# Prevention of Anastomotic Leak in Colorectal Surgery: Current Knowledge and Next Steps

Zhen Hao Ang<sup>1,2</sup>, Shing Wai Wong<sup>1,2</sup>

<sup>1</sup>Department of General Surgery, Prince of Wales Hospital, Sydney, New South Wales, Australia; <sup>2</sup>Randwick Campus, School of Clinical Medicine, The University of New South Wales, Sydney, New South Wales, Australia

Correspondence: Shing Wai Wong, Department of General Surgery, Prince of Wales Hospital, Edmund Blackett Building, Barker Street, Randwick, Sydney, New South Wales, 2031, Australia, Tel +61 2 93822894, Email sw.wong@unsw.edu.au

**Abstract:** Despite vast improvements in training of colorectal surgeons and the care of patients undergoing colorectal resections, contemporary series still show an anastomotic leak rate of 1–19%, which continues to contribute to the morbidity and mortality to these patients. New technologies and more recent studies investigating factors affecting the integrity of colorectal anastomosis have been published. Understanding the factors that increase the risk of anastomotic leak allows surgeons to take steps to prevent and ameliorate these risks. We aim to present an evidence-based narrative review relating anastomotic failure and an algorithm for early detection.

Keywords: dehiscence, join, breakdown, risk

#### Introduction

Over the last 50 years, there has been significant improvement in the perioperative care of patients and techniques used in colorectal resections. This includes the adoption of restorative surgery with minimally invasive (laparoscopic and robotic) approaches for low rectal cancers. With the advent of subspecialty colorectal training and standardized colorectal resections, the overall quality of surgery performed has improved. Anastomotic leaks, however, remain a feared complication contributing to morbidity and mortality. Leak rates have been reported to be as low as 1–3% in right sided colon resections but up to 19% in coloanal anastomoses. Anastomotic leak typically presents on days 5–7 post-operatively with resumption of bowel function, and can be defined either clinically or radiologically. Resumption of bowel function may occur earlier after minimally invasive surgery. Understanding the factors associated with anastomotic leak can allow surgeons to adopt preventative measures. With recent studies examining the effects of sarcopenia and new technologies such as the use of Indocyanine Green (ICG) to assess perfusion at the anastomosis, we review risk factors, preventative measures, diagnosis, and management for anastomotic failure.

#### Methods

Embase and MEDLINE (via PubMED) were searched using the keywords: colon, rectum, anastomo\*leak, and failure. Search was limited to the most recent 15 years (January 2009 to August 2023) to reflect the most up to date studies. Other articles were found from relevant references in the retrieved articles. The search was limited to articles published in English. Only factors that have been reported to increase the risk of anastomotic leak were included in this review.

#### **Review**

For the review, the risk factors have been broken down into systemic and local factors. The post-operative surveillance for signs of anastomotic leak as well as the management options will be presented.

Ang and Wong Dovepress

## **Risk Factors for Anastomotic Leak**

## Systemic Factors

#### Pre-Existing Comorbidities

An American Society of Anesthesiologists (ASA) score of greater or equal to 3 has been found to be associated with high rates of anastomotic leak.<sup>4,5</sup> Specific co-morbidities such as diabetes, pulmonary diseases, and renal diseases have all been implicated in higher risk of anastomotic leak.<sup>4,5</sup> Diabetes has been associated with poor tissue healing and increased risk of post-operative infective complications. Hyperglycemia leads to impairment of inflammatory mediated response and neutrophil function which leads to decreased peripheral blood flow and angiogenesis that can negatively affect the anastomosis.<sup>6</sup> Tan et al, in their meta-analysis of 55 studies (51 retrospective cohort studies-RCS, three prospective cohort studies-PCS, and one randomized controlled trial-RCT), found the presence of diabetes to be associated with a significantly higher risk of anastomotic leak with an odds ratio of 2.40.<sup>6</sup>

#### Anemia and Tissue Hypoxia

Anemia was found to be a modifiable risk factor for anastomotic leak. The LekCheck study, a prospective multi-centered international study, defined anemia as a hemoglobin level (Hb) of less than 10.5 g/dL for males and less than 9.7 g/dL for females. They found that anemia was independently associated with anastomotic leak with an odds ratio of 5.40. This was also found in an older review of the literature by van Rooijen et al, where they found that a Hb of less than 8.4 g/dL predicted anastomotic leak. 8

In a recent systematic review (47 cohort studies and two RCTs), higher intraoperative blood loss was associated with increased risk of anastomotic leak. Twenty-three out of the 49 studies reported the influence of intra-operative blood loss on anastomotic leak with cut-offs varying from 200 mL to 750 mL of blood loss. Larger volume blood loss led to decreased oxygen carrying capacity, with resultant tissue hypoxia affecting the healing of colorectal anastomoses.

An adequate blood pressure is also important for adequate tissue perfusion. A secondary analysis of the LekCheck patient cohort found that 11.7% of patients who required vasopressors in the perioperative period had an anastomotic leak compared to 6.3% in those that did not. Multivariate analysis also showed that phenylephrine use was associated with a higher risk of anastomotic leak compared to noradrenaline with an odds ratio of 4.2. It is thought that vasopressors lead to vasoconstriction, deterioration of microcirculation, and potentially result in local tissue hypoxia. These findings are consistent with those of older studies. 11,12

#### **Emergency Surgery**

A recent systematic review showed that emergency surgery was associated with higher rates of anastomotic leaks. The five studies were included in the meta-analysis (none were RCTs), which showed that emergency surgery was associated with a higher rate of anastomotic leak with an odds ratio of 1.31. The authors postulated that the presence of obstruction or peritonitis may have contributed to reduced integrity of the join.<sup>5</sup>

## Smoking and Alcohol

Multiple regression analysis of 333 consecutive patients who underwent colorectal surgery with anastomosis for both benign and malignant disease revealed that patients who smoked or consumed excessive alcohol were at an increased risk of anastomotic leak, with a relative risk of 3.18 and 7.18, respectively.<sup>13</sup> A recent study by Tsai et al also showed that previous smoking history was a risk factor for anastomotic leak, with smoking cessation for up to 10 years still associated with higher risk compared to never-smokers.<sup>14</sup> Excessive alcohol consumption may be considered a surrogate for poor nutrition, which in itself is a risk factor.<sup>1</sup>

#### Nutritional Status and Sarcopenia

Patients who experienced weight loss of greater than 10% may be at increased risk of anastomotic leak because of malnutrition. In the last decade, there has been growing interest in the effects of sarcopenia in colorectal surgical resections. Sarcopenia is a syndrome characterized by progressive and generalized loss of skeletal muscle mass, seen as an insight into the patient's overall nutritional status. The most common parameter used to measure sarcopenia is the psoas surface area at the level of the third lumbar vertebra on Computed Tomography scan (CT). Whilst individual

