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Contemporary management of anastomotic leak after colon surgery: assessing the need for reoperation

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Abstract

BACKGROUND: We sought to investigate contemporary management of anastomosis leakage (AL) after colonic anastomosis.

METHODS: The American College of Surgeons National Surgical Quality Improvement Program database 2012 to 2013 was used to identify patients with AL. Multivariate regression analysis was performed to find predictors of the need for surgical intervention in management of AL.

RESULTS: A total of 32,280 patients underwent colon resection surgery with 1,240 (3.8%) developing AL. Overall, 43.9% of patients with AL did not require reoperation. Colorectal anastomosis had significantly higher risk of AL compared with ileocolonic anastomosis (adjusted odds ratio [AOR], 1.20; \(P = .04\)). However, the rate of need for reoperation was higher for AL in colocolonic anastomosis compared with ileocolonic anastomosis (AOR, 1.48; \(P = .04\)). White blood cell count (AOR, 1.07; \(P < .01\)), the presence of intra-abdominal infection with leakage (AOR, 1.47; \(P = .01\)), and protective stoma (AOR, .43, \(P = .02\)) were associated with reoperation after AL.

CONCLUSIONS: Nonoperative treatment is possible in almost half of the patients with colonic AL. The anatomic location of the anastomosis impacts the risk of AL. Severity of leakage, the presence of a stoma, and general condition of patients determine the need for reoperation.

Although there is a wide variance in the rate of anastomosis leakage (AL) because of more than 40 definitions of AL in literature, the rate is typically reported between 3.5% and 6% after colorectal operations.1–5 However, AL is one of the main factors of mortality of colorectal patients and mortality of patients with the complication has been reported to be as high as 25% to 30%.2,6 Also, AL significantly increases the risk of local tumor recurrence in colorectal cancer surgery because of the stimulation of locally shed cancer cells by cytokines released during inflammation.1,7,8 In the long-term quality of life can be significantly impaired, especially after rectal anastomosis leaks because of fibrosis and anastomotic stricture.9–11 It is important to recognize high-risk patients and the best treatment strategies of AL to decrease mortality and morbidity of such patients.

It is proposed that reduction in the anastomosis region tissue oxygenation due to ligation and resultant ischemia is the main factor that affects AL.6 Consequences of AL depend on the clinical severity of the complication, which may vary from a subclinical leak which can be detected merely on contrast radiology to generalized peritonitis.1,6 Management usually depends on the severity as well as the experience and the view of the operating surgeon.2 Traditionally, AL was managed with resection of the anastomosis and creation of a stoma.2 Alternative treatments include over sewing the anastomosis with or without protective stoma, medical treatment with or without drainage of perianastomotic abscess, and creating a stoma alone.2,6 However, there is no specific guideline in treatment of AL. Although there are limited data, successful treatment of AL without reoperation has been reported in 50% of cases.6 However, factors affecting the management of AL need more investigation. Considering the relatively low incidence of AL in colorectal surgery, randomized control trials and even defining treatment strategies to manage AL requires large and lengthy multicenter
experiences. In addition, there are difficulties in design regarding homogeneous groups of patients to compare regarding treatment of AL. So, although randomized control trials are ideal, they will likely be limited to specific populations and specific types of anastomoses (eg, low anterior resections), therefore, national retrospective studies using reliable databases are more accessible and practical for evaluating the treatments of anastomotic leakage. Using American College of Surgeons’ National Surgical Quality Improvement Program (ACS NSQIP) database, this study aims to investigate contemporary treatment of AL in patients who underwent colon resections and investigate factors affecting the need for reoperation and mortality of patients with AL.

Methods

We conducted a retrospective cohort study using national participant user files and colectomy target files of the ACS NSQIP database during 2012 to 2013. ACS NSQIP is a nationwide outcome-based database which was collected from medical records and provides preoperative to 30-day postoperative information of surgical patients based on clinical data in the United States. ACS NSQIP database includes more than 150 patient variables using standardized definitions created by the ACS. NSQIP database is exempt to obtain informed consent from individual patients and is covered within the hospitals’ patient consent forms. Approval for the use of the NSQIP patient-level data in this study was obtained from the institutional review board of the University of California, Irvine Medical Center, and NSQIP.

