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Narrative Review

Pre-Operative Risk for Colorectal Anastomotic Leakage: A Narrative Literature Review of Modifiable Risk Factors

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Abstract

Anastomotic leaks (ALs) are a significant and feared postoperative complication, with an incidence of up to 30% despite advances in surgical techniques. With implications such as additional interventions, prolonged hospital stays, and hospital readmission, ALs have important impacts for patients, healthcare providers, and healthcare systems. The Risk of colorectal anastomotic leakage can vary by patient, depending on a variety of factors. The aim of this paper is to explore modifiable pre-operative risk factors, providing a window into areas that can be targeted to reduce the likelihood of AL. A literature search and review was conducted using the following keywords: anastomosis, anastomotic leak, colorectal, and risk factors. Following this, further review was conducted using keywords for these factors (alcohol, smoking, obesity, medications, immunosuppression, nutrition, and hypoalbuminemia; American Society of Anesthesiologists (ASA) physical status classification; mechanical bowel preparation; antibiotics). The significance of different modifiable pre-operative risk factors in the development of colorectal anastomotic leaks varies. Most conclusively, smoking, alcohol consumption, malnutrition (as reflected by hypoalbuminemia), and high ASA scores have strong evidence supporting a role in leak risk. Factors such as obesity (high BMI), non-steroidal anti-inflammatory use, immunosuppression, and mechanical bowel preparation had mixed evidence demonstrating impacts on leak risk. Colorectal anastomotic leakage remains a significant challenge in intestinal surgery, despite medical advancements. Awareness of modifiable pre-operative risk factors enables clinicians to address these factors proactively, minimizing the risk of leaks where possible. Additionally, knowing which patients are high-risk ahead of surgery enables more careful postoperative management.

Keywords: Anastomosis, Anastomotic Leak, Colorectal Surgery, Modifiable Risk Factors

Introduction

Research conducted thus far has identified recurring pre-operative, intraoperative, and post-operative risk factors for anastomotic leaks (AL) after colorectal procedures. In this article, the focus will be directed on preoperative risk factors that elevate a patient's likelihood of suffering from AL. Consideration of risk factors is relevant in the decision-making process for clinicians at various levels of a patient's care – impacting surgeons, anesthesiologists, nurses, and general practitioners, to name only a few. Identifying patients at higher risk may allow for more informed pre-operative patient counselling, planning, and preparation before surgery. The aim of the following article is to provide an overview of the current literature on modifiable pre-operative risk factors contributing to the occurrence of AL after colorectal surgery. Such risk factors include alcohol, smoking, obesity, medications, immunosuppression, nutrition, and hypoalbuminemia, the American Society of Anesthesiologists (ASA) physical status classification, mechanical bowel preparation, and antibiotic use. Ultimately, the goal of this discussion is to draw attention to factors that may be modified prior to a patient's surgery, as well as kept in mind during the perioperative period and postoperative management. This knowledge can help clinicians not only prevent leaks but also predict which patients are at highest risk during the postoperative period. Given the substantial human and economic impact of anastomotic leaks (e.g., cost to healthcare systems for tests to diagnose leaks; impacts of late detection such as reoperation, long-term complications, and even death), a clear

awareness of these factors is of great value to all those managing patients undergoing colorectal surgery.

Table 1. Modifiable and Non-modifiable Pre-Operative Risk Factors for AL*[1-5]

Modifiable
Alcohol consumption
Smoking
Obesity
Medications
Immunosuppression
Nutrition & Hypoalbuminemia
ASA Physical Status Classification
Mechanical Bowel Prep & Pre-op
Antibiotics

*While some risk factors are consistently described in the literature, others are controversial. For completeness and transparency, we include all reported risk factors, noting where controversy has been identified. Ongoing orfuture research in this area may provide additional clarity about the impact of specific risk factors.

Modifiable Risk Factors

As with any significant procedure, the risks associated with colorectal surgery may be increased or decreased in accordance with factors that are modifiable. Given that many of these risks can be mitigated with lifestyle changes, it is critical that a patient's care team explore ways to manage such risks in advance, or (if this is not possible) recognize higher-risk patients and manage the approach to surgery accordingly. This includes considerations about the risk of post-operative complications such as AL, which has shown a significant association with many of the modifiable risk factors explored below.

Smoking

Substance use, including alcohol and tobacco, has been found to be a risk factor for AL across numerous studies. The factors contributing to the increased risk of surgical complications are complex, including other lifestyle factors that may augment the effect of smoking and/or drinking alone.

Smoking is established to have a negative impact on surgical outcomes, regardless of the procedure being performed, with active smoking linked to an increased risk of perioperative cardiovascular, pulmonary, and wound healing complications, including infections, anastomotic dehiscence, reintubation, and respiratory failure.[6] For these reasons, preoperative smoking cessation is highly recommended for improving postoperative results. The optimal duration of smoking cessation to confer operative benefits remains under study and is explored in more detail below.[7]

Across several studies, smoking has been found to put patients undergoing anterior or low anterior resection at risk for AL. Research conducted by Kruschewski et al. (2007) found that smokers had an increased risk of anastomotic leakage following anterior or low anterior resection (multiple regression analysis; OR = 6.42, 95% CI: 2.68-15.36).[8] Similar conclusions were obtained in work by Bertelsen et al. (2009), in a study that aimed to identify risk factors for clinical AL following anterior resection for rectal cancer.[9] These findings were based on a national cohort consisting of 1,495 patients who had curative anterior resection surgery between May 2001 and December 2004. Overall, 11% of patients (n = 163) experienced AL. A significantly higher risk of AL was found in smokers compared to non-smokers (OR = 1.88, 95% CI: 1.02-3.46), once again supporting the link between smoking and this significant post-operative complication. Numerous other studies, undertaken to explore the association between smoking and AL, have yielded similar conclusions.[10–12]

In 2012, Richards et al. evaluated 233 patients (identified from a prospective database) undergoing low anterior resection for benign and malignant disease over a 10-year period at a single surgical unit. In this cohort, the overall anastomotic leak rate was 14% (33/233).[13] On multivariate analysis, current smokers (OR 3.68; 95% CI: 1.38-9.82; P = 0.009) and patients with evidence of metastatic malignant disease (OR 3.43; 95% CI: 1.29-9.13; P = 0.013) were at increased risk of anastomotic leak. The authors concluded that both smoking and the presence of metastatic disease are major risk factors for the development of AL following low anterior resection. It is notable that smoking, a modifiable factor, carries as much, if not more, risk than metastatic disease itself. Furthermore, in a 2015 study conducted by Baucom et al., the effect of smoking on clinical leaks after left-sided anastomoses was evaluated.[14] From the sample of 246 patients included in the study, the anastomotic leak rate was 6.5% (n = 16). Importantly, a significant difference was found in leak rates between smokers and non-smokers (17% and 5%, respectively), with smokers experiencing an over four times greater chance of leak (OR 4.2, 95% CI: 1.3-13.5, P = 0.02). From these results, smoking was concluded to be a significant risk factor for AL after a left colectomy.

Additional work has demonstrated that not only is

smoking associated with AL, but also a patient's smoking history (e.g., heavy smoking) confers additional risk. A 2011 publication from Kim et al. utilized univariate analysis to demonstrate that both smoking history and smoking amount were related to the risk of AL, with a heavy smoking history (more than 40 pack-years) an independently significant risk factor for anastomotic complications after low anterior resection in rectal cancer patients.[15] Along similar lines, evaluations about the impact of smoking cessation on reducing AL risk have also been conducted. A recent study by Tsai et al. (2022) investigated the optimal duration of smoking cessation to reduce the risk of anastomotic leaks.[7] Here, a total of 1,246 patients who underwent curative intent sphincter-preserving surgery without preventative stoma were enrolled between 2000 and 2012. Using a receiver operating characteristic (ROC) curve, a cut-off value of 10.5 years of smoking cessation was identified. Moreover, on multivariate analysis, current smoking (P = 0.022) as well as former smoking with less than ten years of smoking cessation (OR = 2.725, P = 0.029) were both found to be independently related to the development of anastomotic leakage. Thus, current evidence suggests smoking cessation for less than ten years continues to present risks for AL in patients with mid-to-low rectal cancer undergoing sphincter-preserving surgery. Additional studies completed by other research groups have led to similar conclusions regarding the importance of smoking cessation prior to colorectal surgery.[6,14] In a 2016 review, short-term cessation was not found to be effective in reducing the risk of anastomotic leaks; a minimum discontinuation of 4 –8 weeks, if not longer, was suggested for benefit.[16] Importantly, smoking cessation should occur not only prior to surgery but also during the postoperative period.