12 https://doi.org/10.2147/OAS.S429415 Open Access Surgery 2024:17

**Dove**press Ang and Wong

studies have shown sarcopenia to be associated with higher rates of anastomotic leaks, <sup>17,18</sup> a pooled analysis in a recent meta-analysis (32 RCS and 12 PCS) failed to demonstrate a statistical difference. 19

#### Immunosuppressants/Immunomodulators

Systemic corticosteroids are commonly used in patients with autoimmune and chronic inflammatory disorders as well as in post-organ transplant patients, due to their potent immunomodulatory effects. Eriksen et al attempted to address the effect of corticosteroids on anastomotic leak in their systematic review comprising 9,465 patients (11 cohort studies and one RCT) who underwent both right- and left-sided colonic resections.<sup>20</sup> In their review, the leak rate was 6.19% in the steroid group, compared to 3.33% in the non-steroid group. However, the cohort of patients included in this review were highly heterogenous in terms of the duration and dosage of corticosteroid exposure which makes generalizability of the results difficult. Three of the included studies which broke down the dosage to high versus low dose did show higher leak rates with higher dose steroid use (defined as dosage equivalent to 20 mg daily of prednisolone). 21-23 Studies directly comparing the effects of steroid dosage and duration and its effects on anastomotic leak were not found.

The use of biological agents, most commonly TNF-alpha monoclonal antibodies (infliximab and adalimumab), have transformed the management of inflammatory bowel disease (IBD). Approximately 70-90% of patients with Crohn's disease will require at least one surgical intervention throughout their lifetime.<sup>24</sup> The impact of biological agents on the infective complications post-operatively have been reported in two meta-analyses and a Cochrane review.<sup>24–26</sup> While they all concluded that infective complications (not specifically anastomotic leak) were higher in the group treated with biologics, Law et al, in their Cochrane (68 non-randomized studies) review suggested caution when interpreting these results as the studies included were mostly retrospective cohort studies with small numbers. 26 Cira et al, in their metaanalysis of 51 studies (47 RCS, four PCS), did perform subgroup analyses looking specifically at anastomotic leaks and found no difference between treatment and non-treatment groups in the 21 studies that were analyzed.<sup>25</sup> Since then, the largest prospective multi-center observational study (PUCCINI Trial) has added more equipoise to the current evidence.<sup>27</sup> PUCCINI included 947 patients, 382 of whom were treated with at least one anti-TNF alpha agent within 12 weeks of surgery, and showed that there was no difference in post-operative infective complications. PUCCINI also found that detectable serum drug concentration was not associated with higher rates of infective complications postoperatively. The extension of these results to newer classes of biological agents, such as anti-interleukin (ustekinumab) and anti-integrin (vedolizumab), should be done with caution as studies in this subgroup were less robust.

Studies on the effects of immunomodulators commonly used in IBD (including 5-ASA, 6-MP, methotrexate) on anastomotic leak are limited. Most up-to-date evidence suggests that they do not increase post-operative infective complications. 26,27

Immunosuppressants are the cornerstone for the success of solid organ transplant. Mammalian target of rapamycin (mTOR) inhibitors (such as sirolimus and everolimus), a newer class of immunosuppressants, inhibit lymphocyte proliferation and have been shown to impact healing of surgical wounds.<sup>28</sup> Whilst human data is limited, studies in animal models have found mTOR inhibitors to be associated with decreased anastomotic healing.<sup>29</sup> The current recommendation is for cessation of mTOR medications 6 weeks prior to elective surgery.<sup>28</sup>

#### Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs, an integral part of multi-modal analgesic regimens, have been implicated in anastomotic leaks. Through their COX-inhibition mechanism, they have been shown to reduce anastomotic tensile strength as well as impede collagen deposition around the anastomosis.<sup>30</sup> COX-1 blockade, in particular, decreases protective levels of prostaglandins which contributes to epithelial cell migration and mucosal restitution.<sup>30</sup> This higher leak rate seems to only apply with nonselective NSAIDs, with several meta-analyses consistently showing an increased leak rate only in the non-selective group and not in the selective COX-2 group. 31,32

#### Mechanical Bowel Preparation, Pre-Operative Antibiotics Use, and Gut Microbiome

Previous studies have criticized routine mechanical bowel preparation for causing fluid and electrolyte shifts and prolonging fasting times in patients undergoing colorectal surgery without proven benefits in reducing surgical site infections or anastomotic leak. This was the conclusion of a Cochrane review in 2011<sup>33</sup> and a systematic review by

https://doi.org/10.2147/OAS.S429415 Open Access Surgery 2024:17 13 Ang and Wong Dovepress

Leenen et al in 2019.<sup>34</sup> More recent analyses (colorectal-21 RCTs<sup>35</sup> and rectal specific restorative resections: 2 RCTs, 2 RCS, 1 PCS)<sup>36</sup> however showed that the combination of oral antibiotics and mechanical bowel preparation reduced anastomotic leaks. Combination therapy is more effective than bowel preparation or antibiotics alone.<sup>35</sup> The addition of bowel preparation to oral antibiotics is thought to increase the effectiveness of the antibiotic by decreasing colonic bacterial load.

Recent studies into the microbiome associated with anastomotic leaks also add insights into the reasons why antibiotic prophylaxis may decrease anastomotic leak rates. Pathogens such as Pseudomonas aeruginosa and Escherichia coli have been implicated in leaks due to macrophage-mediated downregulation of fibroblast proliferation and increased collagenase activity.<sup>36</sup> Enterococcus faecalis with high-collagenase activity has also been linked to anastomotic breakdown due to its high collagen-degrading properties.<sup>37,38</sup> Hence the administration of broad-spectrum oral antibiotics prior to surgery may help mitigate the potential deleterious effects of colonic bacterial load.