We analyzed the available data on adult patients who underwent partial colon resection with anastomosis during 2012 to 2013 in the US. Using the current procedural terminology (CPT) codes, patients were classified into 4 groups of partial colectomy with colocolonic anastomosis (CCA; 44,140 with 44,204), partial colectomy with colorectal anastomosis (CRA; 44,145 with 44,207), partial colectomy with ileocolic anastomosis (ICA; 44,160 with 44,205), and partial colectomy with colocolonic or ICA with a protective stoma (44,141), and partial colectomy with CRA with a protective stoma (44,146 and 44,208). Patients who underwent total colectomy were excluded from the study because the CPT code for total colectomy does not indicate which patients had protective ileostomy. Patients diagnosis was defined based on the International Classification of Diseases, 9th Revision, Clinical Modifications codes of 153, 153.0 to 154.0, 154.1, 230.3, and 230.4 for colorectal cancer, 211.3 and 211.4 for benign tumors, 562.1, 562.10 to 562.13 for diverticular disease, 564.7 and 564.00 to 564.09 for constipation, 555, 555.0 to 555.9 for Crohn’s disease, 569.1 for rectal prolapse, 557, 557.0 to 557.9 for vascular insufficiency of intestine, and 556, 556.0 to 556.9 for ulcerative colitis. AL was defined as a leak of endoluminal contents through an anastomosis. This could include air, fluid, gastrointestinal contents, or contrast material. Also, the presence of an infection and/or abscess thought to be related to an anastomosis, even if the leak cannot be definitively identified as visualized during an operation, or by contrast extravasation, was considered an anastomotic leak if so indicated by the surgeon.

Patient data on baseline patient demographics, comorbidities, operative details, and postoperative complications were extracted from the database. Definitions for NSQIP collected data points according to ACS definition are online available in the NSQIP user guide. The primary end points investigated were rate and management of AL. Patients were identified for AL complication. Risk-adjusted analysis was performed to report independent predictors of need for reoperation in patients with AL.

Statistical analysis

The SPSS software statistical package version 22 (SPSS Inc., Chicago, IL) was used to perform statistical analysis. The main analyses of the study were multivariate statistical analysis using logistic regression and multivariate linear regressions. Bivariate logistic regression was used for binary outcomes such as mortality and need for reoperation for patients with AL. Linear multivariate regression was used for linear outcomes such as hospitalization length. To eliminate confounding variables and report independent associations between perioperative factors and AL.
adjustment was made for all variables of the study without selection. The adjusted odds ratio (AOR) with a 95% confidence interval (CI) was calculated for each correlation and \( P \) values less than .05 indicate statistical significance.

<table>
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<th>Variables</th>
<th>Surgical management of anastomosis leakage (sample size = 696)</th>
<th>Medical management of anastomosis leakage (sample size = 544)</th>
<th>( P ) value</th>
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<td>3.6 ± 0.7</td>
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<td>Dialysis</td>
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<td>Indication of surgery, n (%)</td>
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<td>Colorectal cancer</td>
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<td>218 (40.1)</td>
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<td>Benign colon tumors</td>
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<td>Diverticular disease</td>
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<td>Crohn's disease</td>
<td>49 (7)</td>
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<td>Ulcerative colitis</td>
<td>4 (0.6)</td>
<td>2 (0.4)</td>
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<td>Chronic constipation</td>
<td>1 (0.1)</td>
<td>0</td>
<td>.37</td>
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<tr>
<td>Mesenteric ischemia</td>
<td>16 (2.3)</td>
<td>13 (2.4)</td>
<td>.91</td>
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<td>Rectal prolapse</td>
<td>1 (0.1)</td>
<td>1 (0.2)</td>
<td>.86</td>
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<td>156 (28.7)</td>
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<td>399 (73.3)</td>
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<td>Operation time</td>
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<tr>
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<td>185 ± 112</td>
<td>202 ± 126</td>
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<td>160</td>
<td>178</td>
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<td>Surgical approach, n (%)</td>
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<tr>
<td>Minimally invasive approaches</td>
<td>356 (51.1)</td>
<td>278 (51.1)</td>
<td>.98</td>
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<tr>
<td>Open</td>
<td>340 (48.9)</td>
<td>266 (48.9)</td>
<td>.98</td>
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<td>Anastomosis type, n (%)</td>
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<tr>
<td>Colorectal</td>
<td>195 (28)</td>
<td>181 (33.3)</td>
<td>.21</td>
</tr>
<tr>
<td>Colocolonic</td>
<td>330 (47.4)</td>
<td>207 (38.1)</td>
<td>.04</td>
</tr>
<tr>
<td>Ileocolonic</td>
<td>171 (24.6)</td>
<td>156 (28.7)</td>
<td>.10</td>
</tr>
</tbody>
</table>