Critically, despite approximately 30% of colon cancers warranting a right hemicolectomy (RH), little data existed until this point regarding the impact of smoking in this context. Recently, Badiani et al. (2022) conducted research to better understand the effect of smoking on postoperative complications following RH.[17] Here, patients who underwent elective RH for colon cancer between 2016 and 2019 were identified from the ACS-NSQIP (American College of Surgeons National Surgical Quality Improvement Program) database. Of the 5,652 RH patients included, 1,884 (33.3%) were identified as smokers. Overall, smoking was found to be a significant risk factor for a variety of serious complications, including a higher rate of organ space infection (4.1% vs. 3.1%, P = 0.034), an unplanned return to the operating room (4.8% vs. 3.7%, P = 0.045), and risk of AL (3.5% vs. 2.1%, P = 0.005). Additionally, smoking was found to be an independent risk factor for wound complications (OR = 1.32; 95% CI: 1.03-1.71; P = 0.032), primary pulmonary complications (OR = 1.50; 95% CI: 1.06-2.13; P = 0.024), and AL (OR = 1.66; 95% CI: 1.19-2.31; P = 0.003). Based on these results, it was concluded that smokers have an increased risk of developing major post-operative complications compared to non-smokers.

Other studies have focused on multiple lifestyle andconcomitant factors that are known to have negative impacts on overall health, including smoking and alcohol consumption (discussed in more detail below). One such early article comes from Sørensen et al. (1999), which focused specifically on the association between AL and smoking and alcohol consumption.[18] Based on 333 patients who underwent colonic or rectal resection with anastomosis between 1993 and 1996, the rate of clinical AL was 15.9% (n = 53). Multiple regression showed that smokers, compared with non-smokers, had an increased risk of anastomotic leakage (relative risk (RR) = 3.18 (95% CI: 1.44 –7.00), as did alcohol abuse (RR = 7.18 (95% CI: 1.20 –43.01). Thus, smoking and alcohol abuse were considered to be important risk factors for anastomotic leakage after colonic and rectal resection.

A 1996 study conducted by Fawcett et al. further supports more recent data exploring the connection between smoking, vascular health, and the risk of AL.[19] Both smoking and hypertension, which contribute to microvascular disease, were found to be associated with an increased incidence of anastomotic dehiscence. Treatment with serotonin antagonists in the perioperative period may be beneficial to maintain microvascular flow (increased serum serotonin and vessel hypersensitivity to serotonin have been observed in smokers, hypertensives, and after surgery). In 2020, an analysis from the National Surgical Quality Improvement Program (NSQIP) identified both smoking and hypoalbuminemia as risk factors for AL after proctectomy and ileal pouch anal anastomosis.[20] From the 910 patients included in this analysis, an overall leak rate of 4.0% (n = 36) was

observed. On multivariate analysis, smoking was found to be the only significant risk factor associated with AL (P = 0.0016). Subgroup analysis of patients with preoperative serum albumin levels revealed that low preoperative albumin was a significant risk factor for AL (P = 0.023).

Research has also been conducted to better understand the pathophysiology behind smoking and increased the risk of surgical complications, including anastomotic leaks.[21] Given the well-established adverse effect of chronic smoking on peripheral vasculature, the negative impact of smoking on rectal mucosal blood flow is posited to play a role. One study measured rectal mucosal blood flow (MBF) in 80 subjects (44 smokers and 36 non-smokers) using laser Doppler flowmetry.[21] Results demonstrated that chronic smokers had significantly lower MBF at the posterior and ventral sites of the rectum compared to non-smokers (P = 0.04 and P = 0.03, respectively). Reduced MBF is thought to impair healing following surgery, increasing the risk of complications such as AL. Additional work found that regular smoking was significantly associated with AL (OR = 6.529, P = 0.007), with the authors suggesting that vascular ischemia from nicotine-induced vasoconstriction and microthromboses, along with carbon monoxide-induced cellular hypoxia, may impair anastomotic circulation in smokers.[22]

In summary, across numerous studies, smoking has been shown to be an important risk factor for anastomotic leaks. While any reduction in smoking is a major win for patients and providers, most evidence points to a significant risk reduction only when smoking cessation has taken place over months or years. Patients with any recent smoking history should thus be monitored carefully for AL following surgery, and additional risk factors should be considered that may further elevate their likelihood of complications alongside smoking.

Table 2. Summary of Findings for Smoking as a Risk Factor

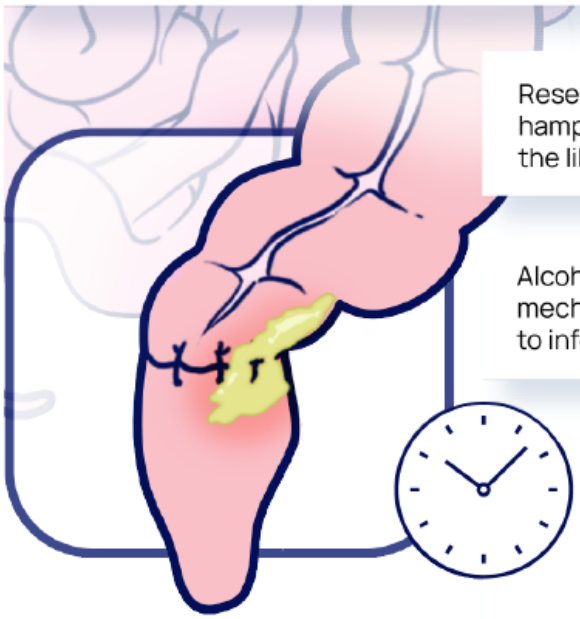
Study Name	Design	Sample Size	Conclusion
Kruschewski et al. (2007)	Multiple regression analysis	N/A	Smoking is known to have a negative impact on cardiovascular health, and so patients with pre-existing coronary heart disease, who also smoke, are likely at an even greater risk than either health concern alone
Bertelsen et al. (2009)	National cohort study	1,495 patients	Smokers have a significantly higher risk of clinical anastomotic leakage following anterior resection for rectal cancer.
Richards et al. (2012)	Prospective database study	233 patients	Both smoking and the presence of metastatic disease are major risk factors for the development of AL following low anterior resection.
Baucom et al. (2015)	Retrospective cohort study	246 patients	Smoking is a significant risk factor for anastomotic leakage after left colectomy.
Kim et al. (2011)	Univariate analysis	154 patients	Heavy smoking history is an independently significant risk factor for anastomotic complications after low anterior resection in rectal cancer patients.
Tsai et al. (2022)	Prospective cohort study	1246 patients	Current and former smoking with less than ten years of smoking cessation are independently related to the development of anastomotic leakage. The optimal duration of smoking cessation to reduce the risk of anastomotic leaks is 10.5 years.