#### Connective Tissue Disorders

The integrity of the anastomosis, like all other wounds, depends on good healing. The extracellular matrix (ECM), particularly collagen composition and metabolism, is thought to be an important factor influencing healing.<sup>39</sup> Degradation of collagen within ECM is required after tissue injury to allow new collagen to be laid down. When this fine balance of degradation and formation is disturbed, it results in poor healing.<sup>40</sup>

Conditions that inhibit collagen formation or formation of structurally defective collagen can also lead to poor healing. 41 Defective collagen metabolism has already been shown to affect tensile strength and mechanical stability of scar tissue formation in inguinal and incisional hernia repairs. 42 Types I and III collagen are generally present together with type III being particularly rich in blood vessels and the gut. 41 Ehler-Danlos Syndrome (EDS) is a connective tissue disorder that can result in defective collagen I and III production. 41 Patients with EDS type 4 (also called vascular subtype) are particularly at risk of developing gastrointestinal complications. Spontaneous colonic perforations have been reported. Case series have warned against performing an anastomosis in patients with Type 4 EDS, with many authors suggesting an end stoma to be the safest approach.<sup>43</sup> Whilst there are no studies specifically looking at EDS and anastomotic leaks, studies have looked at the effects of collagen metabolism in colonic anastomotic complications. Stumpf et al showed that a lower collagen I to III ratio was found in patients who had an anastomotic leak.<sup>39</sup> Matrix metalloproteinase-9 (MMP-9), an enzyme involved in degradation of collagen, has also been investigated for its association with anastomotic leak. Edomskis et al, in their systematic review of 11 studies (human and animal models), reported that five human studies found a correlation between higher levels of MMP-9 and anastomotic leak, while two did not. 40 The studies were however, highly heterogenous and time points of measurements were also highly varied which prevented pooling of data for meta-analysis.<sup>40</sup>

#### Local Factors

## Locally Advanced or Metastatic Disease

There is evidence to suggest that stage IV cancer is associated with higher rates of anastomotic leak. Retrospective studies in Australia<sup>44</sup> and Switzerland<sup>45</sup> found that patients with Stage IV disease were more likely to have anastomotic leaks (13% vs 5.2% and 6.3% vs 1.7%, respectively). Whilst locally advanced disease has been implicated as a risk factor for anastomotic leak, 46 the addition of neoadjuvant therapy to treatment of locally advanced rectal cancer has not been shown to increase risk of a leak.<sup>47</sup>

In colonic resections, neoadjuvant chemotherapy has not been shown to be associated with an increased rate of anastomotic leak. Mankarious et al, in their analysis of the NSQIP-colectomy database, found that there was no difference in post-operative complications including anastomotic leak. Patients with synchronous liver metastases (which accounted for 80% of patients with Stage IV colon cancer) were compared between those who had surgery upfront versus those who had neoadjuvant chemotherapy followed by surgery, and they found no difference in anastomotic leak in both univariate and multivariate analysis.<sup>48</sup> Cheong et al, in their meta-analysis of five RCTs and two observational studies examining the effects of neoadjuvant therapy for locally advanced colon cancer also concurred that there was no associated increase anastomotic leak rates (relative risk of 0.83, p = 0.42).

Open Access Surgery 2024:17 14

Dovepress Ang and Wong

With rectal cancer, neoadjuvant chemoradiotherapy has become the standard of care for locally advanced disease. There is also growing popularity for total neoadjuvant therapy (TNT) as it has been shown to be associated with superior pathological complete response rates compared to traditional short-course (SCT) or long-course radiotherapy alone (LCT).<sup>50</sup> A recent systematic review and meta-analysis (49 studies with a total of 19,502 patients, 10 RCTs and 39 cohort studies) found that neoadjuvant therapy (which included SCT, LCT, and TNT) was associated with high rates of anastomotic leak with an odds ratio of 1.23 (p = 0.004). Subgroup analysis for SCT and LCT also revealed similar results with odds ratios of 1.25 and 1.20, respectively (both statistically significant).<sup>50</sup> Interestingly, when meta-analysis was performed separately for the 10 included RCTs, no increase in anastomotic leak was found in the neoadjuvant therapy group (OR = 1.01, p = 0.91).<sup>50</sup>

Anti-angiogenic agents, such as bevacizumab (Avastin), are often used as part of first-line chemotherapy regimens for metastatic colorectal cancer. It has been well documented that Avastin, through its inhibition of the capillary beds of small bowel villi, can result in spontaneous gastrointestinal perforation due to regression of normal blood vessels. Avastin-containing chemotherapy regimes were associated with higher rates of anastomotic leak in a recent cohort study where 9.6% of patients who were treated with Avastin had an anastomotic leak compared to 0.8% in those who were not treated with it (p < 0.001). Avastin has a half-life of 20 days and pharmaceutical prescribing information recommend ceasing it 4 weeks prior to surgery. The NCCN guidelines adopts a more conservative approach of recommending cessation 6 weeks prior to surgery. Sa

#### Anastomotic Technique

The anastomotic leak rate associated with stapled versus handsewn anastomoses has been a subject of longstanding debate. Whilst a Cochrane review in 2011 reported no significant difference between stapled and handsewn colorectal anastomosis,<sup>54</sup> another in 2012 favored use of the stapler for ileocolic anastomosis in reducing leak rates.<sup>55</sup> Clinical equipoise was again brought about by a more recent meta-analysis of 16 studies (12 RCTs, four cohort studies, includes both ileocolic and colorectal anastomoses), as well as an analysis of six studies (one RCT, five RCS) for ileocolic anastomoses, which showed no significant difference in anastomotic dehiscence rates between handsewn and stapled anastomoses.<sup>56,57</sup>

With colorectal anastomoses, the number of firings required to transect the rectum has been shown to be associated with increased risk of anastomotic leak.<sup>58,59</sup> Efforts should be made to increase the likelihood of a single firing with techniques such as placing the stapler port site lower and using a longer stapler cartridge.

A retrospective analysis showed that the use of robotic stapler (compared to laparoscopic stapler) was associated with fewer radiological leaks (4% vs 7%). Whilst this did not reach statistical significance, the use of a robotic stapler was associated with a lesser number of stapler firings which has been shown to decrease the likelihood of leaks. A meta-analysis revealed a non-statistically significant benefit of robotic stapler over laparoscopic stapler for the prevention of anastomotic leakage after rectal surgery. The main advantage of the robotic stapler is better maneuverability (wider range of motion) in the confined pelvic space which provides more accurate and hence fewer firings. The stable delivery of staples may also contribute to the better result. The new Da Vinci SureForm robotic stapler offers a 120 degrees cone of articulation and Smartfire technology which measures tissue compression before and during firing, pausing if additional compression is required before resumption of firing, to ensure a more consistent staple line. One prospective study found that 70% of rectal transection with the robotic stapler required at least one firing of more than 45 degrees angulation, which is the angulation limit of the laparoscopic powered stapler.

Since the introduction of the Echelon Circular<sup>TM</sup> Powered Stapler (ECPS) in 2019, several studies have compared it to its non-powered counterpart. Early studies have shown mixed results. While studies by Pla-Marti et al<sup>64</sup> and Sylla et al<sup>65</sup> found a lower incidence of anastomotic leak with ECPS, Vignali et al,<sup>66</sup> in their propensity matched cohort study, failed to show a significant difference. Their study also included stapler size, neoadjuvant chemotherapy, and number of linear stapler fires to transect a rectal stump in their matching, which they postulated could have been confounders in the earlier studies.

