International Journal of Surgery

Journal Homepage: ijsopen.org

Research Article

# Non-Gastrointestinal Complications and Short-Term Outcomes in Patients With Anastomotic Leak After Colon Resection: A Propensity Matched Analysis of American College of Surgeons National Surgical Quality Improvement Program Database

***Hazim Hakmi[1], Amir Humza Sohail[1*], Amanda Beneat[1], Shahidul Islam[2], Andrew Morel[1], Hassam Ali[3], Tulio Brasileiro Silva Pacheco[1], Manesh Kumar Gangwani[4], Soban Maan[5] and Jennifer Whittington[1]***

[1]*Department of Surgery, NYU Langone Health - Long Island, New York, USA*
[2]*Division of Health Services Research, NYU Langone Health - Long Island, New York, USA*
[3]*Department of Medicine, East Carolina University, USA*
[4]*Department of Medicine, University of Toledo, Ohio, USA*
[5]*Department of Medicine, West Virginia University, USA*

ARTICLE INFO

*Article history:*
Received: 27 June, 2023
Accepted: 17 July, 2023
Published: 10 August, 2023

Keywords:
*Colorectal anastomosis, leak, failure to rescue*

ABSTRACT

**Introduction:** Anastomotic leak is a devastating complication after colorectal surgery. There is paucity of data on non-gastrointestinal complications after anastomotic leak in this population. We aimed to investigate non-gastrointestinal complications, as well as causes of major morbidity and mortality following anastomotic leak after colorectal resection and hypothesized that non-gastrointestinal complications after anastomotic leak are a sizable proportion of the overall morbidity and mortality in this population. **Methods:** We used the ACS NSQIP database, and searched for CPT codes for colorectal procedures with primary anastomosis between 2015-2019. The cohorts (anastomotic leak vs. no-leak) were aligned using propensity score matching, and 30-day mortality, length of stay, and readmission outcomes were compared. **Results:** We identified 4881 patients with anastomotic leak and 150331 patients with no-leak. The overall leak rate was 3.14%. Anastomotic leak group had an 85% longer length-of-stay. Predicted mean (95% CI) length-of-stay for the leak group was 10.2 (9.9-10.5) days vs. 5.5 (5.4-5.7) days for the no-leak group. Anastomotic leak was associated with a higher 30-day risk of unplanned return to the operating room (OR 34.5; 95% CI 27.2-43.8), and thirty-day mortality (OR 2.8; 95% 2.2-3.5). Anastomotic leak was associated with a higher incidence of pulmonary complications including: pneumonia (OR 4.4; 95% CI 3.5-5.6), unplanned intubation (OR 6.3; 95% CI 4.8-8.3), mechanical ventilation (OR 6.3; 95% CI 5.1-8.0), and pulmonary embolism (OR 4.3; 95% CI 2.6-7.0); cardiac complications, including myocardial infarction (OR 2.9 (95% CI 2.0-4.2) and cardiac arrest (OR 3.2; 95% CI 2.1-4.9); and new-onset renal failure requiring dialysis (OR 3.8; 95% CI 2.6-5.5). There was no significant difference in risk of acute kidney injury (OR 1.1; 95% CI 0.6-2.0), and stroke (OR 1.8; 95% CI 0.9-3.6). **Conclusion:** Colorectal anastomotic leak independently lengthens length-of-stay, and is associated with increased mortality (2.7% vs. 7.2%) after colorectal surgery with an enteric anastomosis.



## 1. Introduction

Anastomotic leaks occur in 6%-27% of patients undergoing colorectal surgery [1]. Leak rates vary dependent upon location of the anastomosis, with entero-enteric anastomosis having the lowest leak rates (1-2%), and colorectal or coloanal anastomosis having the highest rates (5%-19%) [2]. New techniques and devices are continuously developed to mitigate and lower the incidence as well as severity of anastomotic leaks. However, the rate of anastomotic leak continues to be as high in comparison to prior years [1].

*Correspondence to: Amir Humza Sohail, M.D., M.Sc., Department of Surgery, NYU Langone Health - Long Island, 222 Station Plaza North, Suite 300, Mineola, NY 11501, New York, USA; Tel: 5166631525; E-mail: ameer.hamzasohail@gmail.com*


DOI: 10.60122/j.IJS.2023.10.05

The morbidity associated with anastomotic leaks does not pertain only to the gastrointestinal system, but concomitantly affects other vital organ systems such as cardiac, renal, and neurological. Non-gastrointestinal complications are major contributors to readmission, morbidity and mortality after colon resection [1, 3]. It is noteworthy that despite the abundance of research after colon surgery, there remains a paucity of data on non-gastrointestinal complications after anastomotic leak in this surgical population, especially data from large high-quality databases with a heterogeneous patient population.

