ORIGINAL CONTRIBUTION

Risk Factors and Consequences of Anastomotic Leak After Colectomy: A National Analysis

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BACKGROUND: Previous research has identified a number of patient and operative factors associated with anastomotic leak after colectomy; however, a study that examines these factors on a national level with direct coding for anastomotic leak is lacking.

OBJECTIVE: The purpose of this work was to identify risk factors associated with anastomotic leak on a national level and quantify the additional morbidity and mortality experienced by these patients.

DESIGN: We performed a retrospective analysis of patients who underwent segmental colectomy with anastomosis from the 2012 American College of Surgeons National Surgical Quality Improvement Program colectomy procedure-targeted database. Anastomotic leak was defined as minor leak requiring percutaneous intervention or major leak requiring laparotomy. Multivariate logistic regression was used to determine predictors of anastomotic leak and its impact on postoperative outcomes.

SETTINGS: This study was conducted at a tertiary university department.

PATIENTS: This study includes 13,684 patients who underwent segmental colectomy with anastomosis at American College of Surgeons National Surgical Quality Improvement Program–affiliated hospitals in 2012.

MAIN OUTCOME MEASURES: The primary outcome studied was anastomotic leak.

RESULTS: The overall leak rate was 3.8%. Male sex, steroid use, smoking, open approach, operative time, and preoperative chemotherapy were associated with increased anastomotic leaks and diverting ileostomy with decreased incidence of leaks on multivariate analysis. Increased length of stay (13 vs 5 days; $p < 0.001$) and increased 30-day mortality (6.8% vs 1.6%; $p < 0.001$) were also seen in patients who experienced leaks. These patients also experienced increased readmission rates (43.5% vs 8.3%; $p < 0.001$) and were 37 times more likely to require reoperation as a complication of their primary procedure ($p < 0.001$).

LIMITATIONS: The main limitations of this study include its retrospective nature and the limited 30-day outcomes recorded in the American College of Surgeons National Surgical Quality Improvement Program database.

CONCLUSIONS: This study identified patient and operative risk factors for anastomotic leak on a national scale. It also demonstrates that these patients have increased morbidity and 30-day mortality rates, experience multiple readmissions to the hospital, and have a higher likelihood of requiring further operative intervention.

KEY WORDS: Anastomotic leak; Colectomy; Colon cancer; Outcomes.

After colorectal surgery, anastomotic leak (AL) has been shown to be associated with increased morbidity, mortality, and length of hospital stay.[1–3] Reported AL rates in the literature range from 1.8% to 15.9%.[2,4–14] This variability has been attributed to differences in leak rate by type of resection and anastomotic level,[7,9,12,14–19] as well as inconsistent definitions of AL.[20] To

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date, the majority of the literature on this topic has been from single institutions[2,3,5–7,9,14–16,18,21,22] or via administrative databases, which do not directly code AL.[8,17,19,23]

In 2012, the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) began to collect procedure-targeted databases for colectomy.[24] The procedure-targeted colectomy database is the first national database to capture AL defined as a major leak requiring laparotomy or a minor leak requiring percutaneous management or no intervention.[25]

Although previous research has identified a myriad of patient and operative factors, their association with AL is inconsistent. The aims of our study were to identify risk-adjusted predictors for both major and minor ALs on a national level and to quantify the additional morbidity and mortality experienced by these patients.

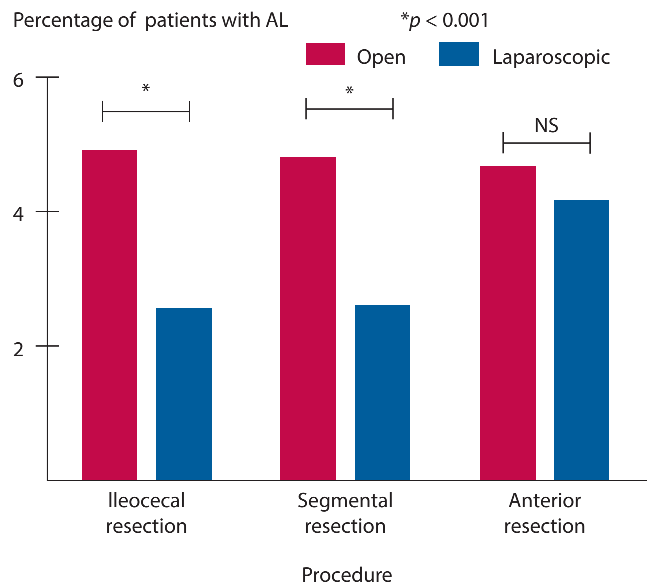

Figure 1. Procedure-specific anastomotic leak (AL) rates after colectomy with anastomosis. NS = not significant.

