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Risk Factors for Anastomotic Leakage After Anterior Resection for Rectal Cancer

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Background: The risk factors for anastomotic leak (AL) after anterior resection have been evaluated in several studies and remain controversial as the findings are often inconsistent or inconclusive.

Objective: To analyze the risk factors for AL after anterior resection in patients with rectal cancer.

Design: Retrospective analysis.

Setting: The Nationwide Inpatient Sample 2006 to 2009.

Patients: A total of 72 055 patients with rectal cancer who underwent elective anterior resection.

Main Outcome Measures: To build a predictive model for AL using demographic characteristics and preadmission comorbidities, the lasso algorithm for logistic regression was used to select variables most predictive of AL.

Results: The AL rate was 13.68%. The AL group had higher mortality vs the non-AL group (1.78% vs 0.74%). Hospital length of stay and cost were significantly higher in the AL group. Laparoscopic and open resections with a diverting stoma had a higher incidence of AL than those without a stoma (15.97% vs 13.25%). Multivariate analysis revealed that weight loss and malnutrition, fluid and electrolyte disorders, male sex, and stoma placement were associated with a higher risk of AL. The use of laparoscopy was associated with a lower risk of AL. Postoperative ileus, wound infection, respiratory/renal failure, urinary tract infection, pneumonia, deep vein thrombosis, and myocardial infarction were independently associated with AL.

Conclusions: Anastomotic leak after anterior resection increased mortality rates and health care costs. Weight loss and malnutrition, fluid and electrolyte disorders, male sex, and stoma placement independently increased the risk of leak. Laparoscopy independently decreased the risk of leak. Further studies are needed to delineate the significance of these findings.

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ALTHOUGH THE INCIDENCE and mortality rates for rectal cancer have decreased during the past 20 years[1] morbidity rates after rectal cancer surgery remain high.[2] The cornerstone of rectal cancer treatment has been surgery, often combined with adjuvant therapies, such as radiotherapy and chemotherapy.[3] Patients undergoing resection for rectal cancer can develop a variety of postoperative complications, anastomotic leak (AL) being the most morbid.

Anastomotic leak after rectal cancer surgery has been reported to occur in 5% to 20% of patients.[4-8] Apart from the immediate clinical consequences, such as intra-abdominal or pelvic abscess, peritonitis, colocutaneous fistula, sepsis, longer hospital stay, and increased in-hospital morbidity and mortality,[9,10] AL also carries long-term effects, including impaired pelvic organ function[11] and, most important, increased local cancer recurrence and cancer-specific mortality.[12,13]

The available data regarding AL come from either single-institution or multicenter trials that include a high number of anterior resections from experienced surgeons. There is a scarcity of data on the incidence and risk factors associated with AL from national databases. Moreover, identification of risk factors associated with AL has been inconsistent owing to the limited power of studies. This retrospective analysis using a large population database evaluates the incidence of AL and risk factors associated with AL after anterior resection for rectal cancer.

METHODS

STUDY POPULATION

Using the Nationwide Inpatient Sample (NIS) database, a retrospective analysis was performed of patients who underwent elective an-

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terior resection for rectal cancer between January 1, 2006, and December 31, 2009. The NIS is the largest all-payer inpatient care database in the United States and contains information from almost 8 million hospital stays each year. The data set approximates a 20% stratified sample of American community hospitals, resulting in a sampling frame that comprises approximately 95% of all the hospital discharges in the United States. Data elements in the NIS are drawn from hospital discharge abstracts. Raw numbers are weighted to reflect the national average. Approval for the use of NIS data was obtained from the institutional review boards of the University of California Irvine and the NIS.

INCLUSION AND EXCLUSION CRITERIA

All the patients with rectal cancer who underwent elective laparoscopic or open anterior resection with or without a diverting stoma were included in this study. *International Classification of Diseases, Ninth Revision (ICD-9)* diagnosis and procedure codes that correspond to rectal cancer (154.0, 154.1, 154.8, 197.5, 209.17, and 230.4) and anterior resection (48.40, 48.41, 48.43, 48.49, 48.63, and 48.69) were used. Laparoscopic modifier codes (54.21 and 54.51) were linked to open procedure codes for anterior resection to identify laparoscopic anterior resection. Codes 46.01, 46.11, 46.20, and 46.21 were used for diverting stoma. Patients who received a stoma at the time of their initial surgery were included in this study to exclude those who received a stoma in response to an AL.