Alcohol Consumption

Similar to smoking, excessive alcohol consumption has been consistently found to be associated with an increased risk for anastomotic leaks. As depicted in Figure 1, there are several factors that are posited to contribute to alcohol's increased risk of AL. Of primary concern are negative impacts on wound healing and increased vulnerability to infection, which may be further heightened by nutritional deficiencies caused by alcohol use. Around the site of the anastomosis, specifically, short-term acute alcohol exposure has been shown to suppress the release of pro-inflammatory cytokines, leading to reduced neutrophil recruitment and phagocytic function, which correlates with a higher risk of post-injury infection.[17] Additionally, ethanol exposure has been shown to affect the proliferative phase of wound healing, disrupting aspects such as re-epithelialization, angiogenesis, collagen production, and wound closure. Most significant is alcohol's impact on wound angiogenesis, which may

The consumption of alcohol has been linked to several negative impacts on the body, such as hindered wound healing and heightened vulnerability to infections. Prolonged alcohol consumption can weaken the immune system, disrupt the formation of new blood vessels (angiogenesis), and interfere with the synthesis of collagen. These processes are vital for effective wound healing.

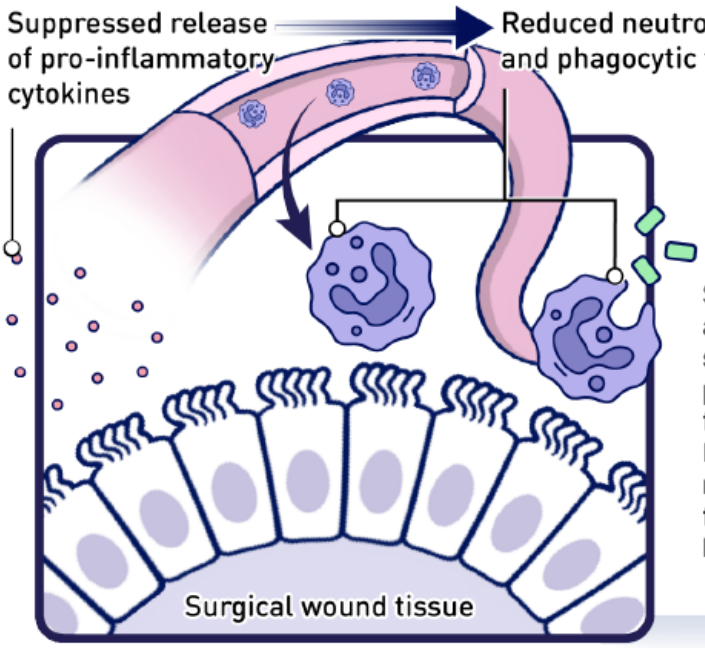
Furthermore, alcohol abuse can lead to nutritional deficiencies, particularly in essential nutrients like vitamin C, which is crucial for collagen synthesis and tissue repair.



Research has demonstrated that alcohol exposure hampers the healing process of wounds and increases the likelihood of infection.

Alcohol exposure weakens the body's defense mechanisms, making individuals more susceptible to infections at the site of the surgical wound.

The effects of alcohol on the body's ability to defend itself are strongly influenced by factors such as the **duration** and **amount** of alcohol consumed, as well as the **timing of exposure** and **withdrawal** from alcohol.



Studies indicate that short-term acute alcohol exposure generally **suppresses the release of pro-inflammatory cytokines** when faced with an inflammatory challenge, leading to **reduced neutrophil recruitment and phagocytic function**, which correlates with a **higher risk of post-injury infection.**

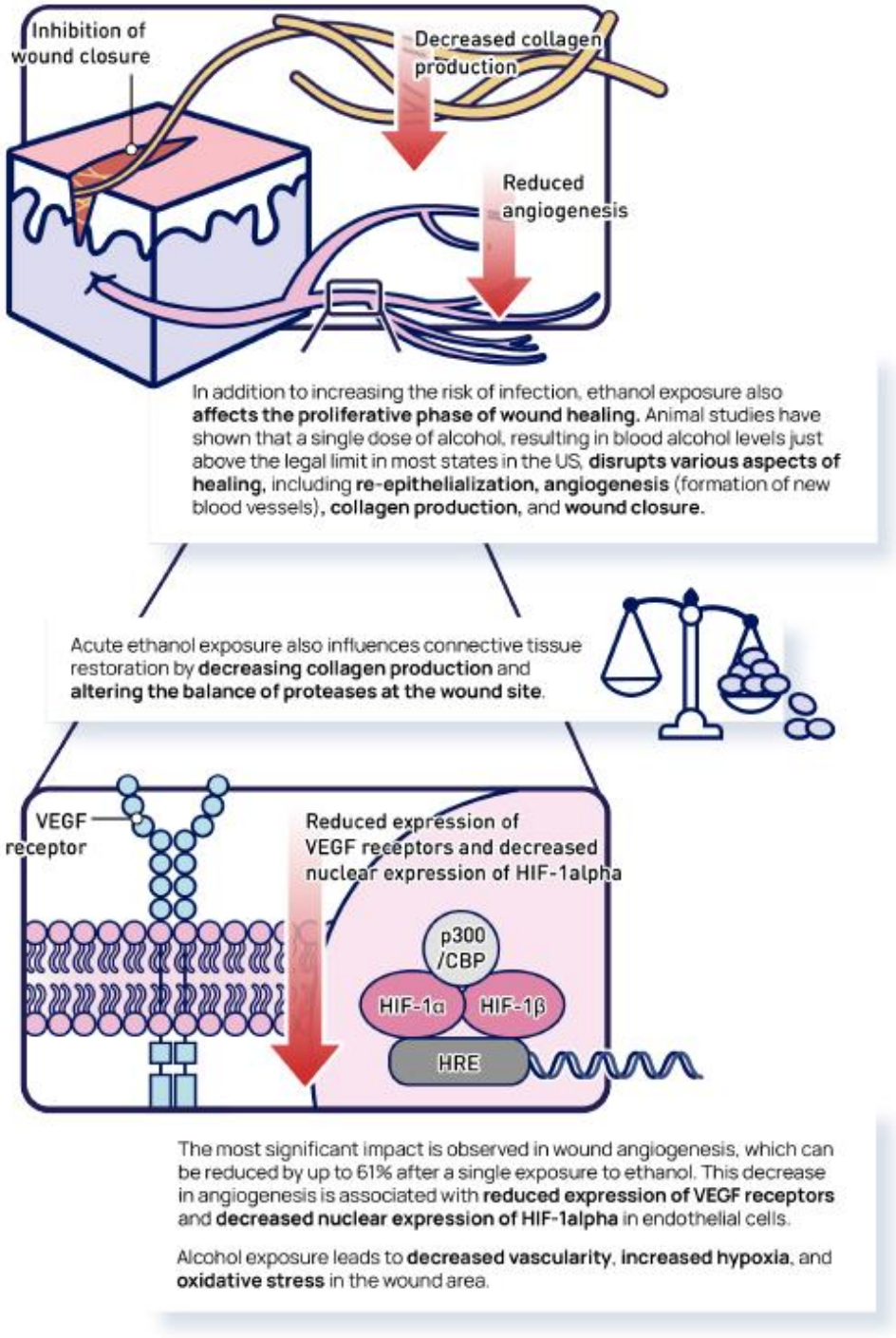


Figure 1. Pathophysiology of Alcohol Consumption and Impaired Wound Healing.[17,22]

be reduced by up to 61% after alcohol exposure. This decrease is associated with reduced expression of VEGF receptors and decreased nuclear expression of HIF-1alpha in endothelial cells.[22] In an early study completed by Mäkelä et al. (2003), patients who consumed alcohol were at a significantly elevated risk for AL compared to those who abstained (OR = 6.19; 95% CI: 2.39-15.99; P = 0.001).[23] Unfortunately, more detailed patient information, including the amount of alcohol consumption patients were reporting, was not provided. A subsequent study completed by Nickelsen et al. (2005) also found a relationship between alcohol consumption and AL.[24] It is important to note that statistically significant results were only obtained for those with heavy alcohol consumption (> 60g/day; OR = 2.48; 95% CI: 1.07-5.77). Those with no/low alcohol consumption were not found to be at increased risk (OR = 0.81; 95% CI: 0.50 –1.31).