Open Access Surgery 2024:17 https://doi.org/10.2147/OAS.5429415

Ang and Wong Dovepress

In a recent multi-center study by Catarci et al, use of a tri-layered stapled anastomosis was associated with significantly lower risk of anastomotic leak. In this study, there was a 4% absolute risk reduction overall for anastomotic leak with the number needed to treat being 25.<sup>67</sup>

#### Perfusion Assessment

As dogmatic as it may sound, performing a well-vascularized, tension-free anastomosis has been the key tenet of an ideal anastomosis. This has led to a belief that hypoperfusion at the anastomosis is the most important risk factor for leak. <sup>68,69</sup> Traditionally, assessment of the blood supply was done by testing for a pulsatile flow in the marginal artery. In recent years, with improved technology, more direct methods of assessment have become available. Indocyanine Green Fluorescence Angiography (ICG-FA) is the most common method used due to the widespread adoption of robotic surgery and availability of near-infrared light function in most laparoscopic cameras. <sup>68</sup> Despite some early concerns about ICG-FA potentially overestimating the perfusion at the anastomosis, <sup>70</sup> recent systematic reviews have shown that perfusion assessment at the anastomosis reduced the risk of anastomotic leak. A recent meta-analysis <sup>68</sup> which included 66 studies (11,560 patients), analyzing all methods of perfusion assessment, found a 5% decrease in anastomotic leak compared with control groups (7.4% vs 12.4%). Two meta-analyses, Safiejko et al (three RCTs and 29 cohort studies) and Xia et al (three RCTs and 19 cohort studies), specifically assessed the benefits of ICG-FA which also revealed a reduction in anastomotic leak rate. <sup>71,72</sup>

#### **Defunctioning Stoma**

Defunctioning loop ileostomies or colostomies are often performed in patients undergoing low anterior resection (LAR) with colorectal or coloanal anastomoses, which are associated with higher risk of anastomotic leak.<sup>3</sup> Defunctioning stomas have been shown to decrease the rate of clinically significant anastomotic leaks in patients undergoing LAR, including leaks which require re-operation. In the meta-analysis of eight RCTs with 892 patients, clinically significant leaks occurred in 6.3% of patients in the defunctioned group compared to 18.3% without defunctioning (p < 0.00001). The re-operation rate was also significantly lower at 5.9% compared to 16.7% (p < 0.00001).<sup>73</sup> A Norwegian national cohort study of 1,018 patients also supported the above findings.<sup>74</sup>

# Diagnosis of Anastomotic Leak

Diagnosis of anastomotic leak, which typically occurs on post-operative days (POD) 5–7, involves assessment of a combination of clinical, biochemical, and radiological parameters.

Symptoms and signs of anastomotic leak typically include increasing abdominal pain, nausea and vomiting, fever, tachycardia, peritonitis, and prolonged ileus.<sup>75</sup> These signs and symptoms may not be apparent until POD 5.<sup>76</sup>

Biochemically, inflammatory markers are typically elevated with high white cell count (with neutrophilia) as well as elevated C-reactive protein (CRP). Earlier studies revealed that CRP was uniformly elevated in patients post-colorectal surgery but typically normalized by POD 3.<sup>75</sup> CRP have also been shown, in a meta-analysis of seven studies, to have a high negative predictive value for leak (NPV = 97%) when a cut-off of 172 mg/L on POD 3 was used.<sup>77</sup> The trajectory of CRP was investigated by a group from Newcastle, Australia.<sup>78</sup> In this international multicenter study of 833 patients, they found that an increase in CRP of greater than 50 mg/L in a 24-hour period from POD 3 has a specificity of greater than 96% for anastomotic leak.<sup>78</sup> This study also reported a high NPV of 96% when using a CRP cut-off of 172mg/L on POD 3.<sup>78</sup>

The use of neutrophil-to-lymphocyte ratio (NLR) as a marker for subclinical inflammatory response has also been studied. Mik et al reported that a NLR of less than 6.5 has a good NPV on POD 4 for anastomotic leak. NLR was also significantly different between the group with and without anastomotic leak (9.03 vs 4.45, p = 0.0012). Paliogiannis et al also supported the above findings in their study of 1,432 patients, which again showed that POD 4 NLR of 6.15 carries a sensitivity and specificity of 100% and 61.8%, respectively. Whilst there is no exact cut-off for NLR, we can infer that an increasing NLR beyond POD 4 is concerning for anastomotic leak.

Radiologically, computed tomography (CT) with intravenous contrast remains the most employed study used in the evaluation of post-operative complications. The presence of perianastomotic free air or fluid collection should raise the

16 https://doi.org/10.2147/OAS.5429415 Open Access Surgery 2024:17

Dovepress Ang and Wong

concern for an anastomotic leak.<sup>75</sup> Oral or rectal contrast can also be added to increase the diagnostic value of the CT, depending on the location of the anastomosis. The addition of intraluminal contrast has been shown to increase the sensitivity for diagnosing a leak from 65% to 75%.<sup>80</sup> Extravasation of intraluminal contrast seen on CT is considered the most specific sign of a clinically significant leak.<sup>80</sup>

# Management of Anastomotic Leak

Management of colorectal anastomotic leak are determined by the severity of the leak, timing of the leak, location of the leak (intraperitoneal versus extraperitoneal), and patient's clinical status.<sup>3</sup> Management options include antibiotics alone, radiological-guided drainage, and surgery. Antibiotics alone is reserved for patients who only have low-grade sepsis and/or a localized collection of less than 3 cm.<sup>81</sup> For collections larger than 3 cm, radiological-guided drainage together with broad-spectrum antibiotics is preferred. Patients who do not respond to treatment and have collections not amenable to percutaneous drainage should be drained surgically.<sup>81</sup>

Surgery is reserved for patients who are hemodynamically unstable or have failed the above mentioned non-operative treatments. The surgical approach depends on whether the anastomosis is accessible or inaccessible (inflammatory phlegmon). <sup>82</sup> In the case of an inflammatory phlegmon, insertion of drains intra-operatively into the perianastomotic area might be the only feasible approach as exploring the inflammatory mass might expose the patient to more harm (such as enterotomies). <sup>81</sup> For accessible anastomoses, surgical options include taking down the anastomosis and forming an end stoma, revising the anastomosis with or without a diverting stoma, or drainage and formation of a diverting stoma.

The chosen surgical approach depends on the patient's hemodynamics as well as intra-operative findings. Intra-operative findings of an ischemic or unhealthy-looking anastomosis, large anastomotic dehiscence (>1 cm), and the requirement of high doses of inotropes would be indications for taking down the anastomosis. This subgroup of patients typically receive an end stoma with a mucous fistula for decompression of the distal bowel. Patients with an anastomotic defect of <1 cm can have the anastomosis repaired or re-anastomosed with proximal diversion if patient's clinical status and the proximal and distal bowel are healthy and well-vascularized. A retrospective study involving left-sided colonic resections found that, in the appropriately selected patient subset, there was no significant difference in mortality and morbidity in patients who had proximal diversion versus Hartmann's procedure. Proximal diversion of the fecal stream with a loop stoma (with or without revision of anastomosis) is preferred to an end stoma, if both procedures are deemed safe, as it has been shown to increase the chance of future stoma reversal.