Emergency hospital admissions were excluded to prevent bias favoring anterior resection with end colostomy. Patients with cancer and concomitant inflammatory bowel disease were excluded.

PRIMARY END POINT

The primary end point for this study is AL as determined by *ICD-9* codes 997.4, 567.22 (abdominopelvic abscess), and 569.81 (fistula of the intestine).

STUDY VARIABLES

Information on patient age, sex, and race; primary payer type; and hospital type (teaching vs nonteaching), location (urban vs rural), and bed size (small vs medium vs large) was available from the NIS data set. The definitions of hospital type, location, and bed size can be found on the Healthcare Cost and Utilization Project NIS website.[14] Preadmission comorbidity variables were also extracted from the NIS data set; they are based on the Elixhauser predictive model.[15] Preadmission comorbidities provided by the NIS are based on *ICD-9* code definitions (**Table 1**). Surgery type was classified into 6 categories using *ICD 9* codes in the procedure variables: open or laparoscopic, with and without the use of a diverting loop ileostomy or colostomy. Postoperative complications were also determined using *ICD-9* codes.

STATISTICAL ANALYSIS

All the statistical analyses were conducted using commercially available (SAS, version 9.3; SAS Institute, Inc) and free (the R statistical environment[16]) software programs. Demographic and comorbidity data are summarized using means and interquartile ranges for continuous variables and counts and proportions for categorical variables. *P* values are not reported for these data as information from these variables are descriptive in nature. Formal statistical tests on these variables would have to consider the inflation of the experimentwise type I error due to multiple comparisons. Thus, *P* values would be misleading and, hence, are not reported.

To build a predictive model for AL using demographic and preadmission comorbidity data, we used the lasso algorithm for logistic regression[17,18] to select variables that are most predictive of a leak. Tenfold cross-validation and the 1-SE rule were used to control for overfitting. A logistic regression model was then refit using the variables selected. Regardless of the variables selected, age, sex, laparoscopy, and presence of a stoma were forced into the model as previous literature has demonstrated their associations with AL, and, thus, these variables were included in the predictive model. Estimated odds ratios (ORs) and 95% CIs based on robust standard errors are reported. Because data-driven methods were used to derive the predictive model, definitive conclusions regarding associations with leakage cannot be drawn as *P* values and 95% CIs will not have their nominal operating characteristics.

In assessing postoperative complications, we estimated ORs using logistic regression for each complication. The Bonferroni correction was used to control for multiple comparisons. Age older than 60 years, sex, race, hospital teaching status, hospital location, hospital size, use of laparoscopy, presence of a stoma, and all the comorbidities (Table 1) were included in the multivariate analysis. The ORs were significantly different than 1 at the .05 level if the *P* value is less than .05/10 = 0.005 (10 comparisons). The corresponding 99.5% CIs are reported.

RESULTS

A total of 72 055 patients with rectal cancer who underwent elective anterior resection between January 1, 2006, and December 31, 2009, were identified. Of this group, 9855 patients developed an AL postoperatively, yielding a leak rate of 13.68%. **Table 2** lists demographic characteristics and hospital type, location, and size for the AL and non-AL groups. Mean in-hospital mortality was higher in the AL group compared with the non-AL group (1.78% vs 0.74%). The AL group had a longer mean hospital stay compared with the non-AL group (14 vs 7 days). This was reflected in the mean total charges, which were higher in the AL group (non-AL vs AL group: $93 110 vs $51 413). The proportion of teaching vs nonteaching hospitals, urban vs rural hospitals, and hospital size were similar in the AL and non-AL groups.

Most patients underwent open anterior resection (94.14%); of those, 15.89% received a diverting stoma at the time of their initial surgery. Of those who underwent laparoscopic anterior resection (5.86%), only 1.17% received a diverting stoma at the time of resection. Open anterior resection with and without a stoma had a higher incidence of AL than laparoscopic anterior resection with and without a stoma (**Table 3**). Laparoscopic and open anterior resections with a diverting stoma had a higher AL rate (15.97%) than laparoscopic and open anterior resections without a diverting stoma (13.25%).