PATIENTS AND METHODS

We performed a retrospective analysis using data from the participant user file from the 2012 NSQIP database. NSQIP is a nationally validated, outcomes-based program that provides a prospective, validated database of preoperative to 30-day postoperative surgical outcomes based on clinical data.[24] We linked the 2012 participant user file data with the 2012 NSQIP colectomy procedure-targeted database using patient identification number and a 100% match was achieved. The procedure-targeted database adds specific variables of interest to patients who underwent colectomy, including the presence of a major or minor AL.

Patients who had an ileocecal resection (Current Procedural Terminology (CPT) code 44160 or 44205), a segmental resection (44140 or 44204), or an anterior resection (44145 or 44207) were included. Operations with a diverting ileostomy were included by examining all of the other procedure codes; however, those with end ostomy without anastomosis were excluded. Rectal cancer resections are not included in the colectomy procedure-targeted database and were therefore not included in our analysis.

Preoperative patient factors, intraoperative variables, and postoperative complications were compared to identify those associated with the primary outcome, AL. The NSQIP database categorizes ALs based on the intervention required. Patients are classified as "no," "yes–no intervention required," "yes–percutaneous intervention required," and "yes–reoperation required." These data are coded based on detailed data abstraction in the 30-day postoperative period by a trained clinical reviewer. Our primary analysis compared patients with no AL with all of the patients with AL. For secondary analysis, AL was categorized into minor AL and major AL, with minor AL defined as those requiring no intervention or percutaneous drainage and major AL as those requiring operative intervention.

Univariate analysis using χ^2 tests was performed to compare categorical variables. Continuous variables were analyzed using the Student *t* tests or ANOVA with the Bonferroni correction. Nonparametric, continuous data were analyzed using Wilcoxon rank-sum tests or Kruskal-Wallis tests where appropriate. Multivariate logistic regression was then performed using all of the variables with a p value < 0.20. The primary analysis was first performed to identify factors associated with overall AL. A secondary analysis was conducted to identify those associated with major leak and minor leak based on the definitions above. All of the analyses were conducted using Stata version 12.1 (StataCorp, College Station, TX). A p value of 0.05 was considered statistically significant, and all of the p values reported are 2 tailed. This study was deemed exempt by our institutional review board.

RESULTS

Patient Characteristics and Operative Factors

A total of 13,684 patients underwent colectomy with an overall leak rate of 3.8% (2.6% laparoscopic vs 4.9% open ileocecal resection; 2.6% laparoscopic vs 4.8% open segmental colectomy; and 4.2% laparoscopic vs 4.7% open anterior resection; Fig. 1). A total of 51.6% of all patients were men, 80.3% were white, and the median age at the time of surgery was 63 years (range, 18–90 years). The indication for colectomy was cancer in 41.5%, diverticulitis in 22.8%, IBD in 5.7%, and a combination of benign polyp, bleeding, obstruction, volvulus, or other colitis for the remaining 30.0% of patients. Almost two-thirds of cases were performed laparoscopically (62.5%), with a conversion rate of 11.6% (based on specific coding in the procedure targeted database), and 9.4% of operations were emergent.

Risk Factors Associated With AL

Table 1 illustrates patient and operative factors associated with AL on univariate analysis. Male sex, diabetes mellitus, smoking, chronic obstructive pulmonary disease, functional status, ASA class, chronic steroid use, preoperative weight loss >10% of baseline, bleeding disorder, preoperative chemotherapy, and preoperative albumin level <3 were patient-specific factors associated with AL. Operative factors associated with AL included operations for IBD, emergent cases, wounds classified as dirty, longer operative times, and open approach.