Table 3. Summary of Findings for Alcohol Consumption as a Risk Factor

Study Name	Design	Odds Ratio (OR)	Conclusion
Mäkelä et al. (2003)	Early study	OR = 6.19; 95% CI: 2.39-15.99; $P = 0.001$	Alcohol consumption is associated with increased risk for AL.
Nickelsen et al. (2005)	Subsequent study	Heavy alcohol consumption: OR = 2.48; 95% CI: 1.07-5.77. No/low alcohol consumption: OR = 0.81; 95% CI: 0.50-1.31	Heavy alcohol consumption is associated with increased risk for AL.
Jannasch et al. (2015)	Prospective study	OR = 1.628; 95% CI: 1.233-2.150, $P = 0.001$	Alcohol history is associated with increased risk for AL.
McDermott et al. (2015)	Systematic review	OR = 7.18; 95% CI: 1.2-43	Heavy alcohol intake is associated with increased risk for AL.
Bertelsen et al. (2010)	Investigation of risk factors	OR = 1.37; 95% CI: 0.51-3.67	No significant association between alcohol consumption and AL.

In a chart review of the American College of Surgeons NSQIP, patient cases (completed January 2003 – April 2006) were reviewed for evidence of anastomotic leaks for 12 months following the operating date.[25] Patients were tracked for up to 10 years to determine survival while assessing morbidity, mortality, and cost for patients who experienced a leak compared to those who did not. Multivariable regression found that AL was associated with alcohol abuse (OR = 3.7; 95% CI: 2.6–381.4, $P = 0.007$), among other factors such as congestive heart failure and peripheral vascular disease. Further, in a prospective study completed by Jannasch et al. (2015), alcohol history was found to be related to the risk of anastomotic leaks.[26] Overall, 17,867 patients with histopathologically confirmed rectal carcinoma and primary anastomosis were included. Multivariate analysis found that alcohol history was a risk factor for AL (OR = 1.628; 95% CI: 1.233-2.150, $P = 0.001$), although no information was provided specifying the criteria for 'alcohol history.' The authors note that lifestyle factors, such as alcohol consumption and smoking, may be biased, depending on the reliability of patient reports. A systematic review completed by McDermott et al. (2015) found that heavy alcohol intake (>21 units weekly) was associated with AL (RR = 7.18; 95% CI: 1.2-43).[27]

Contrary to other findings, a study by Bertelsen et al. (2010) investigating risk factors for AL after anterior resection for rectal cancer found alcohol consumption was not associated with AL.[9] Other factors that were found to be insignificant in this investigation include preoperative weight loss, BMI, ASA score, and self-reported physical fitness. Results were insignificant for even the highest threshold of alcohol consumption, greater than 35 units per week (OR = 1.37; 95% CI: 0.51-3.67). The discrepancy between these results and other research may be explained by biased patient reporting.

Overall, the evidence is strongly suggestive that alcohol – a modifiable lifestyle factor – is significantly associated with anastomotic leakages in colorectal surgery. Varied findings and levels of clinical significance may be attributable to the challenge of obtaining lifestyle data from patients, who may under or overestimate their alcohol consumption. Additionally, some studies failed to define quantities of alcohol consumed, at times only grouping patients into binary categories (alcohol –: yes or no). All this considered, due to the known detrimental effects of alcohol on surgical outcomes and health overall, encouraging patients to decrease alcohol consumption (particularly for heavy drinkers) is advised to minimize AL risk.

Obesity

It is wellestablished that obesity is a risk factor for numerous health conditions and also adds risk in the surgical setting.[28] In the context of colorectal surgery, obesity has been cited as a risk factor, particularly for left-sided anastomotic leaks.[28] The risk for other postoperative complications is also elevated in obese patients, including wound dehiscence and incisional site herniation.[28] Early reviews of the literature found strong evidence for a link between obesity and anastomotic leaks. Retrospective analyses demonstrated that obesity was a strong risk factor for leaks in those with low-level anastomosis; in some cases, a two-fold increased risk over non-obese patients.[29] In one retrospective review, Benoist et al. found a weakly significant difference in leak rates between obese and non-obese patients ($P = 0.05$).[30] Other studies have found increased odds ratios for the risk of anastomotic leak in obese patients, ranging from 1.5 to 2.32, depending on BMI.[31] However, in multivariate analyses,

Table 4. Summary of Findings for Obesity as a Risk Factor

Study Name	Design	Odds Ratio (OR)	Conclusion
Various, 2023	Literature Review	OR = N/A	Obesity is a risk factor for numerous health conditions, and also adds risk in the surgical setting. Obesity has been cited as a risk factor, particularly for left-sided anastomotic leaks. Risk for other postoperative complications is also elevated for obese patients, including wound dehiscence and incisional site herniation. Early reviews of the literature found strong evidence for a link between obesity and anastomotic leaks.
Benoist et al., 2000	Retrospective Analysis	OR = 1.5-2.32	Obesity was found to be a strong risk factor for leaks in those with low-level anastomosis, with a two-fold increased risk over non-obese patients in some cases.
Various, early publications	Retrospective Analysis	OR = N/A	Some studies found no significant association between obesity and anastomotic leak.
Kang et al., 2013	Retrospective Analysis	OR = 7.18; 95% CI: 1.2-43	No higher incidence of obesity or diabetes mellitus was found in those who suffered a leak.
Piecuch et al., 2015	Retrospective Analysis	OR = 0.58	No significant relationship was found between leak and BMI.

these results were found not to be significant, despite other groups finding significant results using similar statistical methods (OR = 9; $P = 0.016$).[32]

Other studies have found less evidence that obesity itself confers risk and, rather, that low-level rectal anastomosis is the major risk factor.[33] Through retrospective reviews of patient records, several research groups have found no significant association between obesity and AL.[18,34,35] It is important to note that a number of these early publications did not provide full descriptions of their study populations and/or data, including incomplete research definitions of 'obesity' and proportions of overweight or obese patients in study cohorts.

More recent work has presented a similarly inconclusive picture of the exact impact of obesity on anastomotic leak risk. In 2013, a retrospective analysis carried out by Kang et al. (n = 72,055 patients) did not find a higher incidence of obesity or diabetes mellitus in those who suffered a leak.[36] Another retrospective study from Piecuch et al. (2015) also did not find a significant relationship between leak and BMI based on logistic regression (OR = 0.58; 95% CI 0.22-1.53; $P = 0.27$).[37] In a large meta-analysis based on thirty-one studies and 32,953 patients, those with obesity were found to have a significant increase in risk for AL (Western study group: OR = 1.57, 95% CI 1.01-2.44; Asian study group: OR = 1.58, 95% CI 1.07-2.32).[38] Importantly, this increase was only found to be clinically significant in rectal anastomotic subgroups, agreeing with previous findings.

Obesity is associated with various parameters that may themselves better predict a patient's risk for AL than BMI. In 2020, Chen et al. investigated such parameters in 589 rectal cancer patients who underwent anterior resection of the rectum.[39] Results found that sex, neoadjuvant chemotherapy, operation time, and anastomosis level from the anal verge were all risk factors ($P < 0.05$). The level of serum triglycerides was found to be an independent risk factor for AL (OR = 2.95; $P = 0.024$); however, other obesity-associated parameters were not (including BMI; visceral, subcutaneous, and total fat area; and serum cholesterol ($P > 0.05$)).

Overall, results remain mixed regarding obesity and the risk of anastomotic leaks. While in some cases, high BMI (greater than 30kg/m^2) has been identified as an independent risk factor for AL, in other cases, this has not been the case (as described above).[5,40–42] It does appear that, particularly for very low rectal anastomoses, obesity increases the likelihood of a leak (potentially due to tension at the anastomotic site).[5] In other cases, it appears that factors commonly associated with obesity may be driving the relationship between high BMI and AL.[29,40] Regardless, controlled weight loss should be encouraged by clinical teams for any obese patient, including healthy lifestyle choices that decrease the overall risk for

postoperative complications and a range of health issues known to be associated with obesity.