Table 4 gives the incidence of comorbidities by group. Fluid/electrolyte abnormalities (22.43%), deficiency anemia (16.54%), and weight loss and malnutrition (8.98%) were more prevalent in the AL group. Univariate analysis did not show a higher incidence of obesity or diabetes mellitus in the AL group. These preadmission comorbidities and their definitions according to the NIS are listed in Table 1.

Table 1. Comorbidity Variables and Definitions

Comorbidity	Definition
Alcohol use	Alcohol dependence syndrome, nondependent abuse of alcohol, alcohol withdrawal, alcohol withdrawal delirium, alcohol-induced mental disorders, alcohol-induced disorders
Anemia, deficiency	Iron deficiency anemia, anemia due to chronic kidney disease, anemia due to chronic disease, anemia NOS
Blood loss anemia	Iron deficiency anemia, anemia, anemia complicating pregnancy/child birth, antepartum anemia
Congestive heart failure	Heart failure, systolic heart failure, diastolic heart failure, rheumatic heart failure, heart failure NOS
Chronic pulmonary disease	Bronchitis, chronic bronchitis, emphysema, asthma, bronchiectasis, allergic alveolitis, chronic airway obstruction, pneumoconiosis, asbestosis, pneumonopathy due to inhalation of other dust, chronic respiratory conditions due to fumes or vapors
Coagulation deficiency	Congenital factor VII/IX/XI disorder, congenital deficiency of clotting factors, von Willebrand disease, acquired coagulation deficiency, thrombocytopenia, heparin-induced thrombocytopenia
Depression	Depressive disorder, dysthymic disorder, chronic depressive personality disorder
Diabetes mellitus without chronic complications	Diabetes mellitus, diabetes with coma, secondary diabetes mellitus due to drugs or infection
Diabetes mellitus with chronic complications	Diabetes with renal/ophthalmic/neurologic manifestations, diabetes with peripheral circulatory disorders
Drug abuse (illicit)	Drug dependence, drug withdrawal, drug-induced disorder, cannabis/hallucinogen/opioid/anxiolytic/cocaine/amphetamine abuse
Electrolytes and fluid disorders	Hyperosmolarity/hypernatremia, acidosis, alkalosis, mixed acid-base disorder, hypopotassemia, hyperpotassemia, fluid and electrolyte disorder NOS
HIV and AIDS	HIV, AIDS-related complex with or without other conditions
Hypertension	Uncomplicated hypertension, benign essential hypertension
Hypothyroid	Congenital hypothyroidism, acquired hypothyroidism, iodine hypothyroidism, unspecified hypothyroidism
Liver disease	Chronic hepatitis C, chronic hepatitis C with hepatic coma, esophageal varices with bleeding, esophageal varices, alcoholic cirrhosis, alcoholic fatty liver, chronic hepatitis, biliary cirrhosis, chronic nonalcoholic liver disease, portal hypertension
Lymphoma	Lymphosarcoma, Hodgkin disease, multiple myeloma, other immunoproliferative neoplasms
Metastatic cancer	Secondary malignant neoplasm of the respiratory and digestive systems, secondary malignant neoplasm of unspecified site, secondary malignant neoplasm of the head and neck lymph nodes, malignant ascites, secondary neuroendocrine tumor
Other neurologic disorders	Cerebral degeneration, Parkinson disease, Huntington chorea, acute dystonia, subacute dyskinesia, restless leg syndrome, spinal cerebellar disease, multiple sclerosis, demyelinating CNS disease, epilepsy, pain, seizures, cataplexy, narcolepsy, hypoxic-ischemic encephalopathy, convulsions, altered mental status, aphasia
Obesity	Overweight, morbid obesity, adult BMI of 30-39, adult BMI >40
Paralysis	Flaccid/spastic hemiplegia, cerebral palsy, other paralytic syndromes, functional quadriplegia
Peripheral vascular disease	Peripheral vascular disease unspecified, atherosclerosis, atherosclerosis of the arteries of the extremities, aneurysm, Buerger disease, septic arterial emboli, chronic vascular insufficiency of the intestine
Psychosis	Schizophrenic disorder, unspecified psychosis, delusional disorders
Pulmonary circulation disorder	Pulmonary hypertension, chronic pulmonary heart disease, history of pulmonary embolus, unspecified disease of pulmonary circulation
Renal failure	Chronic kidney disease stage III/IV/V, end-stage renal disease, renal failure unspecified, renal dialysis status, peritoneal dialysis
Rheumatoid arthritis/collagen vascular disease	Hypertrophic and atrophic conditions of the skin, diffuse diseases of connective tissue, systemic sclerosis, sicca syndrome, dermatomyositis, polymyositis, rheumatoid arthritis, inflammatory polyarthropathy, ankylosing spondylitis, polymyalgia rheumatica
Peptic ulcer disease	Gastric ulcer, chronic gastric ulcer with hemorrhage/perforation/obstruction, chronic gastric ulcer without hemorrhage/perforation/obstruction
Valvular disease	Disease of the aortic/tricuspid/mitral/pulmonary valve, diseases of endocardial structures, rheumatic disease of the valve, endocarditis unspecified, aortic valve stenosis/insufficiency, mitral valve stenosis/insufficiency
Weight loss and malnutrition	Protein-calorie malnutrition, kwashiorkor, marasmus