For patients with extraperitoneal leaks, typically seen in low colorectal anastomosis, endoscopic techniques for anastomotic salvage have been described with varying degrees of success. These techniques negate the need for laparotomy. Self-expanding metal stents have been shown to achieve long-term salvage rates of between 50–100%. However, stents are not suitable for anastomoses encroaching the anal verge as it can lead to significant discomfort as well as the well-documented potential complication of stent migration.

The use of vacuum-assisted wound dressings has been a well-established method of wound care and there has been growing interest in the application of the Endo-SPONGE<sup>TM</sup> system in anastomotic leaks. A systematic review comprising of 14 case series with a total of 197 patients found that Endo-SPONGE<sup>TM</sup> resulted in anastomotic salvage in 88.8% of patients with little adverse outcomes reported. However, application of the Endo-SPONGE<sup>TM</sup> does require patients to be sedated for sponge change every 2–4 days. The median number of sponge changes reported within the systematic review was between 5.4–11.4.<sup>86</sup> These early results are promising.

## **Conclusion**

Despite advancements in surgical technology, anastomotic leaks remain a feared condition in colorectal surgery and continue to result in significant morbidity and mortality. This review not only consolidates the existing knowledge on anastomotic leak but also summarizes studies on new areas such as the use of robotic staplers, utility of perfusion assessment with ICG, and anthropometric studies in sarcopenia. A surgeon's understanding of the potential risk factors, diagnostic pathways, as well as management options can result in improved patient outcome after colorectal anastomosis.

Open Access Surgery 2024:17 https://doi.org/10.2147/OAS.S429415

Ang and Wong **Dove**press

## **Disclosure**

The authors report no conflicts of interest in this work.

#### References

1. Chiarello MM, Fransvea P, Cariati M, Adams NJ, Bianchi V, Brisinda G. Anastomotic leakage in colorectal cancer surgery. Surg Oncol. 2022;40:101708. doi:10.1016/j.suronc.2022.101708

- 2. Ellis CT, Maykel JA. Defining anastomotic leak and the clinical relevance of leaks. Clin Colon Rectal Surg. 2021;34(6):359-365. doi:10.1055/ s-0041-1735265
- 3. Friel C, Kin C. Anastomotic complications. In: Steele S, Hull T, Read T, Hyman N, Maykel J, Whitlow C, editors. The ASCRS Textbook of Colon and Rectal Surgery. 4th ed. Springer; 2022:189.
- 4. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC. Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg. 2015;102(5):462-479. doi:10.1002/bjs.9697
- 5. He J, He M, Tang JH, Wang XH. Anastomotic leak risk factors following colon cancer resection: a systematic review and meta-analysis. Langenbecks Arch Surg. 2023;408(1):252. doi:10.1007/s00423-023-02989-z
- 6. Tan DJH, Yaow CYL, Mok HT, et al. The influence of diabetes on postoperative complications following colorectal surgery. Tech Coloproctol. 2021;25(3):267–278. doi:10.1007/s10151-020-02373-9
- 7. Huisman DE, Reudink M, van Rooijen SJ, et al. LekCheck: a prospective study to identify perioperative modifiable risk factors for anastomotic leakage in colorectal surgery. Ann Surg. 2022;275(1):e189-e197. doi:10.1097/sla.0000000000003853
- 8. van Rooijen SJ, Huisman D, Stuijvenberg M, et al. Intraoperative modifiable risk factors of colorectal anastomotic leakage: why surgeons and anesthesiologists should act together. Int J Surg. 2016;36(Pt A):183-200. doi:10.1016/j.ijsu.2016.09.098
- 9. Charalambides M, Mavrou A, Jennings T, et al. A systematic review of the literature assessing operative blood loss and postoperative outcomes after colorectal surgery. Int J Colorectal Dis. 2022;37(1):47-69. doi:10.1007/s00384-021-04015-4
- 10. Huisman DE, Bootsma BT, Ingwersen EW, et al. Fluid management and vasopressor use during colorectal surgery: the search for the optimal balance. Surg Endosc. 2023;37(8):6062-6070. doi:10.1007/s00464-023-09980-1
- 11. Adanir T, Nazli O, Kara C, et al. The relationship between vasopressor dose and anastomotic leak in colon surgery: an experimental trial. Int J Surg. 2010;8(3):221–224. doi:10.1016/j.ijsu.2010.01.004