(continued on next page)
Results

During the study period, 32,280 patients (16,933 female) with median age of 63 years who underwent partial colectomy were identified from ACS NSQIP database. Most of the patients were Caucasian (86.3%) and the most common comorbidities included hypertension (49.1%), and diabetes mellitus (14.6%). Overall, 1,240 (3.8%) of patients had AL. Of these, 240 (19.4%) were managed medically, 304 (24.5%) were managed with nonsurgical intervention, and 696 (56.1%) underwent reoperation in management of AL. Demographics and clinical factors of the patient with AL based on types of treatment of leakage are described in Table 1.

The mortality rates of patients with and without AL were 8% and 2%, respectively. After adjustment with comorbid factors and demographic data, patients with AL had more than 3 times higher mortality risk (AOR, 3.91; CI, 2.65 to 5.75; \( P < .01 \)). In addition, AL significantly increased the risk of readmission to the hospital (AOR, 1.92; CI, 1.56 to 2.37; \( P < .01 \)). Among patients with AL, patients who underwent reoperation had significantly higher mortality compared with patients managed with medical treatment or interventional treatments (9.5% vs 6.1%; AOR, 1.98; CI, 1.03 to 3.78; \( P < .03 \)). For patients who were managed without reoperation, an interventional procedure was associated with a significant decrease in mortality of patients (4.6% vs 7.9%; AOR, .14; \( P < .04 \)). Overall, patients with AL had significantly longer hospitalization compared with patients without (18 days vs 7 days; adjusted mean difference 5 9; CI, 9 to 10; \( P < .01 \)). The median hospitalization length of patients who underwent reoperation, interventional treatment, and medical treatment of AL were 20, 16, and 12 days, respectively. Patients who underwent reoperation had significantly longer hospitalization compared with patients who were managed with medical treatment or interventional treatments (adjusted mean difference 5 4 days, \( P < .01 \)). Also, patients with interventional treatment had longer hospitalization compared with patients with medical treatment of AL (adjusted mean difference 5 4 days; \( P < .01 \)).

Overall, 1,240 patients had AL. We found a significantly higher risk of AL in CRA compared with ICA (AOR, 1.20; \( P < .04 \)). However, there was not any significant difference in risk of AL between ICA and CCA (AOR, 1.13; CI, .89 to 1.43; \( P < .29 \)). Also, patients who had a protective stoma with anastomosis had significantly lower rate of anastomotic leakage (AOR, .46; CI, .31 to .69; \( P < .01 \)).

Risk-adjusted analysis of factors associated with need for reoperation in management of AL is reported in Table 2. Factors such as emergent surgery, American Society of Anesthesiologists score more than 2, AL with surgical site infection, the absence of a diverting stoma, and preoperative white blood cells count were significantly associated with need for reoperation in management of AL. Also, patients who developed AL for a CCA had a significantly higher risk of unplanned reoperation for management of the leakage compared with patients who had AL for an ICA.

Table 3 describes the associations between perioperative variables and postoperative mortality of patients with AL. Need to reoperation and chronic steroid use were mortality predictors of patients who developed AL.