In multivariate logistic regression analysis, patient factors associated with AL were male sex, preoperative steroid use, preoperative chemotherapy, and smoking status (Table 2). AL was also associated with operations lasting >3 hours and an open approach, and diverting ileostomy was associated with lower overall leak rates.

When AL was categorized into minor and major ALs, open approach and operative time >3 hours were associated with both major and minor ALs (Table 3). Minor leaks were associated with bleeding disorders, dirty/infected wound classification, and preoperative chemotherapy. Diverting ostomy was not protective against minor AL on analysis but remained protective of major AL. Major AL was also associated with male sex, smoking, preoperative steroid use, and anterior resections.

Complications Associated With AL

AL patients experienced increased length of stay (13 vs 5 days; $p < 0.001$) and mortality (6.8% vs 1.6%; $p < 0.001$) when compared with patients without AL. AL patients were also more likely to be readmitted (43.5% vs 8.3%; $p < 0.001$) and 4.6 times more likely to be readmitted more than once in 30 days ($p < 0.001$). Furthermore, AL patients were 37 times more likely to require multiple returns to the operating room because of a complication from their primary procedure ($p < 0.001$; not shown in table form). Both minor and major ALs were associated with dramatically increased complications, as seen in Table 4.

DISCUSSION

The results of this study indicate that ALs after colectomy are associated with identifiable patient and operative variables. Patient-associated characteristics include male sex and modifiable factors including preoperative smoking, chronic steroid use, and preoperative chemotherapy administration within 90 days of surgery. Operative factors associated with AL were cases lasting >3 hours, anterior resections, and an open approach. When AL is divided into minor and major leaks on the basis of intervention, bleeding disorders, preoperative chemotherapy, and contaminated wounds are associated with minor leaks but not major leaks. Interestingly, diverting ileostomy is associated

Table 1. Univariate analysis of factors associated with anastomotic leak after colectomy

Variable	*Leak (N = 520)*	*No leak (N = 13,164)*	*p*
Age (median), y	62	63	0.004[a]
Male sex, %	57.1	48.1	<0.001[a]
Race, %			0.74
White	80.3	79.6	
Black	8.3	9.2	
Other	11.4	11.2	
Diabetes mellitus, %			0.03[a]
Nondiabetic	82.9	85.4	
Noninsulin dependent	10.0	10.0	
Insulin dependent	7.1	4.6	
Current smoker, %	27.3	17.0	<0.001[a]
Severe chronic obstructive pulmonary disease, %	9.0	5.2	<0.001[a]
Functional health status, %			0.009[a]
Fully dependent	1.3	0.4%	
Partially dependent	1.5	2.1	
Independent	97.1	97.4	
ASA classification, %			0.003[a]
1	3.3	2.9	
2	39.9	46.7	
3	48.0	43.5	
4	8.5	5.6	
5	0.4	0.3	
Dialysis dependent, %	1.5	0.8	0.08
Chronic steroid use, %	11.2	6.4	<0.001[a]
Weight loss >10%, %	6.3	4.4	0.03[a]
Bleeding disorder, %	7.5	4.2	<0.001[a]
Preoperative blood transfusion, %	4.2	2.8	0.06
Preoperative albumin level <3, %	10.8	7.4	0.003[a]
BMI >30, %	35.2	33.9	0.25
Preoperative chemotherapy, %[b]	8.2	4.9	0.001[a]
Emergency case, %	12.5	9.3	0.01[a]
Wound classification, %			<0.001[a]
Clean contaminated	70.0	79.6	
Contaminated	16.5	11.6	
Dirty	13.4	8.8	
Indication, %			0.02[a]
Colon cancer	38.3	41.6	
Diverticulitis	21.2	22.9	
IBD	8.5	5.5	
Other	31.9	30.0	
Approach, %			<0.001[a]
Laparoscopic	24.2	33.0	
Laparoscopic with hand assist	18.7	22.7	
Laparoscopic with conversion to open	7.1	7.3	
Open	50.0	37.0	
Operation, %			<0.001[a]
Open segmental resection	25.6	20.0	
Open ileocecectomy	17.7	13.5	
Open anterior resection	13.6	11.9	
Laparoscopic segmental resection	19.0	28.4	
Laparoscopic ileocecectomy	8.1	11.9	
Laparoscopic anterior resection	15.9	14.3	
Protective ileostomy	3.1	3.5	0.63
Operative time >3 hr, %	47.3	36.6	<0.001[a]

[a]*p* Value is significant.
[b]Chemotherapy was administered within 90 days of surgery.