Therefore, we aimed to investigate non-gastrointestinal complications, as well as causes of major morbidity and mortality following anastomotic leak after colon and rectal resection, with the aim to identify opportunities for early intervention to improve outcomes. Further, we hypothesized that anastomotic leak is associated with longer length of hospital stay and higher mortality.

## 2. Methods

The primary objective of this study was to evaluate and compare clinical outcomes in patients undergoing colorectal surgery with primary anastomosis with and without an anastomotic leak. The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database was used to extract national data for patients that underwent colon resection with primary anastomosis over a period of five years from 2015 to 2019. Patients that underwent this procedure were identified using the following CPT codes for open and laparoscopic colorectal procedures with primary anastomosis: 44140 (colectomy, partial; with anastomosis); 44145 (coloproctostomy "low pelvic anastomosis"); 44147 (abdominal and transanal approach); 44160 (colectomy, partial, with removal of terminal ileum with ileocolostomy); 44204 (colectomy, partial, with anastomosis); 44205 (colectomy, partial, with removal of terminal ileum with ileocolostomy); and 44207 (colectomy, partial, with anastomosis, with coloproctostomy "low pelvic anastomosis"). An anastomotic leak was diagnosed based on the NSQIP variable "COL_ANASTOMOTIC".

Demographic characteristics were summarized by groups and described using the median (interquartile range) or frequency (percentage), as appropriate. Baseline characteristics were compared between groups using the wilcoxon rank sum test for continuous variables, and Chi-square or Fisher's exact test for categorical variables, as appropriate. Since this was not a randomized controlled study and our study groups (anastomotic leak vs. no leak) were imbalanced in terms of sample size, demographics, and clinical characteristics, we implemented a propensity score matching (PSM) method to match patients between groups on several relevant variables to reduce the confounding effects of the covariates on the study outcomes [4]. Specifically, we developed a multiple logistic regression model (MLRM) using "group" as the dependent variable and a selected list of patient characteristics (age, body mass index (BMI), race, sex, smoking status, diabetes mellitus, dyspnea, elective surgery status, functional dependency, mechanical ventilation, chronic obstructive pulmonary disease (COPD), ascites, congestive heart failure (CHF), hypertension, renal failure, dialysis, cancer, wound infection, steroid use, weight loss, transfusion, sepsis, emergency status, American Society of Anesthesiologists (ASA) class and surgical approach) based on clinical expertise and literature review as the covariates. The MLRM allowed us to compute the predicted probability (propensity score) of being in the anastomotic leak vs. no leak groups for each subject in the sample.

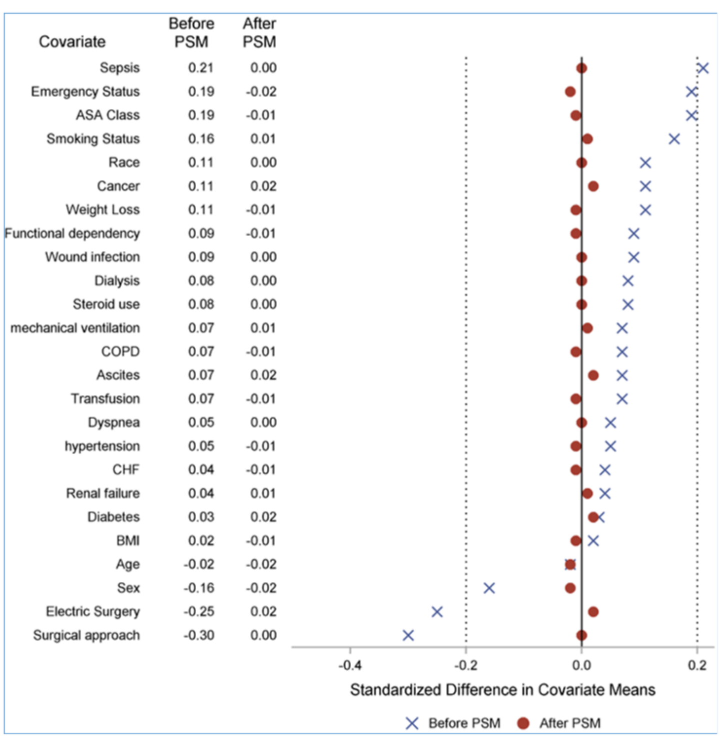


**FIGURE 1:** Love plot depicting standardized differences before and after propensity score matching. The red dots indicate after matching standardized differences, and the blue x marks indicate before matching differences. The red dots are close to zero for all the variables, which suggests a good match. Most of the blue x marks are seen away from the standardized difference of zero for the raw data.