Fig. 1 reports mortality of patients with AL by age. Patients older than 70 years with AL have a significantly high mortality rate. Also, obese patients have significantly higher mortality risk (Fig. 2).
Our analysis shows AL occurs after colon resections at a rate of 3.8%. It was associated with a significant increase in risk of mortality, readmission, and prolonged hospitalization in our study. Our results reinforce the severity of AL after colonic anastomosis. The rate of AL has been reported as 3.5% to 6% in the literature which is in line with our study result.\(^1\)-\(^3,\)\(^5\) Also, poor prognosis of patients with AL has been cited multiple times.\(^1\)-\(^3,\)\(^6,\)\(^14\) Considering that short-term and long-term outcomes of patients are improved if AL is detected and treated in an early phase, high-risk patients for AL may benefit from some diagnostic interventions that can easily be performed in daily postoperative care.\(^15\)-\(^17\) For example, high-risk patients for AL may benefit from drain analysis after operation. Overall, 80% of patients that develop AL have changes in drain fluid aspect, when drains are used.\(^18\) Macroscopic changes in drain production in AL have been reported to occur before other

| **Table 2** Risk-adjusted analysis of factors associated with need for reoperation in management of anastomosis leakage |
|---|---|---|---|
| **Variables** | **Adjusted odds ratio** | **95% Confidence interval** | **P value** |
| **Age, years** | | | |
| Age >70 | .93 | .65-1.34 | .72 |
| **Sex** | | | |
| Female | .84 | .62-1.14 | .28 |
| **Comorbidity** | | | |
| Hypertension | 1.16 | .83-1.63 | .36 |
| Diabetes mellitus | .81 | .53-1.21 | .31 |
| Chronic obstructive pulmonary disease | 1.09 | .59-2.01 | .76 |
| Bleeding disorders | .82 | .44-1.52 | .54 |
| Chronic steroid use | 1.49 | .84-2.64 | .16 |
| Anemia | 1.17 | .78-1.75 | .43 |
| Congestive heart failure | 1.40 | .38-5.10 | .60 |
| Disseminated cancer | .75 | .44-1.27 | .28 |
| Dialysis | 1.37 | .39-4.75 | .61 |
| **Surgery** | | | |
| Emergent | Reference | Reference | Reference |
| Nonemergent | .60 | 10.41-89 | .01 |
| **Surgical approach** | | | |
| Minimally invasive approaches | Reference | Reference | Reference |
| Open | 1.04 | .75-1.45 | .80 |
| **Procedure** | | | |
| Partial colectomy with ileocolonic anastomosis | Reference | Reference | Reference |
| Partial colectomy with colocolonic anastomosis | 1.48 | 1.01-2.23 | .04 |
| Partial colectomy with colorectal anastomosis | 1.22 | .74-2.03 | .42 |
| **Leakage severity** | | | |
| Anastomosis leakage without surgical site infection | Reference | Reference | Reference |
| Anastomosis leakage with surgical site infection | 1.47 | 1.07-2.03 | .01 |
| **Stoma** | | | |
| Anastomosis without a stoma | Reference | Reference | Reference |
| Anastomosis with a stoma | .43 | .21-87 | .02 |
| **Indication of surgery** | | | |
| Benign colon tumors | Reference | Reference | Reference |
| Colorectal cancer | 1.31 | .63-2.72 | .46 |
| Diverticular disease | .77 | .29-1.99 | .59 |
| Crohn’s disease | .32 | .05-1.93 | .21 |
| Ulcerative colitis | 1 | .35-11.74 | .41 |
| Chronic constipation | † | — | — |
| Mesenteric ischemia | 1.02 | .44-2.34 | .95 |
| Rectal prolapse | .18 | .01-2.77 | .22 |
| **Other factors** | | | |
| Body mass index | .98 | .96-1 | .13 |
| Preoperative sepsis* | .67 | .36-1.24 | .20 |
| ASA score > 2† | 1.55 | 1.08-2.22 | .01 |
| White blood cell count | 1.07 | 1.02-1.12 | <.01 |
| Operation time | .99 | .99-1 | .05 |
| Serum albumin level | .83-1.45 | .48 |

*Preoperative sepsis, septic shock, and systemic inflammatory response syndrome.
†The American Society of Anesthesiologists score more than 2.
‡There was not any case to compare.
clinical signs of AL. Also, checking serum C-reactive protein level on postoperative day 3 or 4 has been suggested for high-risk patients. However, accomplished, it is of great importance to detect AL in the early phase. Finally, leak test during operation is a fast and easy procedure which may help detect AL in high-risk patients. However, there remains no "perfect" diagnostic test for anastomotic leakage and values of these techniques in daily practice need more investigation.

