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REVIEW

Anastomotic disruption after large bowel resection

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Abstract

Anastomotic disruption is a feared and serious complication of colon surgery. Decades of research have identified factors favoring successful healing of anastomoses as well as risk factors for anastomotic disruption. However, some factors, such as the role of mechanical bowel preparation, remain controversial. Despite proper caution and excellent surgical technique, some anastomotic leaks are inevitable. The rapid identification of anastomotic leaks and the timely treatment in these cases are paramount.

Key words: Colon; Colectomy; Anastomosis; Surgical complications

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INTRODUCTION

Anastomotic leakage following colorectal resection and primary anastomosis is a major clinical problem. The increased morbidity and mortality following anastomatic leakage are considerable, and lead to prolonged hospital stay. Leakage after partial colectomy with primary anastomosis may result in abscess formation, sepsis, multiple procedures and death. Despite vast improvements in surgical technique and devices, anastomotic leakage continues to be a clinical problem. The prevalence of intraperitoneal anastomotic leak varies in the literature between 0.5% and 30%, but is generally between 2% and 5%[1-3]. The double staple anastomotic technique does not appear to increase the risk for anastomotic leak, which has been reported to be 2.7%[4].

There are many factors that contribute to anastomotic leakage. Certainly, poor surgical technique can lead to an anastomotic leak. However, even when the operation is done technically well, anastomotic leaks are inevitable. Hence, a great deal of research has been done to elucidate the factors, which may decrease the rate of anastomotic leaks. Several factors have been identified that may impact on anastomotic leakage: adequacy of blood flow to the anastomoses, contamination, anastomotic technique, the presence of a pelvic drain, anastomotic tension, absence of active disease or distal obstruction, and the distance from the anal verge[5].

Numerous different techniques have been used to fashion a colorectal anastomosis. These techniques can be divided into 2 categories: hand sewn or stapled anastomosis. Hand sewn techniques include single-layer interrupted or continuous with either absorbable or nonabsorbable sutures, or various double layer techniques. The advent of stapling devices in the last century has made a significant contribution to colorectal surgery. Stapling devices have been widely accepted by surgeons performing gastrointestinal surgery. Numerous studies have been conducted comparing the various anastomotic techniques. Debates have been raised comparing single *versus* double-layered closure, absorbable *versus* nonabsorbale sutures, sutures *versus* staples, and inverting *versus* everting techniques. None of the various methods of anastomosis has been proven to be superior to the others.

HISTORY

During the early 19th century, while writing on intestinal injuries, Travers stressed the uniform contact of cut ends of intestine utilizing everting sutures. Later that century, Lembert countered this idea, instead advocating inverting sutures with serosal to serosal contact. Halsted noted that the submucosal layer was the strength-bearing layer in intestinal anastomoses. By the time that Treves published "A System of Surgery" in 1895 "Lembert Sutures" were recommended in intestinal anastomoses. The first acclaimed mechanical device to create a non-sutured anastomosis was Murphy's button introduced in 1892. It consisted of two mushroom shaped pieces, which were secured within bowel ends by purse string sutures. The pieces were then joined together. The bowel would heal as an inverted anastomosis. The excess inverted tissue would slough and the intact "button" would pass per rectum. Murphy's button gained considerable acceptance for several decades.

Circular end-to-end stapling devices were developed in the Soviet Union during the 1950s. The KT, PKS and SPTU instruments were bulky and unwieldy but served as the prototypes for today's end-to-end staplers[6]. A Soviet instrument was brought to the United States by Ravitch in 1958. Subsequently, such devices have been manufactured in the United States but did not attain widespread use until the 1970s. Thus, today's surgeon has the option of suturing or stapling intestinal anastomoses.

RISK FACTORS

Numerous risk factors have been implicated as predisposing for anastomotic leaks. Schrock *et al*[7] performed a large retrospective analysis of factors relating to leakage of colonic anastomoses. Factors that were found to correlate with an increased leakage rate were older age, anemia, prior radiation therapy, intraperitoneal infection and anatomic level of anastomosis. Conversely, steroid use, nutritional status and experience of the operating surgeon did not significantly influence the anastomotic leak rate. Rullier *et al*[8] analyzed factors associated with leakage and reported male sex and level of anastomosis as independent risk factors. In the same study, low anastomoses in obese patients were reported as associated with higher risk of leak. A higher leak rate with low pelvic anastomosis has also been reported by other investigators[9].