PSM was implemented using the SAS macro One-To-Many Match [5] which used a greedy nearest neighbor matching algorithm without replacement. A caliper size of 0.1 times the logarithm of the standard deviation of the propensity score was used to minimize treatment bias. Patients were matched in a 1:1 ratio of study to comparison groups based on the propensity score. The best matches are those with the highest-digit match on the propensity score. The subjects in the "anastomotic leak" group were matched to those in the "no leak" group on eight digits of the propensity score. For subjects that did not match, seven digits of the propensity score were subsequently used. The algorithm continued to match to the lowest digit. The effectiveness of the propensity score model in achieving covariate balance was assessed using standardized differences in mean responses and displayed using a love plot (Figure 1) [6]. Conditional logistic regression models were used to compare mortality and readmission outcomes between propensity-matched groups. A generalized linear model with random intercept was used to compare length of stay between groups. SAS 9.4 was used to analyze all data, and statistical significance was assumed if p<0.05.

## 3. Results

We identified 4881 patients with anastomotic leak and 150331 patients with no leak using ACS NSQIP data from 2015 to 2019. The overall leak rate was 3.14%. The propensity score matching technique led to matching data with 4181 patients in each group. The demographics and clinical characteristics before and after propensity score matching analysis are shown in (Table 1). Before matching, anastomotic leak was associated with gender, race, current smoking status, dyspnea, diabetes mellitus, hypertension requiring medication, ascites, severe COPD, CHF, need for dialysis, disseminated cancer, functional dependence, ventilator dependence, steroid use for chronic condition, preoperative weight loss (>10%), preoperative transfusion requirement, disseminated sepsis, emergency case, ASA classification-severe, and minimally invasive surgical approach (p-value<0.01 for all). There was no significant association between anastomotic leak and age (p=0.124), and BMI (p=0.48).

Before matching, all the laboratory parameters (serum sodium, serum creatinine, serum albumin, leukocyte count, hematocrit, and international normalized ratio [INR]) were found to be significantly associated with the anastomosis leak (p<0.05 for all), except platelet count (p=0.613) and partial thromboplastin time [PTT] (p=0.546). After matching, anastomotic leak was not associated with any of the demographic, clinical or laboratory parameters (p>0.05 for all), indicating adequate matching (Table 1).