Medications

In addition to substances such as cigarettes and alcohol, certain medications may also play a role in the development of leaks following colorectal surgery. Most research has focused on two classes of prescription

medications and their role in the risk of AL: steroids and anti-inflammatory drugs.

In 2012, a prospective study was carried out by Slieker et al., investigating the risk of AL in 259 patients with left-sided colorectal anastomoses.[43] Importantly, patients involved in this study were prescribed corticosteroids either as a long-term medication or perioperatively for the prevention of postoperative pulmonary complications. Overall, the incidence of AL was 7.3%, with rates significantly higher in those on long-term corticosteroids (50%) or on perioperative steroids (19%). For those with pulmonary comorbidities, the rate of AL was also significantly elevated (22.6%). While this compelling evidence suggests medications can increase the rate of anastomotic leaks, the role of underlying pulmonary disease must be considered. In a 2014 systematic review by Eriksen et al., corticosteroids were found to increase the risk of anastomotic leaks, with an overall AL rate of 6.77% (95% CI: 5.48-9.06) in patients using corticosteroids, compared to 3.26% (95% CI: 2.94-3.58) in those not on the medication.[44] This was based on 12 studies with a total of 9,564 patients. Further evidence supporting a role for corticosteroids in increased risk of AL comes from Jina & Singh (2019), which found an odds ratio of 4.857 (P <0.001) for leaks in patients on corticosteroid therapy compared to those not using the medication.[45]

Conflicting evidence was found in a Danish cohort study by Ostenfeld et al. (2015), which looked at the relationship between AL and preadmission glucocorticoids.[46] Of the overall 18,190 patients with colon cancer, 6.5% experienced an AL. Glucocorticoid use as a whole did not lead to an increase in the risk of AL (6.9% among those who had never used; OR = 1.05; 95% CI: 0.89-1.23). The method of drug administration (oral, inhaled, or intestinal-acting) also did not significantly affect the risk of leakage. Similarly, for those with rectal cancer (n = 5,284 patients), glucocorticoid use slightly elevated the risk (14.6% vs, 12.8% among never-users; OR 1.36; 95% CI: 1.08-1.72), and results did not significantly differ by route of administration. Based on these results, the authors suggested that a moderate risk may be associated with anastomotic leak (particularly after rectal cancer resection), but the absolute risk difference is small and the clinical impact may be limited.

Perioperative use of nonsteroidal anti-inflammatory drugs (NSAIDs) is also associated with a risk of AL. Given that recovery guidelines are increasingly suggesting opioid-sparing medications be used whenever possible following colorectal surgery, post-operative NSAID use is a common occurrence. It is thus important to be aware of the potential impact on the risk of AL from this class of medications.

In 2012, a cohort study was completed evaluating the effect of postoperative use of NSAIDs on AL requiring reoperation following colorectal surgery.[47] Data for this study was drawn from a prospective clinical database and electronic medical records. Overall, NSAID use (specifically, diclofenac and ibuprofen) was found to be significantly associated with the AL rate compared with controls (12.8% and 8.2% vs. 5.1%; P <0.001). After multivariate logistic regression analysis, only diclofenac treatment was found to be a risk factor for leakage (OR 7.2; 95% CI: 3.8-13.4, P <0.001). Based on these results, the authors suggested that medications like diclofenac should be used with caution, but that large-scale, randomized control trials were (at the time) urgently needed to further understand the relationship between NSAIDs and anastomotic leak risk.

While most investigations consider NSAID use broadly, some studies further refine by NSAID type, recognizing that different drugs may confer different risks. Modasi et al. (2018) performed a systematic review whereby the AL rate was assessed following NSAID use for colonic or rectal anastomoses in the post-operative care period.[48] Interestingly, while use of post-operative NSAIDs was associated with an

overall increased risk of AL (OR = 1.58; 95% CI: 1.23-2.03; P = 0.0003), non-selective NSAIDs were associated with increased risk specifically (OR = 1.79; 95% CI: 1.47-2.18; P <0.00001), while selective NSAIDs were not. In this particular review, the non-selective NSAID diclofenac was associated with an increased risk of leakage (OR = 2.79; 95% CI: 1.96-3.96; P <0.00001), while ketorolac was not (OR = 1.36; 95% CI: 0.89-2.06; P = 0.16). These results suggest that certain medications, even within the same drug class, may put patients at higher risk of postoperative complications than others.

A further meta-analysis conducted by Huang et al. (2018) found that, across all studies, there was a significantly lower rate of anastomotic dehiscence in patients not taking NSAIDs (pooled OR = 2.00; 95% CI: 1.48-2.71; P <0.00001).[49] However, when analyses were completed using only randomized control trials, similar dehiscence rates were found between groups (P = 0.17). In subgroup analysis, non-selective NSAIDs were associated with a higher risk of leaks (pooled OR = 2.02; 95% CI: 1.62-2.50; P <0.00001), but there was

no significant difference in the incidence of leaks between patients not taking NSAIDs and those on selective NSAIDs (P = 0.05). Another recent systematic review and meta-analysis by Jamjittrong et al. (2019) found that there was a significant association between NSAID use and anastomotic leakage (OR = 1.73; 95% CI: 1.31-2.29; P <0.0001).[50] Included in this analysis were twenty-four studies with a total of 31,877 patients. Subgroup analyses revealed that non-selective NSAIDs (but not COX-2- selective NSAIDs) were significantly associated with the risk of AL. No significant subgroup difference was found between selective and non-selective NSAIDs. Chen et al. (2022) recently examined postsurgical ketorolac administration and its impact on anastomotic leak rate.[51] In this meta-analysis, which included seven studies and 400,822 patients, an increased risk was observed, though this did not stand up to statistical significance (OR = 1.41; 95% CI: 0.81-2.49; P = 0.23). Subgroup analyses in case-control and retrospective cohort studies did reveal a significantly increased risk of leakage (P <0.05).

Recognizing the many physiological effects that NSAIDs can have, including impacts on wound healing, Hakkarainen et al. (2015) evaluated the relationship between postoperative NSAID administration and anastomotic complications.[52] These results, published in a report from Washington State's Surgical Care and Outcomes Assessment Program (SCOAP), found that NSAIDs were associated with an increased risk of leak, which was isolated to nonelective colorectal surgery (12.3% in the NSAID group vs. 8.3% in the non-NSAID group, OR = 1.70; 95% CI: 1.11-2.68). This was after risk adjustment and based on a retrospective cohort study of 13,082 patients undergoing either bariatric or colorectal surgery.

Some work investigating the impact of NSAIDs on AL leak rates has found conflicting results. In 2020, Arron et al. performed a systematic review and meta-analysis.[53] In this study, which included a cohort of 10,868 patients, the overall anastomotic leak rate was not increased in patients using NSAIDs for postoperative analgesia compared to non-users (RR = 1.23; 95% CI: 0.81-1.86; P = 0.34). Even after stratification for low anterior resections, the effect remained non-significant. When further analyses examined non-selective NSAIDs versus COX-2- selective NSAIDs, again, neither drug sub-type was found to significantly increase the risk of AL (P = 0.19, P = 0.26).