In a more recent study, Makela *et al*[10] compared 44 patients with anastomotic leaks to 44 control patients matched for age, gender and indications for surgery. They found that malnutrition, weight loss, alcohol intake, lengthy operative times, peritoneal contamination, and blood transfusions were independent predictors for leaks. In addition, the presence of multiple risk factors increased the risk for anastomotic leaks.

Law *et al*[11] performed a prospective study to identify risk factors for anastomotic leak in 196 patients undergoing total mesorectal excision for rectal cancer ranging from 3 cm to 12 cm from the anal verge. The overall leakage rate was 10.2%. The leakage rate was significantly higher in men (13.4%) as compared with women (5.2%) ($P=0.049$). As expected, the presence of a proximally diverting stoma significantly decreased the leakage rate especially in patients with risk factors for anastomotic dehiscence and low pelvic anastomosis. Interestingly, ages, level of anastomosis, stage of disease, or techniques of anastomosis were not significant predictors of anastomotic leak.

Mechanical forces

Investigators have used strength measurements to assess colonic healing using either breaking strength or bursting strength[12]. The breaking strength represents the uniaxial force required to break a wound *in vitro* and is a test of the entire anastomotic line. The bursting strength is a multiaxial test that measures the weakest point of an intestinal anastomosis which is the most likely location of an anastomotic leak[13].

The mechanical strength of an anastomosis is related to whether an anastomotic leak occurs. The strength of an anastomosis is dependent on the deposition of collagen. The measurement of tissue collagen content is another tool used in experimental models[14]. Martens *et al*[15] demonstrated that increased production of collagen at the anastomotic site was present 12 h after surgery. Brasken *et al*[16] showed that large amounts of type I and III collagen were present on postoperative day 4 in the anastomosis. In support of Halsted's observations, it is generally appreciated that the ultimate strength of an anastomosis depends on the collagen content in the submucosa.

Nutrition

Bowel rest (with a low-residue diet) lowered the bursting strength of non-operated colon in rats[17]. Interestingly, however, it did not impair the strength of a healing anastomosis. Dietary protein depletion impairs colonic strength in healing rat colon. Data regarding the duration of protein depletion needed to impair colonic healing in rats is conflicting. While some studies suggest that as little as one week of protein depletion has a detrimental effect, others suggest that at least 7 wk of protein restriction are needed[18,19]. In a comparison of alimentation means, Kiyama *et al*[20] showed that colonic anastomoses in rats were stronger after enteral nutrition compared to parenteral nutrition.

Bowel preparation

The role of preoperative bowel preparation has become a matter of controversy. Poth EJ[21] in 1953 proposed use of neomycin and sulfathalidine for intestinal antisepsis with reduction in the postoperative complications. Nichols RL and Condon R[22] also suggested a historic reduction in mortality and morbidity with the use of bowel preparation in a collective review of literature. In a 1973 retrospective study, Irvin TT and Goligher JC[23] reported a significant decrease in anastomotic dehiscence with the use of mechanical bowel preparation than that without mechanical bowel preparation (7% *vs* 24%). Most of the reports favoring the use of mechanical bowel preparation are based on retrospective data. However, some randomized trials have reported significant differences in outcomes with use of oral antibacterial agents and mechanical preparation. Matheson *et al*[24] reported a significant reduction in the incidence of wound sepsis and anastomotic dehiscence using both a mechanical and antibiotic preparation.

In contrast, recent literature suggests no significant advantage utilizing aggressive mechanical preparations. To assess the need for mechanical preparation to decrease the rate of anastomotic leaks in elective colorectal surgery, a number of prospective randomized trials have been completed[25-28]. Recently, Guenaga *et al*[29] conducted a meta-analysis on the existing clinical trials which studied the effect of mechanical bowel preparations on the rate of anastomotic leaks. A total of 1204 patients were enrolled in the various studies. Patients were divided into 2 groups: Group 1 ($n=595$) which received a mechanical bowel preparation; and group 2 ($n=609$) without a mechanical bowel preparation. They showed that the rate of anastomotic leaks in group 1 was obviously higher (5.5%)

compared to group 2 (2.9%) ($P=0.02$). Clearly, controversy exists on whether mechanical bowel preparations influence the rates of anastomotic leaks in elective colorectal surgery. Recent meta-analysis and prospective trials have questioned the usefulness of mechanical bowel preparations and do not support its use.