**TABLE 1:** Demographics and clinical characteristics after propensity score matching.

| | **Before Match** | | | | **After Match** | | | |
|---|---|---|---|---|---|---|---|---|
| | **Anastomotic Leak (N=4881)** | **No Leak (N=150331)** | **P-value[1]** | **Missing N** | **Anastomotic Leak (N=4181)** | **No Leak (N=4181)** | **P-value[1]** | **Missing N** |
| ***Demographics*** | | | | | | | | |
| Age (year) | 63.0 (52.00 - 72.0) | 63.0 (52.00 - 73.0) | 0.124 | 0 | 62.0 (51.00 - 72.0) | 62.0 (51.00 - 72.0) | 0.262 | 0 |
| BMI (kg/m2) | 27.8 (23.88 - 32.8) | 27.8 (24.09 - 32.2) | 0.48 | 2644 | 27.5 (23.65 - 32.4) | 27.6 (23.86 - 32.1) | 0.551 | 0 |
| Female gender | 2200 (45.1%) | 79391 (52.8%) | <.001 | 3 | 1906 (45.6%) | 1946 (46.5%) | 0.38 | 0 |
| Race | | | <0.0001 | | | | 0.994 | |
| White | 3295 (67.5%) | 108862 (72.4%) | | 0 | 2917 (69.8%) | 2927 (70.0%) | | 0 |
| African American | 438 (9.0%) | 13849 (9.2%) | | 0 | 377 (9.0%) | 379 (9.1%) | | 0 |
| Asian | 139 (2.8%) | 4710 (3.1%) | | 0 | 112 (2.7%) | 106 (2.5%) | | 0 |
| American Indian/Alaskan Native | 21 (0.4%) | 739 (0.5%) | | 0 | 17 (0.4%) | 15 (0.4%) | | 0 |
| Native Hawaiian or Pacific Islander | 9 (0.2%) | 332 (0.2%) | | 0 | 5 (0.1%) | 4 (0.1%) | | 0 |
| Unknown | 979 (20.1%) | 21839 (14.5%) | | 0 | 753 (18.0%) | 750 (17.9%) | | 0 |
| Current Smoker | 1086 (22.2%) | 23904 (15.9%) | <.001 | 0 | 957 (22.9%) | 945 (22.6%) | 0.754 | 0 |
| Diabetes | 276 (6.3%) | 7559 (5.6%) | 0.04 | 16288 | 260 (6.2%) | 241 (5.8%) | 0.381 | 0 |
| Dyspnea | 384 (7.9%) | 9762 (6.5%) | <.001 | 0 | 311 (7.4%) | 312 (7.5%) | 0.967 | 0 |
| Elective Surgery | 3237 (66.3%) | 116360 (77.4%) | <.001 | 57 | 2823 (67.5%) | 2786 (66.6%) | 0.389 | 0 |
| Functional Dependent | 182 (3.7%) | 3415 (2.3%) | <.001 | 566 | 159 (3.8%) | 168 (4.0%) | 0.612 | 0 |
| Ventilator dependent | 57 (1.2%) | 815 (0.5%) | <.001 | 0 | 49 (1.2%) | 44 (1.1%) | 0.602 | 0 |
| History of Severe COPD | 320 (6.6%) | 7354 (4.9%) | <.001 | 0 | 270 (6.5%) | 284 (6.8%) | 0.538 | 0 |
| Ascites | 57 (1.2%) | 774 (0.5%) | <.001 | 0 | 51 (1.2%) | 41 (1.0%) | 0.295 | 0 |
| Congestive heart failure | 76 (1.6%) | 1656 (1.1%) | 0.003 | 0 | 58 (1.4%) | 64 (1.5%) | 0.584 | 0 |
| Hypertension requiring medication | 2452 (50.2%) | 71768 (47.7%) | <.001 | 0 | 1968 (47.1%) | 1982 (47.4%) | 0.759 | 0 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Currently on dialysis | 86 (1.8%) | 1316 (0.9%) | <.001 | 0 | 75 (1.8%) | 76 (1.8%) | 0.935 | 0 |
| Disseminated cancer | 423 (8.7%) | 8652 (5.8%) | <.001 | 0 | 366 (8.8%) | 346 (8.3%) | 0.433 | 0 |
| Steroid use for chronic condition | 476 (9.8%) | 11305 (7.5%) | <.001 | 0 | 428 (10.2%) | 433 (10.4%) | 0.857 | 0 |
| >10% loss body weight in last 6 months | 312 (6.4%) | 6026 (4.0%) | <.001 | 0 | 276 (6.6%) | 291 (7.0%) | 0.514 | 0 |
| Transfusion >= 1 units PRBCs in 72 hours before surgery | 159 (3.3%) | 3272 (2.2%) | <.001 | 0 | 129 (3.1%) | 136 (3.3%) | 0.662 | 0 |
| Systemic Sepsis | 624 (12.8%) | 10077 (6.7%) | <.001 | 0 | 519 (12.4%) | 521 (12.5%) | 0.947 | 0 |
| Emergency case | 741 (15.2%) | 13671 (9.1%) | <.001 | 0 | 582 (13.9%) | 612 (14.6%) | 0.348 | 0 |
| ASA classification-Severe | 3201 (65.6%) | 84679 (56.4%) | <.001 | 158 | 2649 (63.4%) | 2667 (63.8%) | 0.683 | 0 |
| Minimally Invasive Surgical Approach | 2494 (51.3%) | 98788 (65.9%) | <.001 | 460 | 2147 (51.4%) | 2141 (51.2%) | 0.896 | 0 |
| ***Laboratories*** | | | | | | | | |
| Serum Sodium | 139.0 (137.0 - 141.0) | 139.0 (137.0 - 141.0) | <.001 | 11540 | 139.0 (137.0 - 141.0) | 139.0 (137.0 - 141.0) | 0.069 | 543 |
| Serum Creatinine | 0.9 (0.701 - 1.1) | 0.9 (0.700 - 1.0) | 0.019 | 10292 | 0.9 (0.700 - 1.0) | 0.9 (0.700 - 1.0) | 0.466 | 500 |
| Serum Albumin | 3.8 (3.300 - 4.2) | 3.9 (3.500 - 4.2) | <.001 | 44520 | 3.8 (3.300 - 4.2) | 3.8 (3.300 - 4.2) | 0.478 | 2190 |
| WBC | 7.5 (6.000 - 9.8) | 7.2 (5.720 - 9.1) | <.001 | 8705 | 7.5 (5.950 - 9.7) | 7.5 (5.900 - 9.8) | 0.719 | 425 |
| Hematocrit | 38.6 (33.90 - 42.3) | 39.0 (34.70 - 42.5) | <.001 | 7754 | 38.8 (34.00 - 42.5) | 38.7 (33.60 - 42.3) | 0.057 | 371 |
| Platelet count | 255.0 (203.0 - 321.0) | 254.0 (207.0 - 314.0) | 0.613 | 9003 | 255.0 (205.0 - 321.0) | 256.0 (203.0 - 320.0) | 0.64 | 436 |
| PTT | 29.1 (26.30 - 32.7) | 29.2 (26.60 - 32.5) | 0.546 | 104556 | 29.2 (26.50 - 32.8) | 29.5 (26.80 - 33.0) | 0.183 | 5410 |
| INR | 1.1 (1.000 - 1.2) | 1.0 (1.000 - 1.1) | <.001 | 84407 | 1.1 (1.000 - 1.2) | 1.1 (1.000 - 1.2) | 0.827 | 4139 |