Table 2. Multivariate analysis of factors associated with anastomotic leak

Variable	*OR*	*95% CI*	*p*
Male sex	1.37	1.10–1.71	0.005[a]
Open approach	1.71	1.27–2.31	<0.001[a]
Operative time >3 hr	1.50	1.19–1.90	0.001[a]
Preoperative chemotherapy	1.71	1.16–2.54	0.007[a]
Preoperative steroids	1.60	1.08–2.34	0.02[a]
Protective ileostomy	0.55	0.31–0.97	0.04[a]
Smoking	1.56	1.20–2.02	0.001[a]

Variables that were not significant on multivariate analysis include age, diabetes mellitus, severe chronic obstructive pulmonary disease, dialysis dependence, weight loss >10% of body weight, bleeding disorder, preoperative blood transfusion, preoperative albumin level <3, emergency case, wound classification, indication, and protective ileostomy.
[a]*p* Value is significant.

with a lower rate of major AL requiring operative intervention but is not associated with lower minor AL rates. Although previous studies have also demonstrated an association with these factors,[6,8,9,12,15–17,22,23,26] none have used a national data set with uniform coding for AL.

Male sex,[3,8,12,15,17,23] steroid use,[5,22] and smoking[6,23] have been shown in numerous studies to be associated with increased risk of AL. Smoking in particular has been associated with increased AL rates in colectomies,[6] and specifically with anterior resections,[23] and future studies are needed to determine whether preoperative abstinence from tobacco use can improve AL rates in these patients. Chemotherapy has not been shown to be consistently associated with AL, because some studies demonstrate no association,[27,28] whereas others suggest a positive association[26]; however, the majority of these studies investigate rectal cancer resections rather than all colectomies. In our study, because chemotherapy was associated with an increase in overall AL, and specifically minor AL, the optimal timing of surgery in relation to perioperative chemotherapy deserves further investigation. Other patient factors frequently identified that were not found to be significant in our study include malnutrition[2,5,8,16] and ASA classification.[9,16,19,21,29] Although these were significant on univariate analysis (Table 1), they were not found to be independently predictive of AL on multivariate analysis.

Long operative time[2,9,16,17,22] and low anastomoses[12,15,17,19,23] have also been described in the literature as being associated with an increased incidence of AL. An open approach, however, has not been correlated previously with AL. It is unclear whether surgeons chose an open approach in cases that they anticipated to be more difficult or if more experienced surgeons tended to perform their procedures laparoscopically. This subject requires further study before drawing firm conclusions.

The effectiveness of diverting ileostomy for anastomotic protection is heavily debated across studies as well,[7,8,16,17,22,30–37] and our study shows that it is protective against overall AL and specifically major ALs that require reoperation but not minor leaks. This has never been described, and, although it may help shed light on the controversy of protective ileostomies, further trials are needed to validate this finding. In addition, protective ileostomy is most commonly used in the setting of rectal resection after neoadjuvant chemotherapy and radiation. Because the NSQIP colectomy procedure-targeted database does not include rectal resection, we are unable to address the controversy of using an ileostomy in that setting. Furthermore, an ileostomy may again be a marker of a more difficult surgery, because it is not routinely performed in the setting of colectomies, which may explain why it was not shown to be protective for overall AL.

Increased morbidity and mortality rates are consistently seen with AL. Our mortality rates of 3.3% for minor AL and 6.8% for major AL are consistent with the current literature, although rates as high as 39.3% have been reported.[5] In addition, our reoperation rate of 60.7% in AL patients is consistent with published rates of 45% to 88%.[14,21] Our data also highlight that, although minor leaks do not require immediate return to the operating room, they are associated with major increases in postoperative complications, such as wound complications, pulmonary complications, deep vein thrombosis, and postoperative mortality.