Our study results show 43.9% of ALs were managed without reoperation in 2012. Previously, successful nonsurgical management of AL in 57% to 58% of cases has been reported for a large colon and rectal surgery training program. As we expected, patients who underwent reoperation for anastomotic leakage had significantly higher mortality compared with patients managed without reoperation. Also, such patients had significantly longer hospitalization. However, the 2 groups of patients with reoperation and nonsurgical treatment were not 2 homogeneous groups of patients, and their severity of leakage may differ broadly. Also, some patients with reoperation might have initial unsuccessful nonsurgical management of AL. As expected, we found in nonsurgical treatment of AL, patients who had interventional treatment with medical treatment had significantly lower mortality compared with patients who were managed with medical treatment alone. Further studies are indicated to explain this correlation.

The anatomic location of the anastomosis impacts risk of AL. We found a significantly higher risk of AL in CRA compared with ICA. The site of colonic anastomosis was reported as a factor related to the risk of AL. This could be at least partially because of preoperative radiotherapy in patients with rectal cancer who underwent CRA. However, because of missing data, we could not evaluate associations

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted odds ratio</th>
<th>95% Confidence interval</th>
<th>P value</th>
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<tr>
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<tr>
<td>Need to reoperation</td>
<td>1.98</td>
<td>1.03–3.78</td>
<td>.03</td>
</tr>
<tr>
<td>Preoperative sepsis*</td>
<td>2.68</td>
<td>1.11–6.44</td>
<td>.02</td>
</tr>
<tr>
<td>ASA score &gt;2</td>
<td>1.89</td>
<td>.76–4.67</td>
<td>.16</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>.96</td>
<td>.90–1.03</td>
<td>.36</td>
</tr>
<tr>
<td>Operation time</td>
<td>.99</td>
<td>.99–1.00</td>
<td>.91</td>
</tr>
<tr>
<td>Serum albumin level</td>
<td>.78</td>
<td>.47–1.27</td>
<td>.31</td>
</tr>
</tbody>
</table>

*Preoperative sepsis, septic shock, and systemic inflammatory response syndrome.

1The American Society of Anesthesiologists score more than two.
between AL and preoperative radiotherapy. Investigation of preventive strategies to decrease risk of AL, especially in high-risk patients such as patients with CRA is essential. Although patients with CRA had higher risk of AL in our study, as expected they have a lower rate of reoperation compared with patients who developed a leakage for a CCA (54.3% vs 62.1%). This can be related to the anatomic location of the anastomosis which determines whether the leak is intraperitoneal or extraperitoneal.\textsuperscript{21,22} Because of

![Figure 1](image1.png)

Figure 1  Mortality of patients with AL by age.

the large exposed peritoneal surface, an intraperitoneal anastomotic leak in CCA represents often with classic signs of peritonitis.\textsuperscript{21,22} However, an extraperitoneal anastomotic leak in CRA may present without peritoneal signs and has a higher chance to be managed without reoperation.\textsuperscript{5,21–23} These differences explain different strategies in treatment of extraperitoneal and intraperitoneal AL.\textsuperscript{21}

Severity of leakage, the presence of a stoma, and general condition of patients are 3 important factors deciding need to reoperation in management of AL. Our study results show 42.9% of patients with AL were managed without reoperation. We found severity of the leakage (presence or absence of intra-abdominal infection with the leakage) is an important factor for deciding on reoperation as 70.3% patients who underwent reoperation in management of AL had intra-abdominal surgical site infection. This is in line with the current wait-and-see strategy which is recommended for patients with limited leakage.\textsuperscript{2} In addition, we found preoperative general condition of the patients (American Society of Anesthesiologists score) is significantly associated with need to reoperation in management of

![Figure 2](image2.png)

Figure 2  Mortality of patients with AL by body mass index.
AL. Other factors which have significant associations with need to reoperation in management of patients in our study were admission type and preoperative white blood cells count which both have close relations with general condition of patients. In current guidelines of treatment of AL severity of leakage and general condition of patients (presence or absence of sepsis) are among the important factors which define the best treatment of patients. 