[1]P-values are from Wilcoxon rank-sum test for continuous variables, and Chi-square or Fisher's exact test for categorical variables. Continuous variables are presented as median (interquartile range) and categorical as frequency (percentage).

Anastomotic leak was associated with a higher incidence of pulmonary complications including pneumonia (OR 4.4; 95% CI 3.5-5.6), unplanned intubation (OR 6.3; 95% CI 4.8-8.3), need for mechanical ventilation (OR 6.3; 95% CI 5.1-8.0), and pulmonary embolism (OR 4.3; 95% CI 2.6-7.0). Among renal complications, there was no significant difference in risk of acute kidney injury between the two groups, however odds of new renal failure requiring dialysis were significantly higher in the anastomotic leak group (OR 3.8; 95% CI 2.6-5.5). Anastomotic leak was also associated with almost three times higher risk of postoperative myocardial infarction (OR 2.9 (95% CI 2.0-4.2) and cardiac arrest (OR 3.2; 95% CI 2.1-4.9). Further, the risk of sepsis and wound complications was also higher in patients with anastomotic leak, (Table 2) for details. Stroke was not associated with anastomotic leak (1.8; 95% CI 0.9-3.6).

**TABLE 2:** Non-gastrointestinal complications and short-term outcomes between matched groups.

| Complications | Anastomotic Leak | No Leak | OR (95% CI) [a] | P-value |
|---|---|---|---|---|
| **Pulmonary complications, n(%)** | | | | |
| Pneumonia | 413(9.9%) | 108(2.6%) | 4.4(3.5-5.6) | <0.0001 |
| Unplanned intubation | 379(9.1%) | 70(1.7%) | 6.3(4.8-8.3) | <0.0001 |
| Pulmonary embolism | 82(2.0%) | 20(0.5%) | 4.3(2.6-7.0) | <0.0001 |
| Mechanical ventilation | 586(14.0%) | 126(3.0%) | 6.3(5.1-8.0) | <0.0001 |
| **Renal complications, n (%)** | | | | |
| Acute kidney injury | 27(0.7%) | 24(0.6%) | 1.1(0.6-2.0) | 0.662 |
| New renal failure requiring dialysis | 128(3.1%) | 34(0.8%) | 3.8(2.6-5.5) | <0.0001 |
| **Central nervous systems complications, n (%)** | | | | |
| Stroke | 21(0.5%) | 12(0.3%) | 1.8(0.9-3.6) | 0.122 |

| | | | | |
|---|---|---|---|---|
| **Cardiac complications** | | | | |
| Postoperative myocardial infarction | 105(2.5%) | 38(0.9%) | 2.9(2.0-4.2) | <0.0001 |
| Cardiac arrest | 95(2.3%) | 31(0.7%) | 3.2(2.1-4.9) | <0.0001 |
| **Sepsis** | | | | |
| Postoperative systemic inflammatory response syndrome | 1287(30.8%) | 149(3.6%) | 11.1(9.7-14.4) | <0.0001 |
| Septic shock | 846(10.1%) | 152(3.6%) | 8.0(6.5-9.9) | <0.0001 |
| **Unplanned return to the operating room within 30 days of the initial procedure** | 2447(58.5%) | 136(3.3%) | 34.5(27.2-43.8) | <0.0001 |
| **Wound complications** | | | | |
| Wound disruption | 199(4.8%) | 39(0.9%) | 5.4(3.8-7.8) | <0.0001 |
| Superficial SSI | 287(6.9%) | 176(4.2%) | 1.7(1.4-2.1) | <0.0001 |
| **Clostridium difficile** | 123(3.2%) | 54(1.4%) | 2.4(1.7-3.4) | <0.0001 |
| **Related Readmission** | 1701(40.7%) | 329(7.9%) | 7.3(6.4-8.4) | <0.0001 |
| **Thirty day mortality** | 299(7.2%) | 115(2.8%) | 2.8(2.2-3.5) | <0.0001 |
| **Length of Stay (days)** | 10.2 (9.9-10.5) | 5.5 (5.4-5.7) | | <0.0001 |

[a] Estimated via conditional logistic regression models; OR: Odds ratio.

