

## Review Article

# Anastomotic leakage following colorectal surgery: definition, diagnosis and treatment

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Received May 1, 2018; Accepted December 7, 2018; Epub January 15, 2019; Published January 30, 2019

**Abstract:** Aim: Anastomotic leakage (AL) is one of the most serious complications after colorectal resection, causing sepsis, reducing overall in-hospital survival and increasing the risk of local and distant recurrences. So, the diagnosis and treatment of AL following colorectal surgery is very important. Method: To improve the diagnosis and treatment of AL following colorectal resection, a number of studies have investigated strategies to diagnose and manage AL. In this review, we summarized the definition, grade, diagnosis and treatment of AL. Result: The results showed that the diagnosis of AL following colorectal resection relied on computed tomography (CT) scans and water-soluble enemas. The AL could be classification into 1 of 3 grades (grades A, B, and C) according to its impact on clinical management. The treatments included conservative treatment, endoscopic treatment and surgical intervention. Clinically, most cases of AL were cured through comprehensive therapy. Conclusion: Departments of medicine and surgery should work hand in glove to treat AL. Besides, we should pay more attention to the use of endoscopy and laparoscopy in treating AL following colorectal resection.

**Keywords:** Anastomotic leakage, colorectal resection, diagnosis, treatment, definition

## Introduction

At present, surgery is the main treatment for colorectal tumors. Enhanced recovery after surgery (ERAS) has gained momentum in the management of the colorectal cancer patient, which reduces morbidity and shortens the hospital stay [1]. Anastomotic leakage (AL) is one of the most serious complications of colorectal resection. AL is a devastating complication, causing sepsis, reducing overall in-hospital survival, and increasing the risk of local and distant recurrences [2, 3]. In addition, AL prolongs the hospital stay and increases the hospitalization expenses, affecting the implementation of the ERAS. Therefore, the diagnosis and treatment of AL following colorectal surgery is very important.

To diagnose and treat AL following colorectal surgery more efficiently, a number of studies have investigated the pathways and strategies used to diagnose and treat AL. In this review, we summarized the definition, grading, diagno-

sis and treatment of AL following colorectal resection.

## Definition of AL

There is a series of studies defining AL. Almeida et al. [4] defined AL as clinical signs of peritonitis and /or clinical evidence of free fecal fluid within the abdomen or emerging from the drain site. Kobayashi et al. [5] showed that clinical AL was defined as clinical symptoms, such as fever or septicemia, in combination with intra-abdominal or pelvic abscess formation, discharge of pus per the rectum, rectovaginal fistula formation or peritonitis within 30 days postoperatively, leading to a clinical and/or radiological examination of the patient or surgery that confirmed the presence of leakage. There are also other definitions of AL. On the whole, the definitions of AL mainly incorporate the symptoms and signs caused by AL. These definitions may provide clues to the diagnosis of AL. The exact diagnosis should depend on the imagological examination or surgical exploration.

### *Diagnosis of AL*

As there are no special clinical signs of AL, it is necessary to explore objective methods to diagnose AL. According to the literature, CT scans and water-soluble enemas have proven useful in diagnosing AL following colorectal resection. CT scans are performed with oral, intravenous, and rectal contrast. A positive CT was defined as demonstrating extraluminal contrast or clear extravasation from the suture line [6]. CT imaging has been reported to be effective in identifying patients with AL and it was done in most of the patients [7]. Besides, CT imaging could show celiac conditions, such as peritoneal effusion, pneumoperitoneum, abscesses and so on. A positive water-soluble enema study was defined by the extravasation of contrast from the anastomotic suture line or a collection of contrast of the bowel lumen [6]. This method has a high specificity to find AL. However, it is easy to miss diagnosis when the orificium fistulae is too small or too sly. There was a series of studies comparing the effect of using water-soluble enemas and CT imaging in the diagnosis of AL. Alves et al. [8] concluded that CT imaging was the first measure to be taken for patients with suspected AL. On the contrary, another study by Nicksa et al. [6] supported the superiority of water-soluble enema over CT imaging. Therefore, these two methods could be both taken for patients with suspected AL.

### *Grading of AL*

To indicate the severity of AL following colorectal resection, the international study group of rectal cancer established a clinical grading system. This classification ranked AL into 1 of 3 grades (grades A, B, and C) according to its impact on clinical management [9]. Grade A: this grade of AL is not associated with clinical symptoms or abnormal laboratory tests. The patient is clinically well and no active therapeutic intervention is required. Grade B: an AL is classified as grade B when the patient's clinical condition requires an active therapeutic intervention that can be managed without operative reintervention. Clinical management of grade B leakage includes commonly-administered antibiotics, and/or radiologic replacement of a pelvic drain, or transanal lavage. Grade C: patients with grade C AL are often quite ill and require

operative re-laparotomy [9]. Kulu et al. [10] performed a study to test the grading system for validity. They concluded that this grading system is a simple, easily applicable, and valid classification. Using this classification system may facilitate the comparison of results from different studies on AL after sphincter-preserving rectal surgery.