Chemo-radiation

Preoperative chemo-radiation has been used in patients with rectal carcinoma and reductions in tumor size can be achieved with its use. Chemo-radiation may predispose to anastomotic problems in patients having colon surgery, particularly in patients with anastomosis in the pelvis. Many surgeons perform a temporary diverting stoma to minimize the consequences of anastomotic disruption in patients who have had pelvic radiation therapy[30]. Anastomotic leak and radiation therapy may contribute to the formation of pelvic fibrosis, rendering the neorectum stiff and noncompliant. After reconstruction, patients may suffer from tenesmus and fecal incontinence[31].

Since many colectomies are performed for cancer, the effects of common chemotherapeutic agents and external beam irradiation on colonic healing are of interest. Immediate post-operative administration of intravenous 5-flourouracil (5-FU) in rats undergoing colectomy resulted in more conflicting data. While 4-8 mg/(kg.d) for 10 d impaired breaking strength of rat colon[32], 20 mg/(kg.d) for 5 d had no significant effect compared to controls[33]. A third study on rats showed that 600 mg/m^2 of 5-FU in the early postoperative period had no effect on colon anastomotic bursting strength[34].

In a study on rats, preoperative vitamin A supplementation protected against impaired colonic healing caused by preoperative radiation therapy[35].

Del Rio *et al*[36] showed that chronic steroids (time released via subcutaneous route) impaired colonic anastomotic strength in rats. In contrast, a large retrospective review in humans suggested no steroid effect[7].

Surgical technique

The technique used to fashion a colorectal anastomosis is largely based on surgeon preference. In order to achieve an adequate colonic anastomosis with a low rate of post-operative anastomotic leak or stricture formation, certain basic surgical principles must be met. First, the technique utilized for the anastomosis must assure an adequate lumen. Second, an adequate blood supply must be maintained for both the proximal and distal colon after resection. Finally, the anastomosis must be performed so that there is no tension to pull it apart (i.e., the surgeon must assure adequate mobilization of the proximal and distal colon). Considerable investigation has been conducted during the last century to determine the best technique for colonic anastomoses. An intestinal anastomosis may be constructed by a variety of techniques, including single layered suture, double layered suture, interrupted or continuous sutures, absorbable or nonabsorbable sutures, stapling devices or with use of a biofragmentable ring. To date, no single technique, single layer suture, double layer suture or stapling has ever been definitely demonstrated to be superior in preventing anastomotic leaks[37,38].

Table 1 Prospective randomized trials comparing the effect of mechanical bowel preparation *versus* no preparation on anastomotic leaks in elective colorectal surgery (*n*, %)

Investigators	Number of patients	Bowel preparation group (leak rate)	No bowel preparation group (leak rate)	*P*
Miettinen *et al*[25]	267	4%	2%	0.28
Zmora *et al*[26]	380	3.7%	2.1%	0.50
Santos *et al*[27]	149	10%	5%	0.52
Burke *et al*[28]	186	7.8%	11%	0.90

Surgical technique has been extensively studied in animal models. When comparing inverting *versus* everting sutured techniques, the everting technique produced less inflammation and less stricture but the inverting technique was less likely to disrupt[39,40]. (Table 1) This was also supported by the work of Irvin *et al*[41] in both animal as well as human studies. In addition, they reported no difference in the two layered *versus* single layer inverting anastomosis technique when doing intestinal anastomosis[41,42]. With disruption being the most serious problem, the inverting technique is more commonly used.

Stapled *versus* various sutured anastomoses have been compared numerous times in animal models. In a detailed study in dogs, Chung *et al*[43] showed a single layered sutured anastomosis resulted in the least reduction in anastomotic blood flow. Stapled anastomoses reduced blood flow the most. Conversely, Kozol *et al*[40] showed that early anastomotic edema was greater in two layered sewn anastomoses than in stapled. It should be noted that in some clinical circumstances, the surgeon's choice of technique is limited. For example, it is generally accepted that for low pelvic colo-rectal anastomoses stapled techniques are easier to perform.