- 12. Choudhuri AH, Uppal R, Kumar M. Influence of non-surgical risk factors on anastomotic leakage after major gastrointestinal surgery: audit from a tertiary care teaching institute. Int J Crit Illn Inj Sci. 2013;3(4):246-249. doi:10.4103/2229-5151.124117
- 13. Sorensen LT, Jorgensen T, Kirkeby LT, Skovdal J, Vennits B, Wille-Jorgensen P. Smoking and alcohol abuse are major risk factors for anastomotic leakage in colorectal surgery. Br J Surg. 1999;86(7):927–931. doi:10.1046/j.1365-2168.1999.01165.x
- 14. Tsai KY, Huang SH, You JF, et al. Smoking cessation for less than 10 years remains a risk factor of anastomotic leakage in mid-to-low rectal cancer patients undergoing sphincter-preserving surgery. Langenbecks Arch Surg. 2022;407(3):1131-1138. doi:10.1007/s00423-021-02381-9
- 15. Kang CY, Halabi WJ, Chaudhry OO, et al. Risk factors for anastomotic leakage after anterior resection for rectal cancer. JAMA Surg. 2013;148 (1):65-71. doi:10.1001/2013.jamasurg.2
- 16. Sun G, Li Y, Peng Y, et al. Can sarcopenia be a predictor of prognosis for patients with non-metastatic colorectal cancer? A systematic review and meta-analysis. Int J Colorectal Dis. 2018;33(10):1419-1427. doi:10.1007/s00384-018-3128-1
- 17. Herrod PJJ, Boyd-Carson H, Doleman B, et al. Quick and simple; psoas density measurement is an independent predictor of anastomotic leak and other complications after colorectal resection. Tech Coloproctol. 2019;23(2):129-134. doi:10.1007/s10151-019-1928-0
- 18. Margadant CC, Bruns ER, Sloothaak DA, et al. Lower muscle density is associated with major postoperative complications in older patients after surgery for colorectal cancer. Eur J Surg Oncol. 2016;42(11):1654-1659. doi:10.1016/j.ejso.2016.05.040
- 19. Trejo-Avila M, Bozada-Gutierrez K, Valenzuela-Salazar C, Herrera-Esquivel J, Moreno-Portillo M. Sarcopenia predicts worse postoperative outcomes and decreased survival rates in patients with colorectal cancer: a systematic review and meta-analysis. Int J Colorectal Dis. 2021;36 (6):1077-1096. doi:10.1007/s00384-021-03839-4
- 20. Eriksen TF, Lassen CB, Gögenur I. Treatment with corticosteroids and the risk of anastomotic leakage following lower gastrointestinal surgery: a literature survey. Colorectal Dis. 2014;16(5):154-160. doi:10.1111/codi.12490
- 21. Lake JP, Firoozmand E, Kang JC, et al. Effect of high-dose steroids on anastomotic complications after proctocolectomy with ileal pouch-anal anastomosis. J Gastrointest Surg. 2004;8(5):547–551. doi:10.1016/j.gassur.2004.01.002
- 22. Ziv Y, Church JM, Fazio VW, King TM, Lavery IC. Effect of systemic steroids on ileal pouch-anal anastomosis in patients with ulcerative colitis. Dis Colon Rectum. 1996;39(5):504-508. doi:10.1007/bf02058701
- 23. El-Hussuna A, Andersen J, Bisgaard T, et al. Biologic treatment or immunomodulation is not associated with postoperative anastomotic complications in abdominal surgery for Crohn's disease. Scand J Gastroenterol. 2012;47(6):662-668. doi:10.3109/00365521.2012.660540
- 24. Moosvi Z, Duong J, Bechtold ML, Nguyen DL. Systematic review and meta-analysis: risks of postoperative complications with preoperative use of anti-tumor necrosis factor-alpha biologics in inflammatory bowel disease patients. Eur J Gastroenterol Hepatol. 2021;33(6):799-816. doi:10.1097/ meg.0000000000001944
- 25. Cira K, Weber MC, Wilhelm D, Friess H, Reischl S, Neumann PA. The Effect of anti-tumor necrosis factor-alpha therapy within 12 weeks prior to surgery on postoperative complications in inflammatory bowel disease: a systematic review and meta-analysis. J Clin Med. 2022;11:23.
- 26. Law CC, Bell C, Koh D, Bao Y, Jairath V, Narula N, Risk of postoperative infectious complications from medical therapies in inflammatory bowel disease. Cochrane Database Syst Rev. 2020;10(10):Cd013256. doi:10.1002/14651858.CD013256.pub2
- 27. Cohen BL, Fleshner P, Kane SV, et al. Prospective cohort study to investigate the safety of preoperative tumor necrosis factor inhibitor exposure in patients with inflammatory bowel disease undergoing intra-abdominal surgery. Gastroenterology. 2022;163(1):204-221. doi:10.1053/j. gastro.2022.03.057
- 28. Sneider E, Davids J. Effect of chemotherapy, radiation, or immunosuppression on the integrity of the intestinal anastomosis. Semin Colon Rect Surg. 2014;25. doi:10.1053/j.scrs.2014.04.008