Table 5. Summary of Findings for Medications as a Risk Factor

Study Name	Design	Odds Ratio (OR)	Sample Size
Slieker et al. (2012)	Prospective study	OR = 50% (longterm) or 19% (perioperative)	259 patients
Eriksen et al. (2014)	Systematic review	OR = 6.77% (95% CI: 5.48-9.06)	9,564 patients across 12 studies
Jina & Singh (2019)	Retrospective Analysis	OR = 4.857 (P<0.001)	156 patients
Ostenfeld et al. (2015)	Cohort study	OR = 1.05 (95% CI: 0.89-1.23) (colon cancer) or 1.36 (95% CI: 1.08-1.72) (rectal cancer)	18,190 patients (colon cancer), 5,284 patients (rectal cancer)
Klein et al. (2012)	Cohort study	OR = 7.2 (95% CI: 3.8-13.4, P<0.001)	2756 patients
Modasi et al. (2018)	Systematic review	OR = 1.79 (95% CI: 1.47-2.18; P<0.00001)	9835 participants across seven included studies

Given that other drugs taken concurrently can bias risk assessment, Rushfeldt et al. (2016) carried out a study specifically investigating the risk of AL associated with NSAIDs and steroids used perioperatively.[54] Based on a total of 376 patients included in the study, the rate of AL in the cohort was 15.7%. When adjusted for age, sex, and multivariable propensity scores, the OR for leak was found to be 1.07 (P = 0.92) for ketorolac, 1.63 (P = 0.31) for diclofenac, and 0.41 (P = 0.19) for dexamethasone. Regular use of steroids conferred an OR of 7.57 (P = 0.009). Other factors included in the study, such as malignancy, use of a vasopressor, and blood transfusions, were similarly found to have a significant risk of leaks. As such, the study authors concluded that factors beyond perioperative drugs may be more crucial for surgical teams to consider, given their modest impact on AL risk.

Overall, conclusions about NSAID use and the risk of anastomotic leaks remain mixed. As outlined in an article by Lee & Fiore Jr. (2021), all evidence points to more benefits from NSAID use as post-operative pain control than downsides from the risk of anastomotic leak.[55] Given the unclear association between NSAID use and AL, more evidence is necessary to continue

elucidating the role of NSAIDs as a risk factor for post-operative leaks. It is important to note that patients on long-term corticosteroids and/or anti-inflammatory drugs would have been prescribed these medications to treat another pre-existing condition, which could also contribute to the development of conditions favoring post-operative complications, such as an AL.

Immunosuppression

When considering preoperative risks for patients undergoing colorectal surgery, immunosuppression is a critical factor that must not be overlooked. Not only is the prevalence of immunosuppression for surgical patients nearly double (~5%) that of the average citizen in the United States, but this number is expected to continue to rise as survival outcomes for immunosuppressed patients improve.[56,57]

In 2014, Snieder & Davids explored the effects of chemotherapy, radiation, and immunosuppression on the integrity of intestinal anastomosis.[58] As discussed above, corticosteroids (which have a significant impact on immunosuppression) are recognized to confer a risk for AL in colorectal surgery. Snider & Davids further explored other agents that result in suppression of the immune system, including immunomodulators (e.g., azathioprine and 6-mercaptopurine) and biologic agents (e.g., infliximab). In a retrospective study involving 417 patients with bowel anastomoses for Crohn's disease, there was no significant difference in risk between patients on immunomodulators versus not (10% versus 14%, $P = 0.263$), though use of corticosteroids was once again found to be a risk factor ($P = 0.007$).[59] Similarly, in a retrospective analysis of 518 patients undergoing elective laparoscopic bowel resection (142 of which were on preoperative infliximab), no difference was found in the rate of AL between patients on the biologic agent versus not (2.1% with infliximab vs. 1.3% without, $P = 0.81$).[60]

In addition to corticosteroids, immunomodulators, and biologic agents, long -term immunosuppression in organ transplant recipients has also been considered. Given the chronic nature of these immunosuppression regimens and the impact they may have on wound healing, studies have been conducted to explore the potential elevation in risk presented for AL. Despite limited clinical data on the use of newer immune-suppressive agents (mTOR inhibitors, such as sirolimus and everolimus), animal studies have investigated the impact on AL. A study in a rat model found that everolimus decreased ileal and colonic anastomotic breaking strength in a dose-dependent manner, up to 73% at the highest dose, 3 mg/kg/24 h ($P < 0.05$).[61] When examined histologically, the anastomoses of rats treated with the mTOR inhibitor demonstrated signs of decreased anastomotic healing, including less collagen deposition and hydroxyproline content. In a follow-up study conducted in the same rat model, no significant changes in anastomotic strength were observed if everolimus administration was withheld in the early postoperative period (first 2-3 postoperative days), suggesting that mTOR inhibitors have the greatest impact on the early, proliferative phase of wound healing.[62] Further experimental evidence exists to suggest that other immunosuppressants may slow wound healing (and, by extension, increase the risk of AL), including mycophenolate mofetil, cyclosporin A, and tacrolimus.[63–65] Other treatments, including recent chemotherapy and antiangiogenic and antimitotic agents, have been suggested to impact AL risk via impaired wound healing, though direct evidence linking these agents and AL in human patients remains lacking.[27]

In 2016, Yamamoto et al. conducted a retrospective, multicentre study to identify risk factors for complications following ileocolonic resection for Crohn's disease, focusing specifically on preoperative immunosuppression and biologic therapy.[66] Based on data from 231 patients across three countries (Japan, Brazil, and Italy), neither immunosuppression nor biologic therapy prior to surgery was found to be significantly associated with complications, including anastomotic leaks. That same year, Thomas & Margolin published an article exploring various considerations in the management of anastomotic leaks, including immunosuppression.[3] Importantly, they point out the challenges for assessing this risk factor, noting that because colorectal anastomoses are frequently carried out in patients with diseases requiring immunosuppressive therapy (who may also be sicker than the average patient, e.g., IBD), it is difficult to tease apart the role of immunosuppression itself from other patient characteristics that play into AL risk. Though corticosteroids are well-recognized as a risk factor, other immunosuppressive drugs have not been studied extensively enough to provide definitive conclusions. Even for immunosuppressive drugs that have been studied (as discussed above), results have been mixed, with some studies finding increased risk

and others having insignificant impacts on the likelihood of AL.

Given this conflicting data in the literature and the often pivotal role immunosuppressive agents play in managing pre-existing conditions patients present to surgeons with, some research has begun to emerge that explores the impact of chronic immunosuppression on outcomes of colorectal surgery. El Hechi et al. (2020) examined the Colectomy-Targeted ACSNSQIP database for patients who underwent emergent colectomies, dividing patients into those using immunosuppressants (IMS) versus those with no immunosuppression use (NIS).[67] Out of the total 17,707 patients who underwent an emergent colectomy, 15,422 were NIS, and 2,285 were IMS. After patients were propensity-score matched on demographics, comorbidities, preoperative laboratory values, and operative variables, a total of 2,882 patients were included for analyses (1,441 NIS, 1,441 IMS). Though other complications were found to be significantly elevated in patients with immunosuppression, the rates of anastomotic leaks were not significantly different between the two groups (P = 0.13). Similarly, other wound infections were not significantly elevated in those receiving immunosuppression (superficial, deep, and organ/space surgical site infection: P = 1, P = 0.61, and P = 0.41, respectively).