Numerous clinical studies have been performed to define the anastomotic leak rate using sutures (Table 2). The largest of these studies was conducted by Max *et al*[44] in 1000 patients. A retrospective study was performed in 1000 consecutive patients who underwent a single layer continuous polypropylene colorectal anastomosis. The clinical anastomotic leak rate was only 1%[44-47].

Similarly multiple studies have been performed utilizing the stapled technique for colorectal anastomoses (Table 3). The leak rates from these studies ranges from 1.5% to 11%[4,48-54]. The largest of these studies was conducted by Detry *et al*[48]. A prospective study was performed in 1 000 consecutive patients undergoing stapled colorectal anastomosis by a single surgical team. The clinical leak rate was 3.5%. Also, Hansen *et al*[53] performed a large prospective study in 615 patients who underwent stapled colorectal anastomoses by a total of 18 surgeons, showing only 1.5% clinical leak rate.

Specific studies have been performed comparing stapled and sutured colorectal anastomoses (Table 4)[55-58]. Docherty *et al*[55] conducted a randomized prospective multicenter trial in 732 patients undergoing either hand-sewn ($n=321$) or stapled ($n=331$) colorectal anastomoses. The location of the anastomosis included ileocolic, colocolic, colorectal, and colostomy closures. There was no difference in the stapled or sutured group with regards to rate of anastomotic leakage. Demetriades *et al*[58] conducted

Table 2 Clinical studies utilizing sutures for fashioning colorectal anastomosis

Investigators	Number of patients	Types of suture	Continuous *vs* interrupted	Leak rate (%)
Max *et al*[45]	1 000	Non-absorbable	Continuous	1
Mann *et al*[46]	320	Absorbable	Interrupted	3.4
Flyger *et al*[47]	105	Absorbable	Continuous	1
Deen *et al*[48]	26	Absorbable	Interrupted	3.9

Table 3 Clinical studies utilizing staples for fashioning colorectal anastomosis

Investigators	Study design	Number of patients	Leak rate (%)
Detry *et al*[49]	Prospective	1 000	3.5
Griffen *et al*[50]	Prospective	75	2.7
Cohen *et al*[51]	Prospective	26	3.8
Laitinen *et al*[52]	Prospective	39	5.3
Baran *et al*[53]	Retrospective	104	2.8
Karanjia *et al*[54]	Prospective	276	11
Hansen *et al*[55]	Prospective	615	1.5
Memon *et al*[56]	Prospective	218	3

Table 4 Comparison of stapled versus sutured colorectal anastomoses

Investigators	Number of patients	Staple technique leak rate (%)	Suture technique leak rate (%)	*P*
Docherty *et al*[57]	732	4.7	4.3	0.93
Fingerhut *et al*[58]	113	13	18.7	0.05
Everett *et al*[59]	100	0	2	NS
Demetriades *et al*[60]	207	6.3	7.8	0.69

NS = not significant.

a prospective multicenter trial comparing hand-sewn to stapled colonic anastomosis in the emergent penetrating trauma setting. A total of 207 patients were enrolled in the study from 19 different centers. All patients underwent colon resection with primary anastomosis. There were 128 hand-sewn anastomoses and 79 stapled anastomoses. The demographics of both groups were similar with respect to age, gender, mechanism of injury, associated injuries, and fecal contamination. They demonstrated that there was no statistically significant difference in the 2 groups with respect to anastomotic leaks.

Surgeons have attempted several intraoperative techniques in hopes of lowering anastomotic leak rates. One is "omentoplasty" which involves wrapping the anastomosis with omentum. This was prospectively studied by the French Associations for Surgical Research[59]. In their randomized study of 705 patients, omentoplasty did not decrease the anastomotic leak rate or the clinical severity of anastomotic leaks compared to the patients without omentoplasty. Some surgeons have routinely placed a pelvic drain after low anterior resections. In a prospective, randomized study of 319 patients, the same French investigators showed that routine pelvic drainage did not lower the rate or severity of anastomotic leaks[9,60].