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CNS, central nervous system; HIV, human immunodeficiency virus; NOS, not otherwise specified.

Multivariate analysis revealed that weight loss and malnutrition (OR, 2.81; 95% CI, 2.32-3.40), fluid and electrolyte disorders (1.79; 1.58-2.03), male sex (1.49; 1.35-1.64), and the presence of a diverting stoma (1.16; 1.02-1.32) were independently associated with AL after controlling for all the comorbidities, age, sex, and race. Age older than 60 years, race, and hospital teaching status, size, and location were not associated with AL on multivariate analysis. Comorbidities, including diabetes with or without chronic complications, deficiency anemia, congestive heart failure, chronic renal disease, liver disease, chronic pulmonary disease, peripheral vascular disease, and obesity, were not associated with AL. The use of laparoscopy was independently associated with a lower rate of AL (OR, 0.71; 95% CI, 0.57-0.90).

The incidence of several postoperative complications was higher in the AL group (**Table 5**). After controlling for comorbidities, age, sex, and race, multivari-

Table 2. Demographic Data of the Selected Sample Stratified by Group

Variable	Non-AL Group (n = 62 200)	AL Group (n = 9855)
Age, mean (IQR), y	63 (53-72)	64 (54-73)
Sex, No. (%)		
Male	33 250 (53.46)	6165 (62.56)
Female	28 715 (46.17)	3690 (37.44)
Missing	235 (0.38)	0
Race/ethnicity, No. (%)		
White	38 500 (61.90)	5910 (59.97)
Black	2860 (4.60)	580 (5.89)
Hispanic	3530 (5.68)	525 (5.33)
Asian or Pacific Islander	1945 (3.13)	290 (2.94)
Native American	245 (0.39)	40 (0.41)
Other	1235 (1.99)	200 (2.03)
Missing	13 885 (22.32)	2310 (23.44)
Primary payer, No. (%)		
Medicare	26 450 (42.52)	4665 (47.34)
Medicaid	2860 (4.60)	395 (4.01)
Private including HMO	30 010 (48.25)	4445 (45.10)
Self-pay	1180 (1.90)	150 (1.52)
No charge	215 (0.35)	35 (0.36)
Other	1415 (2.27)	155 (1.57)
Missing	70 (0.11)	10 (0.10)
Hospital type, No. (%)		
Nonteaching	25 265 (40.62)	4095 (41.55)
Teaching	36 740 (59.07)	5735 (58.19)
Missing	195 (0.31)	25 (0.25)
Hospital location, No. (%)		
Urban	57 705 (92.77)	9170 (93.05)
Rural	4300 (6.91)	660 (6.70)
Missing	195 (0.31)	25 (0.25)
Hospital bed size, No. (%)		
Small	6050 (9.73)	995 (10.10)
Medium	12 845 (20.65)	2005 (20.35)
Large	43 110 (69.31)	6830 (69.30)
Missing	195 (0.31)	25 (0.25)
Total charge, mean (IQR), $	51 413 (28 430-59 558)	93 110 (39 149-109 701)
Length of stay, mean (IQR), d	7 (5-8)	14 (8-16)
In-hospital mortality, No. (%)		
Did not die	61 735 (99.25)	9665 (98.07)
Died	460 (0.74)	175 (1.78)
Missing	5 (0.01)	15 (0.15)

Abbreviations: AL, anastomotic leak; HMO, health maintenance organization; IQR, interquartile range.