Table 3. Multivariate analysis of factors associated with minor and major anastomotic leak

Variable	*Minor leak, OR (95% CI)*	*p*	*Major leak, OR (95% CI)*	*p*
Anterior resection	0.98 (0.64–1.49)	0.92	1.46 (1.05–2.04)	0.03[a]
Bleeding disorder	2.22 (1.21–4.07)	0.01[a]	1.03 (0.58–1.82)	0.93
Dirty or infected wound	2.19 (1.29–3.73)	0.004[a]	1.04 (0.64–1.68)	0.87
Male sex	1.02 (0.72–1.44)	0.91	1.69 (1.27–2.26)	<0.001[a]
Open approach	1.79 (1.12–2.86)	0.01[a]	1.66 (1.14–2.44)	0.009[a]
Operative time >3 h	1.62 (1.13–2.34)	0.009[a]	1.42 (1.05–1.91)	0.02[a]
Preoperative chemotherapy	2.80 (1.64–4.76)	<0.001[a]	1.09 (0.61–1.95)	0.78
Preoperative steroids	1.17 (0.62–2.23)	0.63	1.92 (1.19–3.08)	0.007[a]
Protective ileostomy	1.02 (0.52–2.00)	0.95	0.21 (0.07–0.67)	0.008[a]
Smoking	1.34 (0.89–2.02)	0.17	1.72 (1.24–2.38)	0.001[a]

Variables that were not significant on multivariate analysis include age, diabetes mellitus, severe chronic obstructive pulmonary disease, dialysis dependence, weight loss >10% of body weight, preoperative blood transfusion, preoperative albumin level <3, emergency case, and indication.
[a]*p* Value is significant.

Table 4. Complications associated with anastomotic leak

Variable	No leak (N = 13,164), %	Minor leak (N = 213), %	Major leak (N = 307), %	p
Superficial SSI	6.6	7.5	10.1	0.04[a]
Deep SSI	1.0	7.5	5.2	<0.001[a]
Wound dehiscence	0.9	6.1	7.8	<0.001[a]
Pneumonia	1.8	5.6	12.1	<0.001[a]
Pulmonary embolism	0.6	1.4	3.9	<0.001[a]
Unplanned intubation	1.5	8.0	11.4	<0.001[a]
Ventilator dependence >48 h	2.1	6.1	22.8	<0.001[a]
Acute renal failure	0.6	1.9	3.9	<0.001[a]
Urinary tract infection	2.8	8.9	6.5	<0.001[a]
Stroke	0.2	0.0	0.7	0.26
Cardiac arrest	0.5	1.9	2.6	<0.001[a]
Myocardial infarction	0.7	0.9	1.3	0.47
Bleeding requiring transfusion	9.8	16.9	21.8	<0.001[a]
DVT requiring treatment	1.2	4.7	6.2	<0.001[a]
Septic shock	1.3	4.7	24.4	<0.001[a]
Ileus	13.0	33.0	36.2	<0.001[a]
30-day mortality	1.8	3.3	6.8	<0.001[a]
Readmission				
1	8.2	48.8	34.9	<0.001[a]
≥2	0.3	1.4	1.3	<0.001[a]

Minor leak was defined as leak requiring no intervention or percutaneous drainage. Major leak was defined as leak requiring operative intervention.
DVT = deep vein thrombosis; SSI = surgical site infection.
[a]*p* Value is significant.

Our overall AL rate was 3.8%, which is relatively low compared with published rates. The majority of studies with similar or lower AL rates are from academic centers and excluded rectal resections, similar to our study.[2,5,9,10] Higher rates of AL are typically seen after total mesorectal excision and coloanal anastomosis for rectal cancer, often in the setting of neoadjuvant chemotherapy and radiation.[3,15,17,19,23] Although our study included anterior resections (CPT codes 44145 and 44207), less than half were for cancer or IBD, and the most common indication was diverticulitis, suggesting that most of these may have been sigmoid resections consistent with our lower AL rate. In addition, to participate in the NSQIP procedure-targeted database, hospitals must voluntarily enroll and provide a trained data abstractor to this cause. It is likely that this database may be skewed toward including only hospitals that have a particular interest in colectomy outcomes. This is also supported by the fact that >60% of the cases in this data set were performed laparoscopically. We believe that the true rate of AL would likely be higher if all hospitals were included.