https://doi.org/10.2147/OAS.S429415 18 Open Access Surgery 2024:17 Dovepress Ang and Wong

29. van der Vliet JA, Willems MC, de Man BM, Lomme RM, Hendriks T. Everolimus interferes with healing of experimental intestinal anastomoses. *Transplantation*. 2006;82(11):1477–1483. doi:10.1097/01.tp.0000246078.09845.9c

- 30. Jamjittrong S, Matsuda A, Matsumoto S, et al. Postoperative non-steroidal anti-inflammatory drugs and anastomotic leakage after gastrointestinal anastomoses: systematic review and meta-analysis. *Ann Gastroenterol Surg.* 2020;4(1):64–75. doi:10.1002/ags3.12300
- 31. Bhangu A, Singh P, Fitzgerald JE, Slesser A, Tekkis P. Postoperative nonsteroidal anti-inflammatory drugs and risk of anastomotic leak: meta-analysis of clinical and experimental studies. *World J Surg.* 2014;38(9):2247–2257. doi:10.1007/s00268-014-2531-1
- 32. Modasi A, Pace D, Godwin M, Smith C, Curtis B. NSAID administration post colorectal surgery increases anastomotic leak rate: systematic review/meta-analysis. *Surg Endosc*. 2019;33(3):879–885. doi:10.1007/s00464-018-6355-1
- 33. Güenaga KF, Matos D, Wille-Jørgensen P. Mechanical bowel preparation for elective colorectal surgery. *Cochrane Database Syst Rev.* 2011;2011 (9):Cd001544. doi:10.1002/14651858.CD001544.pub4
- 34. Leenen JPL, Hentzen J, Ockhuijsen HDL. Effectiveness of mechanical bowel preparation versus no preparation on anastomotic leakage in colorectal surgery: a systematic review and meta-analysis. *Updates Surg.* 2019;71(2):227–236. doi:10.1007/s13304-018-0526-4
- 35. Willis MA, Toews I, Soltau SLV, Kalff JC, Meerpohl JJ, Vilz TO. Preoperative combined mechanical and oral antibiotic bowel preparation for preventing complications in elective colorectal surgery. *Cochrane Database Syst Rev.* 2023;2. doi:10.1002/14651858.CD014909.pub2
- 36. Hansen RB, Balachandran R, Valsamidis TN, Iversen LH. The role of preoperative mechanical bowel preparation and oral antibiotics in prevention of anastomotic leakage following restorative resection for primary rectal cancer - a systematic review and meta-analysis. *Int J Colorectal Dis*. 2023;38(1):129. doi:10.1007/s00384-023-04416-7
- 37. Liu Y, Li B, Wei Y. New understanding of gut microbiota and colorectal anastomosis leak: a collaborative review of the current concepts. *Front Cell Infect Microbiol.* 2022;12:1022603. doi:10.3389/fcimb.2022.1022603
- 38. Williamson AJ, Alverdy JC. Influence of the Microbiome on Anastomotic Leak. Clin Colon Rectal Surg. 2021;34(6):439-446. doi:10.1055/s-0041-1735276
- 39. Stumpf M, Klinge U, Wilms A, et al. Changes of the extracellular matrix as a risk factor for anastomotic leakage after large bowel surgery. *Surgery*. 2005;137(2):229–234. doi:10.1016/j.surg.2004.07.011
- 40. Edomskis P, Goudberg MR, Sparreboom CL, et al. Matrix metalloproteinase-9 in relation to patients with complications after colorectal surgery: a systematic review. *Int J Colorectal Dis.* 2021;36(1):1–10. doi:10.1007/s00384-020-03724-6
- 41. Kivirikko KI. Collagens and their abnormalities in a wide spectrum of diseases. Ann Med. 1993;25(2):113-126. doi:10.3109/07853899309164153
- 42. Stumpf M, Cao W, Klinge U, Klosterhalfen B, Kasperk R, Schumpelick V. Collagen distribution and expression of matrix metalloproteinases 1 and 13 in patients with anastomotic leakage after large-bowel surgery. *Langenbecks Arch Surg.* 2002;386(7):502–506. doi:10.1007/s00423-001-0255-9
- 43. Burcharth J, Rosenberg J. Gastrointestinal surgery and related complications in patients with Ehlers-Danlos syndrome: a systematic review. *Dig Surg.* 2012;29(4):349–357. doi:10.1159/000343738
- 44. Ng SC, Stupart D, Bartolo D, Watters D. Anastomotic leaks in stage IV colorectal cancer. ANZ J Surg. 2018;88(9):E649–E653. doi:10.1111/
- 45. Kaser SA, Mattiello D, Maurer CA. Distant metastasis in colorectal cancer is a risk factor for anastomotic leakage. *Ann Surg Oncol*. 2016;23 (3):888–893. doi:10.1245/s10434-015-4941-1
- 46. Kryzauskas M, Bausys A, Degutyte AE, et al. Risk factors for anastomotic leakage and its impact on long-term survival in left-sided colorectal cancer surgery. World J Surg Oncol. 2020;18(1):205. doi:10.1186/s12957-020-01968-8
- 47. Hu MH, Huang RK, Zhao RS, Yang KL, Wang H. Does neoadjuvant therapy increase the incidence of anastomotic leakage after anterior resection for mid and low rectal cancer? A systematic review and meta-analysis. *Colorectal Dis.* 2017;19(1):16–26. doi:10.1111/codi.13424
- 48. Mankarious MM, Portolese AC, Hoskins MA, et al. Neoadjuvant chemotherapy does not increase risk for anastomotic leak for simultaneous resection of primary colon cancer with synchronous liver metastasis: a NSQIP-colectomy analysis. J Surg Oncol. 2023;128(1):58–65. doi:10.1002/jso.27242
- 49. Cheong CK, Nistala KRY, Ng CH, et al. Neoadjuvant therapy in locally advanced colon cancer: a meta-analysis and systematic review. *J Gastrointest Oncol.* 2020;11(5):847–857. doi:10.21037/jgo-20-220
- 50. Yang J, Luo Y, Tian T, Dong P, Fu Z. Effects of neoadjuvant radiotherapy on postoperative complications in rectal cancer: a meta-analysis. *J Oncol.* 2022;2022:8197701. doi:10.1155/2022/8197701
- 51. Saif MW, Elfiky A, Salem RR. Gastrointestinal perforation due to bevacizumab in colorectal cancer. *Ann Surg Oncol.* 2007;14(6):1860–1869. doi:10.1245/s10434-006-9337-9
- 52. Kim S, Shin JK, Park Y, et al. Bevacizumab increases the risk of anastomosis site leakage in metastatic colorectal cancer. *Front Oncol.* 2022;12:1018458. doi:10.3389/fonc.2022.1018458
- 53. Benson AB, Venook AP, Al-Hawary MM, et al. Colon cancer, version 2.2021, NCCN clinical practice guidelines in oncology. *J National Compr Cancer Network*. 2021;19(3):329–359. doi:10.6004/jncen.2021.0012
- 54. Neutzling CB, Lustosa SA, Proenca IM, da Silva EM, Matos D. Stapled versus handsewn methods for colorectal anastomosis surgery. *Cochrane Database Syst Rev.* 2012;2:CD003144. doi:10.1002/14651858.CD003144.pub2
- 55. Choy PY, Bissett IP, Docherty JG, Parry BR, Merrie A, Fitzgerald A. Stapled versus handsewn methods for ileocolic anastomoses. *Cochrane Database Syst Rev.* 2011;9:CD004320. doi:10.1002/14651858.CD004320.pub3
- 56. Oliveira A, Faria S, Goncalves N, Martins A, Leao P. Surgical approaches to colonic and rectal anastomosis: systematic review and meta-analysis. Int J Colorectal Dis. 2023;38(1):52. doi:10.1007/s00384-023-04328-6
- 57. Abounozha S, Kheder A, Alshahri T, Ibrahim R. Best evidence topic: is ileocolic anastomotic leak rate higher in handsewn or stapler's anastomosis? *Ann Med Surg.* 2020;60:619–622. doi:10.1016/j.amsu.2020.11.075
- 58. Balciscueta Z, Uribe N, Caubet L, et al. Impact of the number of stapler firings on anastomotic leakage in laparoscopic rectal surgery: a systematic review and meta-analysis. *Tech Coloproctol*. 2020;24(9):919–925. doi:10.1007/s10151-020-02240-7
- 59. Braunschmid T, Hartig N, Baumann L, Dauser B, Herbst F. Influence of multiple stapler firings used for rectal division on colorectal anastomotic leak rate. *Surg Endosc.* 2017;31(12):5318–5326. doi:10.1007/s00464-017-5611-0
- 60. Tejedor P, Sagias F, Nock D, et al. Advantages of using a robotic stapler in rectal cancer surgery. *J Robot Surg.* 2020;14(2):365–370. doi:10.1007/s11701-019-00993-4
- 61. Tejedor P, Sagias F, Flashman K, Kandala NL, Khan J. The use of robotic or laparoscopic stapler in rectal cancer surgery: a systematic review and meta-analysis. J Robot Surg. 2020;14(6):829–833. doi:10.1007/s11701-020-01126-y