We found patients who had a protective stoma had a significantly lower risk of reoperation in management of AL. They also had a significantly lower risk of AL. This is in line with previous reports showing that creation of a temporary stoma during the first procedure may avoid occurrence of symptomatic AL in high-risk patients.24 The effectiveness of a diverting stoma for anastomotic protection is heavily debated across studies.3,23,25–29 Although a temporary stoma does not necessarily decrease the risk of AL, it significantly decreases the risk of symptomatic AL, septic effects of the leakage, and need for reoperation in patients with AL.3,23,25–28 However, the protective stoma did not significantly decrease mortality of patients who suffered anastomotic leakage in our study. The benefits of creating a stoma in high-risk patients deserve more investigation, especially considering the cumulative morbidity and mortality of patients who then require a second operation for stoma closure.30

This study introduces mortality predictors of patients with AL in colon surgery which can influence the current guidelines of treatment of AL. Our analyses show older age (Fig. 1), obesity (Fig. 2), and chronic steroid use significantly increase risk of mortality. We found mortality of patients with AL has a wide variation of 0% to 19% in different age groups (Fig. 1). Also, chronic steroid use was the strongest predictor of mortality after age. Both corticosteroid and nonsteroidal anti-inflammatory drugs have been reported to have adverse effects on wound healing and increase risk of AL.31,32 Also, patients with chronic steroid use have a high risk of septic complications.32 Such high-risk patients have led to proposals for preventive strategies for AL such as reinforcement of CRA by fibrin glue or cyanoacrylate glue, which remain unproven, however.33,34 Also, placement of one or more drains after colon resection and/or anastomosis may limit the consequences of anastomotic failure such as sepsis in patients with AL.19,28 Tsujinaka et al19 reported existing drain along with conservative treatment resulted in resolved anastomotic leakage in 47.6% of cases with AL. However, the risk of AL may increase in the presence of an irrigation-suction drain.35 Further studies are indicated to investigate the best preventive strategies in high-risk patients for AL.

Study limitations

Our study has a number of limitations. The main limitation is the retrospective nature of the study and as with such studies, is limited in its ability to produce cause–effect relationships as well as control for all possible confounders. Also, coding errors could potentially have occurred.36 The study’s data were collected from a national database and the wide variation in definitions of AL (more than 40 definitions),4 hospital setting, hospital quality, surgical strategy, and surgeons’ expertise can confound the study. We could not investigate AL in patients who underwent total colectomy because of the lack of a reliable CPT code for total colectomy without a stoma creation. An important limitation of our study has been the wide heterogeneity of the patients’ indication of colectomy which may affect the results even after adjustment. NSQIP did not collect some important information such as diagnosis day of AL, any detail in type of procedure was done for surgical treatment of AL, the diagnosis methods of AL, suture technique for the anastomosis, using a drain after resection, preoperative nutritional support, and technique of the colon anastomosis. Also, some patients with anastomotic leak may be diagnosed more than a month after surgery, and we did not have information of patients beyond 30 days of operation.37 We found significant higher risk of AL in CRA compared with CCA. However, patients with CRA may have preoperative radiotherapy and we could not evaluate effects of preoperative radiotherapy on AL. In addition, we did not have information on bowel preparation and/or antibiotic usage and perioperative pain management methods such as narcotic usage that may impact anastomotic leakage and/or outcomes from a leakage. Nevertheless, this study provides a large sample size to
report risk factors and contemporary treatment of AL after partial colectomy.

Conclusions

Postoperative anastomotic leak is associated with increased mortality, hospitalization length, and readmission of patients in colon surgery. The anatomic location of the anastomosis impacts risk of AL. The risk of AL in CRA is significantly higher compared with ICA. However, patients with AL after an ICA have a lower rate of reoperation in treatment of the leakage compared with patients who developed a leakage for a CCA. It is unclear if the correlation is related to the differences in inherent anatomic or physiologic situations of these 2 anastomoses and this deserves more investigations. Severity of leakage, presence of a stoma, and general condition of patients are 3 important factors deciding need to reoperation in management of AL. Our analyses show older age, chronic steroid use, and obesity significantly increase mortality risk of patients. Such high-risk patients may benefit from preventive strategies for AL such as creation of a temporary stoma and intensive perioperative support in treatment of AL to attempt to limit the consequences.

References


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