Limitations of this study include its retrospective nature and potential limitations of the data source. Although NSQIP uses standard coding criteria and trained data abstractors, it is impossible to know whether some cases of AL were mistakenly coded as organ/space surgical site infection. However, we feel that the prospective coding conventions used by NSQIP are superior to administrative data sources that require the use of surrogate measures to define AL. The NSQIP database is also limited to outcomes within 30 days of surgery, and previous studies have shown that ≤12% of ALs can be seen more than a month after surgery.[14] This is particularly significant with respect to patients with protective ileostomies who may have delayed presentation of their AL outside of this 1-month window. Furthermore, coding for operative procedures is based on CPT code rather than anastomotic level, and, therefore, sigmoid resections may be coded as anterior resections rather than segmental resection, and this may create a falsely low AL rate for this group of patients.

CONCLUSION

Our study is the first national study to examine patient and operative risk factors for both major and minor AL after colectomy. These data, along with future prospective databases and trials, will hopefully lead to the development of predictive models for AL to allow better counseling of patients on their individual risk, as well as to assist surgeons in their operative decisions.

REFERENCES

1. Bertelsen CA, Andreasen AH, Jørgensen T, Harling H; Danish Colorectal Cancer Group. Anastomotic leakage after curative anterior resection for rectal cancer: short and long-term outcome. *Colorectal Dis.* 2010;12(7 online):e76–e81.
2. Telem DA, Chin EH, Nguyen SQ, Divino CM. Risk factors for anastomotic leak following colorectal surgery: a case-control study. *Arch Surg.* 2010;145:371–376.