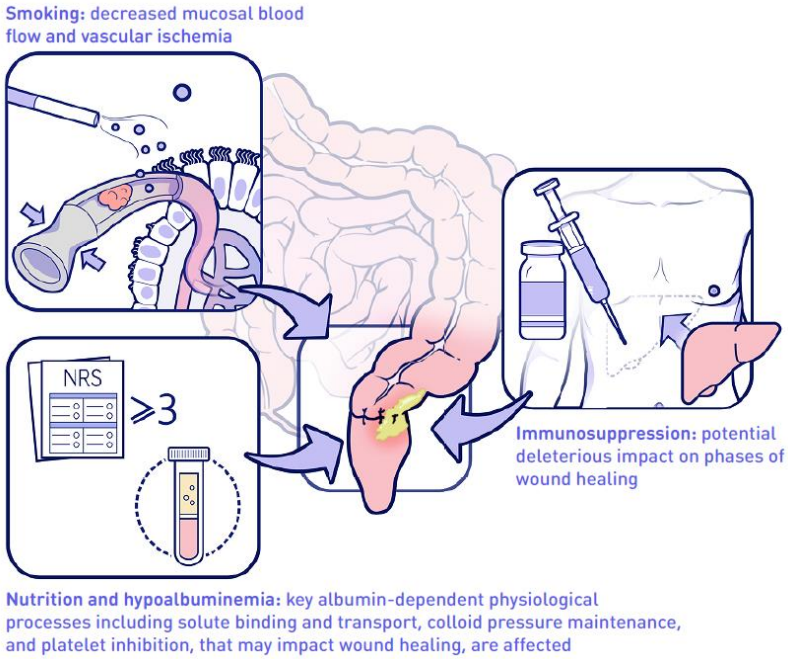


Figure 2. Pathophysiology of Certain Modifiable Risk Factors in AL Patients.[21,62,68]

Table 6. Summary of Findings for Immunosuppression as a Risk Factor

Study Name	Design	Sample Size	Conclusion
Snieder & Davids (2014)	Prospective study	417 patients	No significant difference in the risk of anastomotic leak (AL) between patients on immunomodulators and those not on immunomodulators. Corticosteroids were found to be a risk factor for AL.
Eriksen et al. (2014)	Retrospective Analysis	518 patients	No difference in the rate of AL between patients on the biologic agent (infliximab) and those not on the biologic agent.
Jina & Singh (2019)	Animal study	156 patients	Everolimus (mTOR inhibitor) decreased ileal and colonic anastomotic breaking strength and impaired anastomotic healing.
Yamamoto et al. (2016)	Cohort study	231 patients	Preoperative immunosuppression and biologic therapy were not significantly associated with complications, including anastomotic leak.
El Hechi et al. (2020)	Cohort study	2,882 patients	Rates of anastomotic leaks were not significantly different between patients with immunosuppression and those without. Other wound infections were also not significantly elevated in patients receiving immunosuppression.

Nutrition and Hypoalbuminemia

Given the impact of nutrition (and malnutrition) on processes throughout the body, including those relevant to postoperative complications (e.g., wound healing), it is not surprising that associations have been found between malnutrition and anastomotic leaks. Alongside nutritional deficits more broadly, specific physiological outcomes such as hypoalbuminemia have been observed as particularly important biomarkers for AL risk.

Research conducted by Kang et al. (2013) found that, within 72,000 rectal resections, preoperative weight loss and malnutrition (OR = 2.81; 95% CI: 2.32-3.40) and fluid and electrolyte disturbances (OR = 1.79; 95% CI: 1.58-2.03), conferred an increased risk for AL.[36] Shortly thereafter, Kwag et al. (2014) identified poor nutrition as an independent risk factor for postoperative morbidity in patients undergoing surgery for colorectal cancer.[68] In this study, 352 patients (enrolled prospectively) had nutritional risk screening (NRS) scores calculated on admission, alongside other clinical characteristics (e.g., tumor status, surgical procedure, etc.). Those at nutritional risk (based on the NRS score) were significantly more likely to experience postoperative complications, including anastomotic leakage (P = 0.027) and wound infection (P = 0.01). A follow-up study carried out by Lee et al. (2018) aimed at further evaluating the association between NRS scores and AL again found significant results.[69] Here, retrospective reviews of data from rectal cancer surgeries found that high NRS scores (increased nutritional risk) were an independent risk factor for AL (OR = 2.044; 95% CI: 1.085-3.851).

Albumin remains a gold standard for preoperative markers of nutrition and, thus, is an important parameter to explore when understanding the risks of anastomotic leaks. In a prospective observational quality-improvement study by Sameer M.D. et al. (2018), a cohort of 100 patients undergoing small and large bowel resections was included.[70] Uni- and multivariate analyses identified several factors that were significantly associated with AL risk, including serum albumin <= 3.0 g/dl and serum pre-albumin <= 20 mg/dl. This study also found that pre-albumin was a better indicator of AL risk compared to albumin (P = 0.002), suggesting that pre-albumin may be a better marker to use when assessing the nutritional status of patients as it relates to the risk of anastomotic leaks. More recent research from Xu & Kong (2019) further clarifies the role of malnutrition-related factors and how these contribute to an elevated risk for anastomotic leakage in the context of surgery for rectal cancer.[71] Based on perioperative clinical data from 382 patients, multivariate analysis revealed that low postoperative albumin (P = 0.044) was a significant independent risk factor for postoperative AL. This suggests that monitoring patient albumin levels both prior to and following surgery may be valuable in discerning nutritional status and the risk of leakage. Further, in a NSQIP investigation carried out in 2020, subgroup analysis for the 543 patients with available preoperative serum albumin levels revealed that low albumin levels prior to surgery were significantly associated with a risk for AL (P = 0.023).[20]

In 2008, a prospective review of patient and operative characteristics that contribute to anastomotic leaks was undertaken in a cohort of 672 patients.[72] Here, several variables were found to be significant risks for AL in colorectal resection, including baseline albumin levels less than 3.5 g/dl (P = 0.04). Other risk factors discussed previously in this article (or to follow) were also identified, such as male sex (P = 0.03) and steroid use at the time of surgery (OR = 3.85; 95% CI: 1.24-11.93; P = 0.02). A subsequent retrospective audit of anastomotic leaks in 1,246 patients (137 of whom experienced a leak) also found albumin levels less than 3.5 g/dl to be an independent risk factor, as were factors including anemia, hypotension, use of inotropes, and blood transfusion.[73] These findings were confirmed once again in 2017 by Anandan et al., in a cohort of 112 patients (preoperative serum albumin <3.5 g/dl significantly associated with leaks; P = 0.0418), and later by Awad et al. (2021) (P = 0.015).[74,75]

Other research has assessed not only the impact of serum albumin on the risk of AL but also how monitoring albumin levels may be beneficial for detecting leaks. Shimura et al. (2018) enrolled 200 colorectal cancer patients undergoing curative laparoscopic surgery, of whom 11 cases (5.6%) experienced a leak.[76] Here, there was no difference in preoperative serum albumin levels between the leakage group and the non-anastomotic leakage group, though postoperative serum albumin levels were significantly lower in those patients with an AL. On multivariate analysis, lower average serum albumin levels on postoperative days 1 and 3 were found to be

independent risk factors for anastomotic leakage (OR = 7.53; 95% CI: 1.60-55.80; *P* = 0.0095). This suggests that daily monitoring of postoperative serum albumin levels may help determine which patients are at greatest risk of developing an anastomotic leak.

Additional work has focused not only on passively assessing the impact of nutritional status (including pre-albumin/albumin), but also on evaluating how nutritional interventions may help reduce the risk of AL. Tian et al. (2020) assessed whether early enteral nutrition (EEN) could reduce the risk of recurrent leakage in colorectal cancer surgery.[77] Here, 12 out of a total of 133 patients experienced recurrent leakage in the EEN group, compared to 28 cases (40%) in patients receiving a standard postoperative nutritional protocol. This suggests that optimizing nutrition in the postoperative period may be beneficial for reducing the risk of recurrent leaks.

Overall, the evidence available thus far strongly supports an association between pre-, peri-, and postoperative hypoalbuminemia (a key marker for malnutrition) and the risk of anastomotic leaks following colorectal surgery. Given albumin's key physiological functions, including binding and transport of solutes, platelet inhibition, antithrombosis, and maintenance of colloid pressure, it is well-established that hypoalbuminemia has a deleterious effect on wound healing in colorectal surgery (among other surgical procedures).[78,79] Thus, a focus on both pre- and postoperative nutritional protocols that maintain albumin levels above 3.5 g/dl should be a priority in preventing anastomotic leaks, among other complications.