Many surgeons utilize intraoperative air/water testing of colon anastomoses. With this technique, after completing the anastomosis, the patient is placed in reverse Trendelenburg position. The pelvis is filled with sterile saline solution and an assistant places a sigmoidoscope (flexible or rigid) into the rectum, below the anastomosis. The colon is then insufflated with air, and the surgeon views the pelvic saline bath for bubbling (a sign of an inadequate or leaky anastomosis). If bubbling is seen, the leak is identified and repaired with sutures. There are at least two studies of the efficacy of this technique. In a study of 145 patients, Beard *et al*[61] were able to lower the "radiologic" leak rate from 29% to 11% using air/water testing in order to plan the placement of additional sutures as needed. In a study of 82 patients, Pritchard *et al*[62] found the air/water test helpful in higher anastomoses but unreliable in very low anastomoses. This may be due to the difficulty in suture repairing very low anastomoses.

In many series, the leak rates were higher for anastomoses below the peritoneal reflection[8,63,64]. One large study revealed a 12.7% leak rate in colorectal anastomoses compared to 2.9% in colo-colonic anastomoses[65]. Anastomotic leak can be a serious complication of resection for low rectal resection. Several studies have been conducted to identify risk factors that contribute to anastomotic dehiscence in patients undergoing low anterior resection (LAR) and proctectomy with coloanal anastomosis. Leaks after coloanal anastomoses are no more frequent than with colorectal anastamoses with a range of 6% to 8%[66,67]. Certain risk factors are more frequently associated with rectal resection. Meade *et al*[68] reported that a distance of less than 5 cm from anal verge, male sex, alcoholism and smoking were the risk factors for anastomotic breakdown after low rectal resections. Similar results were reported by Rudinskaite *et al*[69].

Law *et at.* investigated operative results and oncological outcomes of anterior resection for rectal and rectosigmoid cancer. They reported a significantly higher leak rate (8.1%) in patients who underwent a total mesorectal excision than those who underwent partial mesorectal excision (1.3%). Additionally, they reported that higher anastomotic leakage rate was associated with the male gender, absence of stoma, and increased blood loss[70]. Recently, Matthiessen *et al*[71] reported similar results, but they did not report any advantage of performing a temporary stoma. It should be noted that the creation of a proximally diverting stoma to protect a low pelvic or technically inadequate anastomosis does not alter the risk for dehiscence but does ameliorate the septic effects of the leak[7,71,72].

Recently, emphasis on the quality of surgical care offered has increased tremendously. There is an increasing awareness of the outcomes of surgical care as a marker of quality. Dimick *et al*[73] reported lower mortality rates in patients undergoing surgery for colorectal cancer when these procedures were performed in high volume centers. Similarly, Hannan *et al*[74] suggested an inverse relationship between in-hospital mortality rates and case volume for patients undergoing certain procedures. They reported that individual physician volume has more significant influence on the mortality rates for certain procedures. The same

authors[75] recently reported a significant reduction in mortality of patients who underwent colectomy when these procedures were performed by high-volume surgeons at high-volume centers. Conversely, the data reported by Urbach *et al*[76] did not support superior outcomes when colon operations were done at high volume centers.

CLINICAL PRESENTATION AND DIGNOSIS

Anastomotic leakage typically occurs between the 3rd and the 6th post-operative days. The clinical manifestation of anastomotic dehiscence varies in magnitude from failure to thrive to profound sepsis. The presentations in a given patient depend, in part, on the location and magnitude of the leak, and whether any adjacent tissues such as omentum or small intestine contain the leak. Indeed, a less severe leak may be walled off by adjacent organs or omentum and may present with vague abdominal pain, failure to thrive, temperature elevation, tachycardia, prolonged ileus, diarrhea or intestinal obstruction. Recognition of this situation may be delayed as the nonspecific symptoms can be attributed to delayed recovery from a major operation rather than to an anastomotic failure. However, the physician must have a high index of suspicion to make an early diagnosis. Most patients with anastomotic dehiscence will have prolonged ileus, increased postoperative abdominal pain, fever, and leucocytosis. However, the spectrum can include sepsis, peritonitis and/or hemodynamic instability. Longo *et al*[77] described the initial symptoms in 56 patients with postoperative pelvic abscess that developed after colon surgery, showing that 93% had intestinal dysfunction and 4% were in shock.

