.[26] In a randomized multicenter trial including patients undergoing laparoscopic colorectal surgery, Rose et al[27] reported a 16.8% leak rate for anastomoses less than 10 cm from the anal verge. In our study, we experienced a similar percentage, which is consistent with the published literature.

There was no significant difference in the incidence of low rectal cancer between males and females, but the relative risk for AL in males was 2.3 times higher. Other studies have reported that the male sex is a predisposing factor for AL.[28–30] One possible explanation for this difference is a narrower pelvis in males, which makes the surgical dissection and creation of an anastomosis technically more challenging than in females.

An individual surgeon's preferences regarding anastomotic technique make it difficult to evaluate the overall effect of the operating surgeon's experience on the clinical outcome. The severity of the patient's illness and individual surgeon's case mix are also impeding factors. In this study, a surgeon's influence on the AL rate was simply evaluated by 2 variables: years of experience and board certification. We did not find significant differences among the individual surgeons in assessing these variables. Although this is hardly a complete measure of an individual surgeon's mastery of his or her craft, the surgeons in this study had already been preselected by their appointment to a university hospital faculty and by their specific interest in colon and rectal surgery. One study reported that surgeons with colorectal training were able to preserve the anal sphincter more often in patients undergoing low anterior resection (LAR) than surgeons not having this type of training ($P < 0.001$).[31] Read et al[32] linked a better outcome for patients undergoing surgery with rectal cancer and neoadjuvant therapy to colorectal specialty training. Another study by Prystowsky et al[33] did not find specialty training a factor influencing patient outcome. Further analyses like propensity score matching may further clarify the surgeon's influence on AL rates and overall patient outcome.

In our study, intraoperative complications were defined as unexpected adverse events (surgical or anesthetic) occurring in the operating room during the surgical time and documented in the operative and anesthetic reports at the time of surgery by the study nurse in collaboration with the surgeon and anesthesiologist. Surgical complications included injury of bowel, other organs or blood vessels, bleeding, stapling device malfunction, and others. Anesthetic complications were defined as hypotension less than 20% of the baseline measurement, or any systolic mean pressure of less than 85 mm Hg or mean arterial pressure of less than 60 mm Hg and a patient treated pharmacologically or with fluids, myocardial infarction, oxygen saturation less than 90% for more than 5 minutes, and metabolic acidosis (in patients with arterial line and any pH less than 7.30). Intraoperative bleeding was considered a complication if intraoperative blood transfusion was needed. Patients with intraoperative adverse events were 4.1 times more likely to leak than those not having complications. Other studies have also reported intraoperative adverse events as independent risk factors for AL.[5,34] Intraoperative complications in some instances may directly affect the anastomotic creation or in other instances may cause abdominal contamination, for example, bowel injury increasing the chances of AL.

Even though this prospective study may contribute to the understanding of the AL, it is not without its limitations. The study was conducted in a large metropolitan university hospital, and there may be patient selection bias in terms of population treated, and variety and severity of colorectal conditions. In addition, this study cannot provide answers to such questions as to when a diverting stoma should be created to protect against an AL and its consequences. Surgeons should continue to use their experience and discretion when deciding to create a diverting stoma. Furthermore, in this study, the surgeon's experience was evaluated in a very limited way by using only 2 variables: experience in years and type of board certification. Irrespective of the participating surgeon's experience, we did not find any

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difference between the individual surgeons. This may be due to the fact that this study was not powered to establish the AL rate between surgeons. Also, we did not use parameters like case-mix index or caseload that could have contributed to a better understanding of the impact of the surgeon's experience on the AL rate. Finally, no set protocol for surveillance, such as a computerized tomography scan or other measurements beyond the standard treatment, was performed for each patient. This could have provided uniform and additional valuable information about AL. For this reason, subclinical leaks could have been missed.

This study is one of the very few prospective observational trials designed to evaluate predisposing factors for AL as the main outcome. Although some risk factors for leak have been previously reported in retrospective studies, new factors not studied before in relation to AL were evaluated in this study, such as CCI and detailed evaluation of the major arterial vessels ligated during colorectal resection. The data from this study also provide information for the development of mathematical predictive models that weight the importance of each variable.

In summary, this study found the following variables to be independent risk factors for anastomotic leak: CCI of 3 or more, level of anastomoses less than 10 cm from the anal verge, high inferior mesenteric artery ligation (above left colic artery), intraoperative complications/adverse events, and the male sex.

CONCLUSIONS

Multiple factors should be taken into consideration before and during colorectal surgery to comprehensively assess the risk for AL. In particular, the CCI is a new useful tool for the prediction of leaks and assessing preoperative comorbidities.

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