Open Access Surgery 2024:17 https://doi.org/10.2147/OAS.S429415

Ang and Wong **Dove**press

- 62. SureForm Staplers. Available from: https://www.intuitive.com/en-us/products-and-services/da-vinci/stapling/sureform. Accessed October, 2023.
- 63. Somashekhar SP, Saldanha E, Kumar R, Pandey K, Dahiya A, Ashwin KR. Prospective analysis of 164 fires of da Vinci SureForm SmartFire stapler in oncological cases: Indian cohort of 76 consecutive cases. J Minim Access Surg. 2023;19(3):384–389. doi:10.4103/jmas.jmas\_154\_22
- 64. Pla-Marti V, Martin-Arevalo J, Moro-Valdezate D, et al. Impact of the novel powered circular stapler on risk of anastomotic leakage in colorectal anastomosis: a propensity score-matched study. Tech Coloproctol. 2021;25(3):279-284. doi:10.1007/s10151-020-02338-y
- 65. Sylla P, Sagar P, Johnston SS, et al. Outcomes associated with the use of a new powered circular stapler for left-sided colorectal reconstructions: a propensity score matching-adjusted indirect comparison with manual circular staplers. Surg Endosc. 2022;36(4):2541–2553. doi:10.1007/s00464-021-08542-7
- 66. Vignali A, Gozzini L, Gasparini G, Calef R, Rosati R, Elmore U. Impact of powered circular stapler on anastomotic leak after anastomosis to the rectum: a propensity score matched study. Int J Colorectal Dis. 2023;38(1):211. doi:10.1007/s00384-023-04506-6
- 67. Catarci M, Guadagni S, Masedu F, et al. Three-row versus two-row circular staplers for left-sided colorectal anastomosis: a propensity score-matched analysis of the iCral 2 and 3 prospective cohorts. Int J Surg. 2023;109(8):2312-2323. doi:10.1097/JS9.0000000000000480
- 68. Renna MS, Grzeda MT, Bailey J, et al. Intraoperative bowel perfusion assessment methods and their effects on anastomotic leak rates: meta-analysis. Br J Surg. 2023;110(9):1131–1142. doi:10.1093/bjs/znad154
- 69. Kojima S, Sakamoto T, Nagai Y, Matsui Y, Nambu K, Masamune K. Laser speckle contrast imaging for intraoperative quantitative assessment of intestinal blood perfusion during colorectal surgery: a prospective pilot study. Surg Innov. 2019;26(3):293-301. doi:10.1177/1553350618823426
- 70. Buxey K, Lam F, Muhlmann M, Wong S. Does indocyanine green improve the evaluation of perfusion during laparoscopic colorectal surgery with extracorporeal anastomosis? ANZ J Surg. 2019;89(11):E487–E491. doi:10.1111/ans.15320
- 71. Safiejko K, Tarkowski R, Kozlowski TP, et al. Safety and efficacy of indocyanine green in colorectal cancer surgery: a systematic review and meta-analysis of 11,047 patients. Cancers. 2022;14:4.
- 72. Xia S, Wu W, Luo L, Ma L, Yu L, Li Y. Indocyanine green fluorescence angiography decreases the risk of anastomotic leakage after rectal cancer surgery: a systematic review and meta-analysis. Front Med. 2023;10:1157389. doi:10.3389/fmed.2023.1157389
- 73. Phan K, Oh L, Ctercteko G, et al. Does a stoma reduce the risk of anastomotic leak and need for re-operation following low anterior resection for rectal cancer: systematic review and meta-analysis of randomized controlled trials. J Gastrointest Oncol. 2019;10(2):179-187. doi:10.21037/
- 74. Myrseth E, Nymo LS, Gjessing PF, Norderval S. Diverting stomas reduce reoperation rates for anastomotic leak but not overall reoperation rates within 30 days after anterior rectal resection: a national cohort study. Int J Colorectal Dis. 2022;37(7):1681-1688. doi:10.1007/s00384-022-04205-8
- 75. Hernandez PT, Paspulati RM, Shanmugan S. Diagnosis of anastomotic leak. Clin Colon Rectal Surg. 2021;34(6):391–399. doi:10.1055/s-0041-1735270
- 76. Mik M, Dziki L, Berut M, Trzcinski R, Dziki A. Neutrophil to lymphocyte ratio and C-reactive protein as two predictive tools of anastomotic leak in colorectal cancer open surgery. Dig Surg. 2018;35(1):77-84. doi:10.1159/000456081
- 77. Singh PP, Zeng IS, Srinivasa S, Lemanu DP, Connolly AB, Hill AG. Systematic review and meta-analysis of use of serum C-reactive protein levels to predict anastomotic leak after colorectal surgery. Br J Surg. 2014;101(4):339-346. doi:10.1002/bjs.9354
- 78. Stephensen BD, Reid F, Shaikh S, Carroll R, Smith SR, Pockney P. C-reactive protein trajectory to predict colorectal anastomotic leak: PREDICT Study. Br J Surg. 2020;107(13):1832-1837. doi:10.1002/bjs.11812
- 79. Paliogiannis P, Deidda S, Maslyankov S, et al. Blood cell count indexes as predictors of anastomotic leakage in elective colorectal surgery: a multicenter study on 1432 patients. World J Surg Oncol. 2020;18(1):89. doi:10.1186/s12957-020-01856-1
- 80. Samji KB, Kielar AZ, Connolly M, et al. Anastomotic leaks after small- and large-bowel surgery: diagnostic performance of CT and the importance of intraluminal contrast administration. AJR Am J Roentgenol. 2018;210(6):1259-1265. doi:10.2214/ajr.17.18642
- 81. Phitayakorn R, Delaney CP, Reynolds HL, et al. Standardized algorithms for management of anastomotic leaks and related abdominal and pelvic abscesses after colorectal surgery. World J Surg. 2008;32(6):1147-1156. doi:10.1007/s00268-008-9468-1
- 82. Hedrick TL, Kane W. Management of acute anastomotic leaks. Clin Colon Rectal Surg. 2021;34(6):400–405. doi:10.1055/s-0041-1735271
- 83. Saur NM, Paulson EC. Operative management of anastomotic leaks after colorectal surgery. Clin Colon Rectal Surg. 2019;32(3):190-195. doi:10.1055/s-0038-1677025
- 84. Stafford C, Francone TD, Marcello PW, Roberts PL, Ricciardi R. Is diversion with ileostomy non-inferior to Hartmann resection for left-sided colorectal anastomotic leak? J Gastrointest Surg. 2018;22(3):503-507. doi:10.1007/s11605-017-3612-x
- 85. Krarup PM, Jorgensen LN, Harling H. Management of anastomotic leakage in a nationwide cohort of colonic cancer patients. J Am Coll Surg. 2014;218(5):940–949. doi:10.1016/j.jamcollsurg.2014.01.051
- 86. Clifford RE, Fowler H, Govindarajah N, Vimalachandran D, Sutton PA. Early anastomotic complications in colorectal surgery: a systematic review of techniques for endoscopic salvage. Surg Endosc. 2019;33(4):1049-1065. doi:10.1007/s00464-019-06670-9
- 87. Eisenstein S, Stringfield S, Holubar SD. Using the National Surgical Quality Improvement Project (NSQIP) to perform clinical research in colon and rectal surgery. Clin Colon Rectal Surg. 2019;32(1):41-53. doi:10.1055/s-0038-1673353
- 88. Tsai YY, Chen WT. Management of anastomotic leakage after rectal surgery: a review article. J Gastrointest Oncol. 2019;10(6):1229-1237. doi:10.21037/jgo.2019.07.07

## **Open Access Surgery**

# **Dovepress**

## Publish your work in this journal

Open Access Surgery is an international, peer-reviewed, open access journal that focuses on all aspects of surgical procedures and interventions. Patient care around the peri-operative period and patient outcomes post-surgery are key topics for the journal. All grades of surgery from minor cosmetic interventions to major surgical procedures are covered. Novel techniques and the utilization of new instruments and materials, including implants and prostheses that optimize outcomes constitute major areas of interest. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/open-access-surgery-journal