Length of stay: Anastomotic leak group had 85% greater [estimate=0.6138(0.016)] length of stay than the no-leak group. Predicted mean (95% confidence interval) length of stay for the leak group was 10.2 (9.9-10.5) days vs. 5.5 (5.4-5.7) for the no-leak group.

We found that patients in the leak group had a significantly higher risk of unplanned return to the operating room within thirty days (OR 34.5; 95% CI 27.2-43.8), as well as thirty-day mortality (OR 2.8; 95% 2.2-3.5). Patients in the anastomotic leak group had an 85% longer length of stay than those in the no-leak group. Predicted mean (95% CI) length of stay for the leak group was 10.2 (95% CI 9.9-10.5) days vs. 5.5 (95% CI 5.4-5.7) for the no leak group.

## 4. Discussion

Our results show that patients with anastomotic leak after colon resection have a higher incidence of pulmonary, cardiac, septic and wound complications as well as need for dialysis requirement after acute renal failure. Further, anastomotic leak is associated with a longer length of stay, higher readmission rate, unplanned return to the operating room, and thirty-day mortality. This is one of the first studies in a nationally representative sample investigating non-gastrointestinal outcomes in patients with anastomotic leak after colonic surgery.

Our results showed a mortality rate of 7.2% following anastomotic leak. Previous estimates of this figure range from 12·0% to 18·6% [7, 8]. Predictors of mortality after anastomotic leak include patient age, comorbidities, emergency surgery, and location of colonic resection and anastomosis (vs. rectal resection and anastomosis, which has a significantly lower leak rate of 0·7-4%) [9-11]. Anastomotic leaks after rectal resection tend to be more localized and contained in the pelvis, as compared to colonic leaks, which are more likely to result in generalized peritonitis. Of note, data also show that emergency surgery is associated with higher leak and mortality rates [9-11]. There are several explanations for this observation. Emergency surgery is often required in patients with colonic obstruction or perforation, which are predisposing factors for anastomotic leak. Further, emergency surgery, often required during evening or night time, is often performed by surgeons with lower case-specific volume. There is data to suggest that surgeon-experience and thus technical proficiency is a predictor of postoperative mortality [15, 16].

Our data showed that patients in the anastomotic leak group had an 85% longer length of stay than those in the no-leak group (10.2 days vs 5.5 days). While data from other health systems showed a similar trend, the length of stay was longer (16.78 vs. 14.22 days; p<0.0001) in Korea [17]. Espin *et al.* investigated outcomes in patients with anastomotic leak after right hemicolectomy and reported a mean (standard deviation) length of stay of 29.7 (19.4) days [18]. Similarly, in a Danish national cohort of colon cancer patients, Krarup *et al.* reported a significantly increased mean length of stay in anastomotic leak patients (8.7 days vs 23.3 days; p < 0.001) [19]. Moreover, patients with anastomotic leak and a charlson score of >2, had an even higher mean length of stay (25.5 days) [19]. The widespread variation in length of stay in anastomotic leak patients is a result of differences in myriad factors, such as procedure type, demographic characteristics, surgical technique, comorbidities, and administration of enhanced recovery after surgery (ERAS) pathway.

Interestingly, there was no significant difference in baseline age and BMI in the anastomotic leak vs. no-leak groups. While detailed multivariate analyses to analyze these associations were not conducted, data on the effect of age and BMI on anastomotic leak are well-documented. Evidence suggests that advanced age is a protective factor for anastomotic leak [20-22]. While the reason for this observation is unclear, it is believed to be an artifact of survivor bias, which selects the fittest of individuals that ‘survive’ and reach a certain age group. Similarly, the effect on BMI on anastomotic leak has previously been described in literature, and is consistent with our results. While higher BMI can lead to greater technical difficulty, operating time and blood loss, outcomes, operative outcomes (such as conversion to open, anastomotic leak, reoperation) and even oncologic outcomes (lymph node yield and R0 resection) are similar [23].

Importantly, although anastomotic leak is associated with a significantly higher incidence of acute kidney injury, patients with anastomotic leak had a significantly higher risk of new onset renal failure requiring dialysis. There are several possible explanations for this. It is possible that the leak group has a lower baseline renal function, leading to need for dialysis when acute kidney injury occurs postoperatively. The factors leading to poorer kidney function may also be predisposing these patients to higher risk of leak. Secondly, patients with leak have a higher incidence of sepsis and septic shock, and the associated inflammatory cytokine storm, which may lead to greater kidney decline in kidney function and need for dialysis in these patients.