3. Law WL, Chu KW. Anterior resection for rectal cancer with mesorectal excision: a prospective evaluation of 622 patients. *Ann Surg*. 2004;240:260–268.
4. Schrock TR, Deveney CW, Dunphy JE. Factor contributing to leakage of colonic anastomoses. *Ann Surg*. 1973;177:513–518.
5. Golub R, Golub RW, Cantu R Jr, Stein HD. A multivariate analysis of factors contributing to leakage of intestinal anastomoses. *J Am Coll Surg*. 1997;184:364–372.
6. Sørensen LT, Jørgensen T, Kirkeby LT, Skovdal J, Vennits B, Wille-Jørgensen P. Smoking and alcohol abuse are major risk factors for anastomotic leakage in colorectal surgery. *Br J Surg*. 1999;86:927–931.
7. Alves A, Panis Y, Trancart D, Regimbeau JM, Pocard M, Valleur P. Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients. *World J Surg*. 2002;26:499–502.
8. Suding P, Jensen E, Abramson MA, Itani K, Wilson SE. Definitive risk factors for anastomotic leaks in elective open colorectal resection. *Arch Surg*. 2008;143:907–911.
9. Buchs NC, Gervaz P, Secic M, Bucher P, Mugnier-Konrad B, Morel P. Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. *Int J Colorectal Dis*. 2008;23:265–270.
10. Leichtle SW, Mouawad NJ, Welch KB, Lampman RM, Cleary RK. Risk factors for anastomotic leakage after colectomy. *Dis Colon Rectum*. 2012;55:569–575.
11. Bellows CF, Webber LS, Albo D, Awad S, Berger DH. Early predictors of anastomotic leaks after colectomy. *Tech Coloproctol*. 2009;13:41–47.
12. Lipska MA, Bissett IP, Parry BR, Merrie AE. Anastomotic leakage after lower gastrointestinal anastomosis: men are at a higher risk. *ANZ J Surg*. 2006;76:579–585.
13. Morse BC, Simpson JP, Jones YR, Johnson BL, Knott BM, Kotrady JA. Determination of independent predictive factors for anastomotic leak: analysis of 682 intestinal anastomoses. *Am J Surg*. 2013;206:950–955.
14. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg*. 2007;245:254–258.
15. Rullier E, Laurent C, Garrelon JL, Michel P, Saric J, Parneix M. Risk factors for anastomotic leakage after resection of rectal cancer. *Br J Surg*. 1998;85:355–358.
16. Mäkelä JT, Kiviniemi H, Laitinen S. Risk factors for anastomotic leakage after left-sided colorectal resection with rectal anastomosis. *Dis Colon Rectum*. 2003;46:653–660.
17. Matthiessen P, Hallböök O, Andersson M, Rutegård J, Sjödahl R. Risk factors for anastomotic leakage after anterior resection of the rectum. *Colorectal Dis*. 2004;6:462–469.
18. Lee MR, Hong CW, Yoon SN, Lim SB, Park KJ, Park JG. Risk factors for anastomotic leakage after resection for rectal cancer. *Hepatogastroenterology*. 2006;53:682–686.
19. Jestin P, Påhlman L, Gunnarsson U. Risk factors for anastomotic leakage after rectal cancer surgery: a case-control study. *Colorectal Dis*. 2008;10:715–721.
20. Bruce J, Krukowski ZH, Al-Khairy G, Russell EM, Park KG. Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *Br J Surg*. 2001;88:1157–1168.
21. Choi HK, Law WL, Ho JW. Leakage after resection and intraperitoneal anastomosis for colorectal malignancy: analysis of risk factors. *Dis Colon Rectum*. 2006;49:1719–1725.
22. Konishi T, Watanabe T, Kishimoto J, Nagawa H. Risk factors for anastomotic leakage after surgery for colorectal cancer: results of prospective surveillance. *J Am Coll Surg*. 2006;202:439–444.
23. Bertelsen CA, Andreasen AH, Jørgensen T, Harling H; Danish Colorectal Cancer Group. Anastomotic leakage after anterior resection for rectal cancer: risk factors. *Colorectal Dis*. 2010;12:37–43.
24. American College of Surgeons. ACS National Surgical Quality Improvement Program. http://site.acsnsqip.org/. Accessed March 20, 2014.
25. American College of Surgeons. User Guide for the 2012 ACS NSQIP Participant Use Data File. http://site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf. Accessed March 20, 2014.
26. Trencheva K, Morrissey KP, Wells M, et al. Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. *Ann Surg*. 2013;257:108–113.
27. Kawada K, Hasegawa S, Hida K, et al. Risk factors for anastomotic leakage after laparoscopic low anterior resection with DST anastomosis. *Surg Endosc*. In press.
28. Akiyoshi T, Ueno M, Fukunaga Y, et al. Incidence of and risk factors for anastomotic leakage after laparoscopic anterior resection with intracorporeal rectal transection and double-stapling technique anastomosis for rectal cancer. *Am J Surg*. 2011;202:259–264.
29. Eberl T, Jagoditsch M, Klingler A, Tschmelitsch J. Risk factors for anastomotic leakage after resection for rectal cancer. *Am J Surg*. 2008;196:592–598.
30. Matthiessen P, Hallböök O, Rutegård J, Simert G, Sjödahl R. Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer: a randomized multicenter trial. *Ann Surg*. 2007;246:207–214.
31. Hüser N, Michalski CW, Erkan M, et al. Systematic review and meta-analysis of the role of defunctioning stoma in low rectal cancer surgery. *Ann Surg*. 2008;248:52–60.
32. Tan WS, Tang CL, Shi L, Eu KW. Meta-analysis of defunctioning stomas in low anterior resection for rectal cancer. *Br J Surg*. 2009;96:462–472.
33. Chude GG, Rayate NV, Patris V, et al. Defunctioning loop ileostomy with low anterior resection for distal rectal cancer: should we make an ileostomy as a routine procedure? A prospective randomized study. *Hepatogastroenterology*. 2008;55:1562–1567.
34. Giannakopoulos GF, Veenhof AA, van der Peet DL, Sietses C, Meijerink WJ, Cuesta MA. Morbidity and complications of protective loop ileostomy. *Colorectal Dis*. 2009;11:609–612.
35. Kienle P, Weitz J, Benner A, Herfarth C, Schmidt J. Laparoscopically assisted colectomy and ileoanal pouch procedure with and without protective ileostomy. *Surg Endosc*. 2003;17:716–720.
36. Ulrich AB, Seiler C, Rahbari N, Weitz J, Büchler MW. Diverting stoma after low anterior resection: more arguments in favor. *Dis Colon Rectum*. 2009;52:412–418.
37. Weston-Petrides GK, Lovegrove RE, Tilney HS, et al. Comparison of outcomes after restorative proctocolectomy with or without defunctioning ileostomy. *Arch Surg*. 2008;143:406–412.