American Society of Anesthesiologist (ASA) Physical Status Classification

The ASA physical status examination is used by anesthesiologists to classify the preoperative physical condition of surgical patients. The scale ranges from 1 (healthy patient) to 5 (patient not likely to survive 24 hours).[80] As might be expected, ASA scores have been found to be associated with the risk of anastomotic leakages, with higher ASA scores indicating a higher risk. Multiple factors are taken into account when assigning an ASA classification level, including smoking status, alcohol consumption, BMI, diabetes mellitus, hypertension, and pulmonary conditions.[80] Other factors are also considered in pediatric or obstetric cases. Notably, many of the factors that elevate an ASA grade have also been discussed throughout this article as risk factors for anastomotic leaks. Unsurprisingly, research has conclusively shown a strong association between higher ASA scores and increased risk for AL.

In 2013, Tan et al. (2013) completed a retrospective study (n = 505 patients), in which a significant association was found between AL and ASA score (OR = 2.99; 95% CI: 1.345- 6.670; *P* = 0.007).[81] Once matched for age, BMI, and Charlson comorbidity index (CCI) on logistic regression, higher ASA scores were independently related to increased risk for leaks,

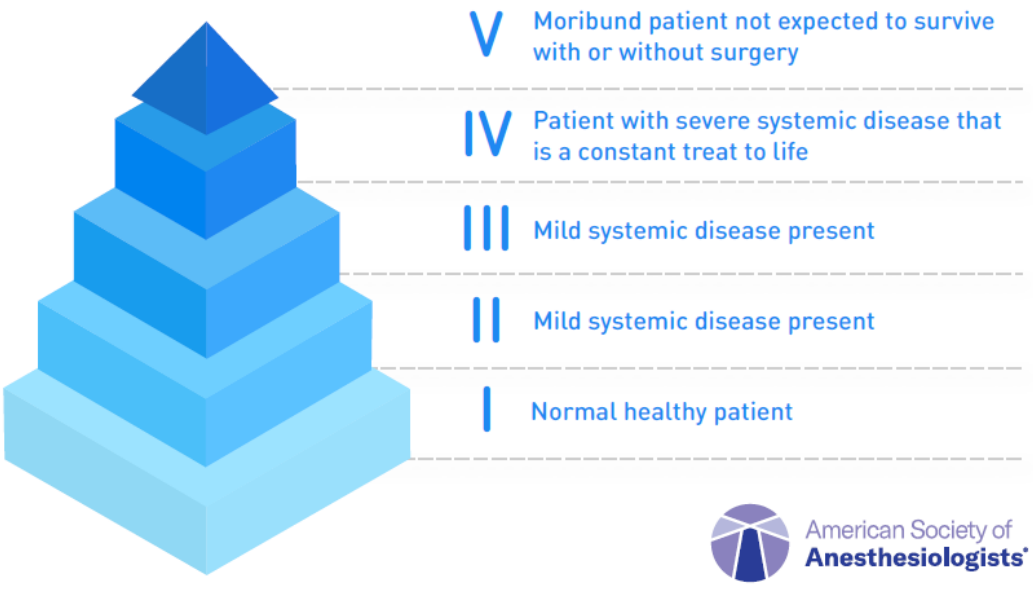


Figure 3. American Society of Anesthesiologists (ASA) Physical Status Classification Score Scale.[80]

when compared to the combined lower ASA scores (ASA I and II) cohort. OR (steroids) = 14.35, P <0.01; OR (ASA_ III v I-II) = 2.02, P = 0.18; OR (ASA_IV vI-II) = 8.45, P = 0.03). In a study by Park et al. (2018), which looked at the influence of ASA scores on a range of postoperative complications after laparoscopic colorectal surgery, results demonstrated that rates of complications did indeed increase with ASA scores.[82] As with a previous study that found higher ASA scores were a risk factor for AL, ASA scores of 3 or above were an independent risk factor for complications such as leaks.[83] Similarly, Jina & Singh (2019) and Kryzauskas et al. (2020) found that ASA grade III or IV conferred a significant risk for anastomotic leaks, with odds ratios of 3.607 and 10.54, respectively.[45,84] These findings were based on multivariable analysis performed on data from 900 patients who underwent sigmoid or rectal resection for left-sided colorectal carcinoma. Most recently, Sripathi et al. (2022) provided a comprehensive report that summarized the current agreement regarding a positive association between ASA scores and anastomotic leaks, whereby ASA grades of 3 or above have been shown to be a key risk factor for AL.[85–88]

In summary, higher ASA scores have consistently been shown to confer a higher risk for patients experiencing postoperative complications, including anastomotic leaks. Clinical teams should be aware of a patient's ASA grade and provide careful monitoring for anastomotic leaks for those evaluated at grade III or above.

Mechanical Bowel Preparation and Pre-Operative Antibiotics

Mechanical bowel preparation (MBP) has traditionally been used to decrease the colon's stool burden, improve visualization during intraoperative endoscopy, and ease the introduction of stapling devices. MBP is unpleasant for patients and has not been shown, on its own, to reduce rates of AL.[27,90] In a study by Contant et al. (2008), a multicentre randomized trial was carried out with 1,431 patients.[91] Overall, no significant difference was found in anastomotic leak rate between patients who received mechanical bowel preparation versus those who did not (difference: 0-6%, 95% CI: 1.7%-2.9%, P = 0.69). Additional randomized control trials have similarly found no advantage to including MBP in a patient's preoperative preparation to reduce the risk of AL.[92–94] In a systematic review by Güenaga et al. (2011), which involved over 5,000 patients, again, no evidence was found to support MBP, either orally or by enema.[95] While one study did find that there was a lower morbidity rate with MBP, there was no difference in

AL rate was found between patients receiving MBP and those who were not.[95] There is some variation in the literature regarding the usefulness of MBP, which could be attributable to the lack of standardization of MBP types among surgeons.[89] Given all of the currently available evidence, though MBP may be useful for other aspects of surgery (e.g., facilitating endoscopy or stapler insertion), it does not appear to make a meaningful difference in patients' anastomotic leak risk.

Broad -spectrum antibiotics are routinely administered intravenously before elective and emergency colorectal surgery.[27] The goal of using pre-operative antibiotics is to reduce post-operative infections. Some surgeons in the United States use non-absorbable oral antibiotics, including Tobramycin and Amphotericin B, to perform selective decontamination of the digestive tract (SDD), reducing AL rates from 7.4% to 3.3%.[27] According to the American College of Surgeons National Surgical Quality Improvement database (NSQIP), using MBP along with preoperative oral antibiotics lowered the rate of AL from 5.7% to 2.8%.[89] Based on these findings, it was concluded that neither oral antibiotics nor MBP alone independently lower the rate of AL. Later studies using the same NSQIP database demonstrated that only oral antibiotics confer any benefit when used alone, and their combination with MBP does not provide any additional advantage.[89,96,97]

Conclusion

Despite continued advancements in clinical medicine, defining, detecting, and treating anastomotic leaks continues to pose significant challenges. By understanding factors that put patients at risk for developing anastomotic leaks, not only may this complication be predicted earlier but also mitigated or prevented altogether. This narrative review identified and outlined the evidence for modifiable risk factors associated with anastomotic leaks, finding differing levels of evidence in support of each. Those factors most conclusively linked to increased leak risk included smoking, alcohol consumption, malnutrition (hypoalbuminemia), and

higher ASA scores. Mixed evidence is available at this time for other risk factors, such as obesity, NSAID use, immunosuppression, and mechanical bowel preparation. Continued work should investigate these and other potential modifiable risk factors to further elucidate their impact on preoperative risk for AL. Overall, the use of risk factors to predict the likelihood of leaks in patients undergoing colorectal surgery is of great value, including further exploration of incorporating these factors into risk models for increasingly accurate predictions of postoperative complications.

Conflict of Interest

The authors declare no conflicts of interest.

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