Table 3. Anastomotic Leak (AL) by Procedure Type

Procedure	Patients, No. (%)		AL Incidence, %	Average AL Incidence, %
	Non-AL Group, (n = 62 200)	AL Group (n = 9855)		
Open resection without colostomy or ileostomy	49 350 (79.34)	7705 (78.18)	13.50	16.06
Open resection with ileostomy	2590 (4.16)	485 (4.92)	15.77	
Open resection with colostomy	6455 (10.38)	1245 (12.63)	16.17	
Laparoscopic without colostomy or ileostomy	3380 (5.43)	350 (3.55)	9.38	14.14
Laparoscopic resection with ileostomy	230 (0.37)	55 (0.56)	19.30	
Laparoscopic resection with colostomy	195 (0.31)	15 (0.15)	7.14	

ate logistic regression analysis revealed that the most common associated complication was postoperative ileus, which was found to occur in 80.72% of patients with AL (OR, 47.43; 99.5% CI, 39.43-57.07). This was followed by wound infection (OR, 6.09; 99.5% CI, 4.85-7.65), which occurred in 15.73% of the AL group vs 2.97% of the non-AL group, followed by other infectious complications, such as urinary tract infection (2.73; 2.06-3.61) or pneumonia (2.69; 1.91-3.79). Respiratory failure (OR, 3.29; 99.5% CI, 2.46-4.41) and renal failure

(2.84; 2.27-3.55) were also associated with AL, as were postoperative cardiac complications, such as myocardial infarction (1.88; 1.28-2.77).

COMMENT

The AL rate of 13.68% falls within the range of previously published series.[5-10] This rate is, however, higher than the average leakage rate of 10% reported in a systematic review by Paun et al.[2] It is also higher than the leakage rate reported in a similar study from Sweden looking at this complication using a population database[19]; however, survival from rectal cancer is reportedly higher in the United States than in Europe.[20] The higher leakage rate in the present study could be explained by the fact that the codes for abdominopelvic abscess and intestinal fistula were included in the definition of AL. This might overstate the leakage rate because some abscesses and intestinal fistulas occur independent of an AL. The high leakage rate may also be a reflection of technically inadequate surgery. Failure to mobilize the splenic flexure, failure to perform high ligation of the inferior mesenteric artery to ensure the collateral blood supply, and failure to test the integrity of the anastomosis or to redo the anastomosis (if there is a concern) can contribute to the high leakage rate.

The true incidence of AL, however, could be higher if we consider that a small portion of ALs can occur after hospital discharge. Jörgren et al[21] showed that AL occurs at a median of 12 days (range, 3-30 days), suggesting that a leak may occur at a later date. Animal studies[22,23] show that the bursting pressure of a colonic anastomosis is lowest between postoperative days 4 and 7, when the anastomosis is most vulnerable to dehiscence and leakage, which corresponds to the average day of hospital discharge or even after the date of discharge for some patients. Anastomotic breakdown that occurred after hospital discharge was excluded from this analysis owing to the limitations of the NIS.

However, hospital type (teaching or nonteaching), location (urban or rural), and size (small, medium, or large) did not seem to affect leakage rates in any of the analyses. One could argue that a difference was not seen in teaching vs nonteaching institutions because a distinction between teaching institutions with and without a colorectal specialist or fellowship could not be made. Also, hospital size was determined by number of beds, which may not always correlate with hospital volume, which may explain why a difference in AL rates was not seen. Specific details such as these are not available in the NIS. However, previously published data from the NIS[24-27] has shown that hospital size is not associated with improved outcomes but rather that surgeon volume and specialized practice are associated with reduced inpatient morbidity, length of stay, and cost. The present results suggest that hospital type, location, and size may not be as important as surgeon experience.