### **Treatment of AL**

#### *General conservative treatment of AL*

The conservative management of AL including absolute diet, total parenteral nutrition, oxygen uptake, anti-infective therapy, keeping abdominal drainage unobstructed and so on. It is important to keep the pelvis and abdomen as clean as possible draining out any detrimental material. There were studies showing that the ability to discharge fecal and purulent fluids from the pelvis offered a chance for conservative treatment in some cases, avoiding the need for a laparotomy [11]. For AL with grade A, these conservation treatments are enough to self-cure.

#### *Endoscopic therapy of AL*

Recently, the use of endoscopic therapy appears to offer a minimally invasive and effective way to manage AL, reducing the risk of permanent stoma and resulting in acceptable bowel function [12]. There was a series of studies exploring endoscopic technologies to cure AL following colorectal resection. These studies are summarized in **Table 1**. According to the table, endoscopic vacuum is a safe treatment for post-surgical AL, with a high success rate [12, 15, 18, 21]. Glitsch et al. [18] performed a study to confirm that endoscopic transanal vacuum-assisted rectal drainage (ETVARD) is a new method for treating AL after extraperitoneal rectal anastomoses. Their treatment began with the endoscopic debridement of the leak/cavity; nylon sponges were then endoscopically fitted into the cavity. Continuous suction was applied by suction tubes inserted into the sponges. Repeat endoscopies and sponge exchanges, including further debridement, were essential. They conclude that ETVARD was a well-tolerated and effective therapeutic option for the treatment of major leaks after extraperitoneal rectal anastomoses. Srinivasamurthy et al. [12] also reported their initial experience of

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**Table 1.** The baseline characteristics of the studies articles about endoscopic technologies to cure AL

First author, year, reference	Strategy	Study design	Num of patients	Cure rate	Technique detail
Srinivasamurthy, 2012, [12]	Using transanal vacuum therapy	Retrospective	8	87.5%	Use endoscopic transanal vacuum-assisted rectal drainage sponge therapy to reduce the size of the abscess cavity and limit pelvic sepsis.
Bège, 2011, [13]	Totally endoscopic strategy	Prospective	27	100%	This strategy involved successive procedures for endoscopic drainage of the residual cavity, diversion of the fistula with a stent, and then closure of the residual orifice with surgical clips or sealant.
DiMaio, 2012, [14]	Covered esophageal self-expandable metal stents	Retrospective	5	100%	Patients were sedated with monitored anesthesia care and underwent a standard flexible sigmoidoscopy. A guidewire was placed endoscopically. The endoscope was withdrawn and exchanged over the wire. The CSEMS was then advanced over the wire, and deployment of the CSEMS was performed under fluoroscopic guidance.
Arezzo , 2010, [15]	Endoluminal vacuum therapy	Case report	3	100%	The sponge should be changed every 48-72 h according to instructions for use.
Abbas, 2009, [16]	Endoscopic Management With Temporary Stent	Case report	1	100%	The procedures were performed in the endoscopy suite with the patient under intravenous sedation. The patients were placed in the left lateral decubitus position.
Zhou, 2012, [17]	Endoscopic needle knife therapy	Case report	1	100%	The orifice was enlarged by cutting through the septum between the sinus and the adjacent bowel lumen using an Olympus Triple Lumen Needle Knife at a setting of endoscopic retrograde cholangiopancreatography 'Endocut' on ERBE.
Glitsch, 2007, [18]	Endoscopic transanal vacuum assisted rectal drainage		17	94.1%	Treatment began with endoscopic debridement of the leak/cavity; nylon sponges were then endoscopically fitted into the cavity. Continuous suction was applied via suction tubes inserted into the sponges.
Perez, 2013, [19]	Biodegradable expandable polydioxanone stents	Retrospective and descriptive observational study	5	100%	A coated biodegradable stent or totally coated metal stent was inserted. The stent was sufficiently long to cover the fistula or to join both ends of the dehiscence. Metal stents were changed every 2 weeks, and biodegradable stents were checked every 2 to 4 weeks to ensure that the fistula or dehiscence had resolved.
Lippert, 2011, [20]	Endoscopic treatment with fibrin glue	Retrospective		–	The application of fibrin glue was performed with a double injection system "Duploject" only after rinsing the insufficiency/fistulae with sterile NaCl 0.9%. The syringe with fibrin glue as well as with the thrombin solution can be applied through this system.
Arezzo, 2014, [21]	Endoscopic vacuum therapy	Retrospective	14	79%	The sponge is connected to an evacuation tube advanced by a pusher tube with handle into the over-tube once removed the scope. We connected the tube to a vacuum system producing continuum negative pressure up to 700 mmHg when in hospital, and a portable system producing continuum negative pressure up to 200 mmHg when discharged.
Lamazza , 2013, [22]	Self-expandable metal stents	Prospective			The length of the stent placed ranged from 60 to 105 mm and the length of the stricture ranged from 20 to 55 mm (mean 33.5 mm).The stent was placed at least 2 cm above and 1 cm below the stricture. The lower end of the stent was always placed at least 1 cm above the dentate line to avoid tenesmus and anal pain.
Blot, 2015, [23]	Double-pigtail stents	Retrospective			The orifice of the fistula was dilated with a 0.035-in. guide wire (Tracer Metro DirectTM, WilsonCook Medical, Bloomington, IN, USA), in order to drain the peri-anastomotic abscess as much as possible. A DPS (Zimmon Biliary Stent, Cook Ireland Ltd, Limerick, Ireland) was inserted through the orifice of the fistula (between the peritoneal cavity and the lumen of the colon or rectum). It should be noted that the DPS never sticks out through the anus but always remains in the rectal lumen.