Patients with leak had a significantly higher incidence of *Clostridium Difficile* infection. Given the need for antibiotic coverage after anastomotic leak, this is not a surprising finding. However, with regards to this finding, the effect of reverse causality cannot be ruled out. Using advanced machine learning and propensity-score analysis, Baker *et al.* showed that *Clostridium Difficile* infection increases anastomotic leak in a dose-dependent manner with increasing ASA Class [24]. Thus, it is possible that a significant proportion of patient's in the leak group acquired pre-leak *Clostridium Difficile* infection that predisposed them to anastomotic leak, as opposed to *Clostridium Difficile* infection being a result of antibiotic administration post-leak.

The present study has several limitations. It is a retrospective observational study with its inherent biases. It is possible that some leak patients were not captured or categorized properly as a result of errors or variations in data entry. Further, absence of data on certain important baseline variables, such as smoking status and alcohol intake, may have resulted in residual confounding in analyses for outcomes, especially pulmonary and cardiac complications. For the patients requiring dialysis after new onset renal failure, we were unable to determine and compare the long-term risk of dependence on dialysis between the two groups. Finally, early (within 3 days of index surgery) incidence of anastomotic leak is associated with worse outcomes in comparison to late leaks [25]. Due to absence of data on the exact timing of leak, we were unable to perform a subgroup analysis investigating outcomes in these two groups. Future studies are required to investigate non-gastrointestinal outcomes in patients in each colon surgery subgroup after anastomotic leak. Further, identification of predictive factors associated with each negative outcome within the leak subgroup may lead to a higher index of suspicion, facilitate early diagnosis and thus lead to reduction in morbidity and mortality.

## 5. Conclusion

Patients with anastomotic leaks after colorectal surgery are known to have a higher risk of morbidity, susceptibility to failure to rescue and mortality. Multiple complications are seen after anastomotic leak with pulmonary and sepsis complications being the most common. Possible lookout and early treatment of the most common complications after anastomotic leak could play a role in reducing rescue to failure.

## Level of Evidence

Level II.

## References

[1] Freek Daams, Misha Luyer, Johan F Lange "Colorectal anastomotic leakage: aspects of prevention, detection and treatment." *World J Gastroenterol*, vol. 19, no. 15, pp. 2293-2297, 2013. View at: Publisher Site | PubMed

[2] Nicole M Saur, E Carter Paulson "Operative Management of Anastomotic Leaks after Colorectal Surgery." *Clin Colon Rectal Surg*, vol. 32, no. 03, pp. 190-195, 2019. View at: Publisher Site | PubMed

[3] I S Bakker, I Grossmann, D Henneman et al. "Risk factors for anastomotic leakage and leak-related mortality after colonic cancer surgery in a nationwide audit." *Br J Surg*, vol. 101, no. 4, pp. 424-432, 2014. View at: Publisher Site | PubMed

[4] Paul R. Rosenbaum, Donald B. Rubin "Reducing Bias in Observational Studies Using Subclassification on the Propensity Score." *Journal of the American statistical Association*, vol. 79, no. 387, pp. 516-24, 1984. View at: Publisher Site

[5] Lori S. Parsons "Performing a 1:N Case-Control Match on Propensity Score." InProceedings of the 29th Annual SAS users group international conference, vol. 1, p. e11, 2004. Montreal, Canada: SAS Institute.

[6] Thomas Love "Displaying Covariate Balance after Adjustment for Selection Bias." InJoint Statistical Meetings, 2002.

[7] R Kube 1, P Mroczkowski, D Granowski, et al. "Anastomotic leakage after colon cancer surgery: a predictor of significant morbidity and hospital mortality, and diminished tumour-free survival." Eur J Surg Oncol, vol. 36, no. 2, pp. 120-124, 2010. View at: Publisher Site | PubMed

[8] Arnaud Alves, Yves Panis, Danielle Trancart, et al. "Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients." *World J Surg*, vol. 26, no. 4, pp. 499-502, 2002. View at: Publisher Site | PubMed

[9] Dutch Institute for Clinical Auditing. *Rapportages* 2011. accessed 26 November 2022.