Weight and nutrition are important factors when evaluating patients with a colorectal anastomosis. Obesity was not associated with AL, contrary to findings in a study by Suding et al.[28] However, weight loss and malnutrition before surgery have an important role in AL, correlating with findings from previously reported data.[29] There is evidence in the literature to suggest that obesity becomes a risk factor for leaks in very low rectal anastomoses because it may be related to tension at the anastomotic site.[30]

Table 4. Anastomotic Leak (AL) by Comorbidity

Comorbidity	Patients, No. (%) Non-AL Group (n = 62 200)	AL Group (n = 9855)
Alcohol abuse	890 (1.43)	205 (2.08)
Anemia, deficiency	7925 (12.74)	1630 (16.54)
Chronic blood loss anemia	1090 (1.75)	225 (2.28)
Congestive heart failure	2225 (3.58)	485 (4.92)
Chronic pulmonary disease	7175 (11.54)	1250 (12.68)
Coagulation deficiency	995 (1.60)	290 (2.94)
Depression	3115 (5.01)	460 (4.67)
Diabetes, uncomplicated	9775 (15.72)	1460 (14.81)
Diabetes with chronic complications	780 (1.25)	140 (1.42)
Drug abuse (illicit)	265 (0.43)	45 (0.46)
Fluid and electrolyte disorders	7955 (12.79)	2210 (22.43)
HIV and AIDS	60 (0.10)	5 (0.05)
Hypertension	28 880 (46.43)	4360 (44.24)
Hypothyroidism	4130 (6.64)	545 (5.53)
Liver disease	835 (1.34)	125 (1.27)
Lymphoma	215 (0.35)	40 (0.41)
Metastatic cancer	18 580 (29.87)	3085 (31.30)
Other neurologic disorders	1340 (2.15)	270 (2.74)
Obesity	4920 (7.91)	770 (7.81)
Paralysis	285 (0.46)	85 (0.86)
Peripheral vascular disorders	1610 (2.59)	280 (2.84)
Psychosis	700 (1.13)	165 (1.67)
Pulmonary circulation disorders	515 (0.83)	140 (1.42)
Peptic ulcer disease	5 (0.01)	0
Renal failure	1715 (2.76)	380 (3.86)
Rheumatoid arthritis/collagen vascular diseases	620 (1.00)	60 (0.61)
Valvular disease	2035 (3.27)	250 (2.54)
Weight loss and malnutrition	1810 (2.91)	885 (8.98)

Abbreviation: HIV, human immunodeficiency virus.

The present data suggest that the use of a diverting stoma is predictive of AL. The evidence is conflicting as some researchers have shown that the absence of a stoma is associated with higher leakage rates.[31] Moreover, Dehni et al[32] reported that the use of a diverting stoma reduced the incidence of a clinical leak (symptoms of generalized or pelvic infection). Matthiessen et al[33] further supported this finding in a multicenter randomized trial in which 234 patients underwent a low anterior resection. In the series by Matthiessen et al, a diverting stoma was found to reduce the rate of AL. In a systematic review and meta-analysis by Hüser et al,[34] the occurrence of anastomotic failures was unaffected by the presence of a diverting stoma; however, the use of a diverting stoma seemed to ameliorate the consequences and reduce the incidence of pelvic sepsis. Our findings could be explained by the fact that more difficult and complicated cases, patients with very low anastomoses and those with a history of radiotherapy, which are more prone to leakage, will be more likely to receive a diverting stoma at the time of their operation owing to the surgeons' judgment. This can also explain why only 1.17% of patients who underwent laparoscopic anterior resection had a diverting ostomy placed at the time of initial surgery. Perhaps the conditions of these patients are less complicated (ie, without previous abdominal surgery or a history of radiotherapy) and these patients

Table 5. Postoperative Complications by Group

Complication	Patients, No. (%) Non-AL Group (n = 62 200)	Patients, No. (%) AL Group (n = 9855)	OR (99.5% CI)	*P* Value
Ileus	5045 (8.11)	7955 (80.72)	47.43 (39.43-57.07)	<.001[a]
Wound infection	1850 (2.97)	1550 (15.73)	6.09 (4.85-7.65)	<.001[a]
Respiratory failure	1475 (2.37)	730 (7.41)	3.29 (2.46-4.41)	<.001[a]
Renal failure	3025 (4.86)	1250 (12.68)	2.84 (2.27-3.55)	<.001[a]
Urinary tract infection	1825 (2.93)	750 (7.61)	2.73 (2.06-3.61)	<.001[a]
Pneumonia	1200 (1.93)	495 (5.02)	2.69 (1.91-3.79)	<.001[a]
Deep-vein thrombosis	265 (0.43)	110 (1.12)	2.64 (1.29-5.39)	<.001[a]
Cardiac complications[b]	1210 (1.95)	355 (3.60)	1.88 (1.28-2.77)	<.001[a]
Cerebral vascular accident	80 (0.13)	20 (0.20)	1.58 (0.33-7.59)	.41