The presence of the aforementioned risk factors should raise the index of suspicion for leaks. Suspicion of a leak should lead to diagnostic imaging. A gastrografin enema is a quick and inexpensive way to evaluate the integrity of a colonic anastomosis. A gastrografin enema is less useful for right colonic anastomoses because it becomes too dilute to accurately define the anastomosis. A CT scan with intravenous, oral and rectal contrast material may also be obtained in those patients with suspected anastomotic leak and should demonstrate any abscess or extravasation of contrast from the intestine. Barium enema should not be used in this circumstance because of the increase in morbidity and mortality associated with barium-induced peritonitis. Indium-labeled leukocyte scans are occasionally helpful to identify abdominal abscesses that are suspected but not seen using conventional imaging.

MANAGEMENT

The specific method of management of an anastomotic dehiscence depends on the manifestation of the leak and the clinical condition of the patient. As many as 36% to 49% of patients with a pelvic anastomosis will have a leak demonstrated when gastrograffin enemas are routinely used during the first postoperative week[78,79]. Most of these are "subclinical" leaks. In a patient with evidence of low-grade sepsis and documentation of a contained anastomotic leak with abscess, drainage of the abscess and broad-spectrum parenteral antibiotic therapy are required and may be sufficient therapy. Drainage of an abscess can be accomplished percutaneously or operatively. A CT scan of the abdomen and pelvis with intravenous, oral, and rectal contrast medium is advocated whenever an anastomotic leak and abscess is suspected. CT scan is highly sensitive and accurate (95%) in determining the presence of abdominal or pelvic abscess[80]. CT-guided percutaneous drainage is successful in as many as 85% of appropriately selected patients[81]. For a low colorectal anastomosis, abscess drainage can be accomplished through the anastomosis if the dehiscence is readily apparent at endoscopic examination. The defect can be gently enlarged to allow better drainage, and transrectal drains can be placed in the cavity for continuous or intermittent irrigation. Transvaginal and transperineal drainage can also be performed.

Clinically ill patients with sepsis, pain and tenderness will require reoperation. Creation of a proximal colostomy or ileostomy plus peritoneal lavage and placement of drains are indicated. Some studies have advocated proximal diversion without resection if the anastomosis has been used with good results[82,83].

Gross peritonitis requires laparotomy, resection of the anastomosis with end colostomy and mucous fistula or Hartmann pouch. Diversion alone without resection of the leaking anastomosis is not ideal because of persistent sepsis from the leaking anastomosis. In such cases, wide drainage of the anastomosis should be performed. Repair of the anastomosis, either alone or in combination with a proximal stoma, is not recommended because of the high risk of recurrent anastomotic failure and/or anastomotic stricture in the presence of intra-abdominal sepsis.

Unrecognized anastomotic leaks may present as enterocutaneous fistulas. A fistulogram and/or CT scan should be obtained to determine the site of the defect in the intestine and whether any undrained collection of pus is present. Any adjacent fluid collection should be drained to facilitate closure of the fistula. After control of the source of sepsis and in the absence of distal bowel obstruction or a foreign body, the majority of colocutaneous fistulas will close without operative intervention. Other important management guidelines include correction of anemia and fluid and electrolyte abnormalities, excellent wound care, and adequate nutrition. Bowel rest and total parenteral nutrition may be necessary to facilitate closure. A late manifestation of unrecognized anastomotic leaks is anastomotic stricture. Strictures may require endoscopic dilation. Refractory strictures will require surgical revision or resection and reanastomosis.

CONCLUSION

In summary, surgeons should be aware of risk factors for colonic anastomotic leaks. The ideal is avoidance of a colonic anastomotic leak by use of proper surgical technique. In fashioning a colorectal anastomosis, some basic surgical techniques must be followed to have an acceptable result. These include the presence of adequate blood flow to the anastomosis, minimal

contamination, absence of anastomotic tension, absence of active disease, and no distal obstruction. The utility of preoperative mechanical bowel preparation in decreasing the anastomotic leak rate has been questioned by findings from several recently performed randomized prospective studies. The use of sutures or staples to create a colorectal anastomosis has never been shown to significantly alter the anastomotic leak rate.

Even when excellent surgical technique is used, a small percentage of leaks are inevitable. Characteristics, such as male gender, obesity, level of anastomosis, peritoneal contamination, age, operative time and blood transfusions, have all been implicated as potential risk factors for anastomotic leakage in various studies[84]. The clinicians must have a high index of suspicion to diagnose an anastomotic leak early. If a leak occurs, it must be identified and treated expediently. Treatment is based on the patient's conditions and the magnitude of the leak.

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