[10] M den Dulk 1, C A M Marijnen, L Collette, et al. "Multicentre analysis of oncological and survival outcomes following anastomotic leakage after rectal cancer surgery". *Br J Surg*, vol. 96, no. 9, pp. 1066-1075, 2009. View at: Publisher Site | PubMed

[11] H S Snijders, M W J M Wouters, N J van Leersum, et al. "Meta-analysis of the risk for anastomotic leakage, the postoperative mortality caused by leakage in relation to the overall postoperative mortality." *Eur J Surg Oncol*, vol. 38, no. 11, pp. 1013-1019, 2012. View at: Publisher Site | PubMed

[12] Nicolas C Buchs, Pascal Gervaz, Pascal Bucher, et al. "Lessons learned from one thousand consecutive colonic resections in a teaching hospital." *Swiss Med Wkly*, vol. 137, no. 17-18, pp. 259-264, 2007. View at: Publisher Site | PubMed

[13] O H Sjo, S Larsen, O C Lunde, et al. "Short term outcome after emergency and elective surgery for colon cancer." *Colorectal Dis*, vol. 11, no. 7, pp. 733-739, 2009. View at: Publisher Site | PubMed

[14] Martin D Zielinski, Amit Merchea, Stephanie F Heller, et al. "Emergency management of perforated colon cancers: how aggressive should we be?" *J Gastrointest Surg*, vol. 15, no. 12, pp. 2232-2238. View at: Publisher Site | PubMed

[15] A Karliczek, N J Harlaar, C J Zeebregts, et al. Surgeons lack predictive accuracy for anastomotic leakage in gastrointestinal surgery. *Int J Colorectal Dis*, vol. 24, no. 5, pp. 569-576, 2009. View at: Publisher Site | PubMed

[16] Stefan W Leichtle, Nicolas J Mouawad, Kathleen B Welch, et al. "Risk factors for anastomotic leakage after colectomy." *Dis Colon Rectum*, vol. 55, no. 5, pp. 569-575, 2012. View at: Publisher Site | PubMed

[17] Jeonghyun Kang, Hyesung Kim, HyeJin Park, et al. "Risk factors and economic burden of postoperative anastomotic leakage related events in patients who underwent surgeries for colorectal cancer." *PloS One*, vol. 17, no. 5, pp. e0267950, 2022. View at: Publisher Site | PubMed

[18] E Espin, F Vallribera, E Kreisler, et al. "Clinical impact of leakage in patients with handsewn vs stapled anastomosis after right hemicolectomy: a retrospective study." *Colorectal Dis*, vol. 22, no. 10, pp. 1286-1292, 2020. View at: Publisher Site | PubMed

[19] Peter-Martin Krarup, Andreas Nordholm-Carstensen, Lars Nannestad Jorgensen, et al. "Association of Comorbidity with Anastomotic Leak, 30-day Mortality, and Length of Stay in Elective Surgery for Colonic Cancer: A Nationwide Cohort Study." *Dis Colon Rectum*, vol. 58, no. 7, pp. 668-676, 2015. View at: Publisher Site | PubMed

[20] Jeonghyun Kang, Hyesung Kim, HyeJin Park, et al. "Risk factors and economic burden of postoperative anastomotic leakage related events in patients who underwent surgeries for colorectal cancer." *PloS One*, vol. 17, no. 5, pp. e0267950, 2022. View at: Publisher Site | PubMed

[21] Ina Zaimi, Cloë L Sparreboom, Hester F Lingsma, et al. "The effect of age on anastomotic leakage in colorectal cancer surgery: A population-based study." *J Surg Oncol*, vol. 118, no. 1, pp. 113-120. View at: Publisher Site | PubMed

[22] Emily F Midura, Dennis Hanseman, Bradley R Davis, et al. "Risk factors and consequences of anastomotic leak after colectomy: a national analysis." *Dis Colon Rectum*, vol. 58, no. 3, pp. 333-338, 2015. View at: Publisher Site | PubMed

[23] Sofoklis Panteleimonitis, Sotirios Popeskou, Mick Harper, et al. "Minimally invasive colorectal surgery in the morbid obese: does size really matter?" *Surg Endosc*, vol. 32, no. 8, pp. 3486-3894, 2018. View at: Publisher Site | PubMed

[24] Sarah E Baker, Dominique J Monlezun, Wayne L Ambroze Jr, et al. "Anastomotic leak is increased with Clostridium difficile infection after colectomy: machine learning-augmented propensity score modified analysis of 46 735 patients." *Am Surg*, vol. 88, no. 1, pp. 74-82, 2022. View at: Publisher Site | PubMed

[25] Richard T Spence, Dhruvin H Hirpara, Sachin Doshi, et al. "Anastomotic leak after colorectal surgery: does timing affect failure to rescue?" *Surg Endosc*, vol. 36, no. 1, pp. 771-777, 2022. View at: Publisher Site | PubMed