Abbreviations: AL, anastomotic leak; OR, odd ratio.
[a] $P < .005$ is considered significant.
[b] Cardiac complications include myocardial infarction and cardiac arrest or insufficiency resulting from a procedure.

had a lower indication for a diverting stoma. Earlier publications, including our own, have shown that when examining the selective use of a diverting stoma, a higher leakage rate is seen in patients who receive a diverting stoma attributed to surgeons' good judgment.[35] Therefore, the use of a diverting stoma should be decided on a case-by-case basis because closure is associated with its own morbidity, with some researchers reporting an overall complication rate of ostomy closure of 17%.[36] Small-bowel obstruction, wound infection, and incisional hernia can occur because a second operation is required for closure. Also, a proportion of these patients will never have their stoma reversed.[37] Owing to the conflicting results of previous studies, future confirmatory studies should be performed to investigate the impact of stoma on leakage.

Laparoscopy was found to be associated with a lower risk of AL. Laparoscopy causes less tissue trauma and is associated with more favorable immunologic outcomes and a lower inflammatory response,[38,39] which could lead to improved anastomotic healing and lower leakage rates. Having a history of abdominal surgery[9] and preoperative radiotherapy,[40] factors previously shown to increase leakage rates and that we could not control for in the analysis, could bias the findings in favor of open surgery, which could explain why the data showed that open surgery had higher leakage rates.

Sex was found to be associated with AL, with males having a higher leakage rate. This finding has been observed in other series[9,30,31,41,42] showing male sex as a risk factor. This could be explained by the fact that males have a narrower pelvis, which makes dissection technically more difficult and more prone to complications.

After examining the risk factors associated with leakage, it is worth noting that AL is associated with higher hospital charges, longer hospital stays, and, most important, higher morbidity and mortality rates. This is most clearly seen in the incidence of wound infection and ileus. Ileus occurs more frequently in patients with AL due to inflammation in the peritoneal cavity. Higher incidences of cardiac, renal, and pulmonary complications occur with AL, which may be due to these patients having more comorbidities or may reflect the stress that an AL puts on patients. Also, longer hospital stays and intensive care unit admission can make these patients more prone to nosocomial infections and other complications, including pneumonia and deep vein thrombosis. The present data show that mortality is higher in the AL group, as expected, which is comparable with other studies.[19,31,43]

This is a retrospective analysis of a national database with limitations. Coding errors can occur but are likely to affect both groups. Information about other important factors, such as history of abdominal surgery, tumor location, cancer stage, and the height of the anastomosis, is unavailable in the NIS. Also, surgeon experience, operative technique, difficulty of the dissection, requirement for blood transfusion,[44-46] and other intraoperative details are unavailable. More important, factors used by the surgeon that influenced the decision to place a stoma are unknown. Factors, such as history of radiotherapy, long protracted surgery, and leak detected at the time of anastomosis, are not provided by the NIS. Smoking, also shown to be associated with AL,[47] was not included in the analysis because smoking history was not coded frequently for these patients. The NIS provides information during a hospital admission only. Thus, the true incidence of leakage could be even higher if we consider that a small percentage of AL occurs after discharge and was undetected in this analysis. For this same reason, the true mortality rate is likely underestimated. Oncologic and functional sequelae after AL also cannot be determined owing to this limitation because patients cannot be tracked. In addition, coding for comorbidities and postoperative complications may result in skewed results due to the vague nature of *ICD-9* definitions for these variables. This retrospective review, however, is one of the largest and most comprehensive studies investigating the risk factors for AL after anterior resection.

In conclusion, the incidence of AL after rectal cancer surgery continues to be a substantial problem despite surgical advances. It is associated with higher mortality and morbidity rates. Male sex, preoperative weight loss and malnutrition, and fluid and electrolyte status were found to considerably increase the risk of AL. The use of laparoscopy was associated with a lower risk of AL. Although more prospective trials are needed, this study provides major insights into identifying important risk factors for the development of AL after anterior resection.

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