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**Table 2.** The baseline characteristics of the studies articles about surgical treatment to cure AL

First author, year, reference	Method	Study design	Num of patients	Cure rate	Technique detail
Basilico, 2014, [24]	Re-operation	Prospective	78	88.50%	Minor leak: anastomotic salvage and loop ileostomy; major leak: anastomotic take-down and terminal stoma
Blumetti, 2012, [25]	Transanal repair	Retrospective	5	80%	Transanal repair consisted of a simple suture, curettage or a flap procedure. The opening in the anastomosis was identified and excised. A broad, U-shaped flap was raised and the opening of the cavity was closed with an absorbable suture. To allow for a tension-free anastomosis, a small portion of anoderm was mobilized distally and the flap was secured with an absorbable suture
Dauser, 2014, [26]	Transanal repair	Retrospective	3	100%	
Thornton, 2011, [27]	Reoperation	Retrospective	30		
Krarup, 2014, [28]	Anastomotic salvage	Prospective	74	100%	In salvage patients, 73% had a loop-ostomy (loop ileostomy or loop-transversostomy). 27.0% of the salvage patients underwent an anastomotic repair or redo without a loop-ostomy
Fracalvieri, 2012, [29]	Anastomotic salvage	Observational study	39	84.60%	Salvage of anastomosis with loop ileostomy
Kirat, 2009, [30]	Salvage surgery	Retrospective	25		Pouch repair and new pouch creation
Uzun, 2012, [31]	Salvage repair with expanded polytetrafluoroethylene graft	Case report	1	100%	Surgery was performed, and the suprapubic mass that invaded the urinary bladder was excised with a wedge resection of the bladder. Additional procedures involved a gastric wedge resection for a nodular lesion located at the gastric corpus, a peritonectomy for peritoneal nodules, and a right hemicolectomy for nodules located on the cecum and the proximal transverse colon
Kwak, 2011, [32]	Laparoscopic Approach	Retrospective	57		Compared with conventional open treatment of anastomotic leakage, the laparoscopic approach resulted in fewer wound complications and tendency of early recovery of bowel movement without an increase in adverse outcomes
Cimitan, 2016, [33]	Laparoscopic reoperation	Prospective			Laparoscopic reoperation can be performed in most cases of anastomotic leaks occurring after minimally invasive colorectal resection for cancer
Boyce, 2017, [34]	Laparoscopy	Single-institute case series	44		Anastomotic leakage can be managed with laparoscopy in the majority of cases

using transanal vacuum therapy in pelvic AL. They showed that early use of endoscopic vacuum therapy appears to offer a minimally invasive and effective way of closing the presacral cavity after a pelvic AL, reducing the risk of permanent stoma and resulting in acceptable bowel function.

An endoscopic strategy with a stent for the management of AL after colorectal resection has been widely tried [13, 14, 16, 19, 22, 23]. Bege et al. designed a prospective study to assess a new, totally endoscopic strategy to manage AL. This strategy involved a successive procedure for endoscopic drainage of the residual cavity, diversion of the fistula with a stent, and then closure of the residual orifice with surgical clips or a sealant. Their results showed that this strategy achieved resolution of the fistulas with minimal morbidity [13]. Further, self-expandable metallic stents were tried to treat patients with AL. A self-expandable metal stent is a metallic tube, which is placed at the level of the colorectal obstruction and expanded to resume their original diameter. Owing to this characteristic, several studies were performed to explore its use in the treatment of AL. The results showed that self-expandable metal stents represent a valid option to treat patients with symptomatic anastomotic complications after colorectal resection for cancer. They have a complementary role to balloon dilatation in the case of simple anastomotic stricture, and they improve the rate of healing when the stricture is associated with a leak [14, 19, 22]. Also, double-pigtail stents were used in endoscopic treatment to treat AL. The endoscopic procedure involved a double-pigtail stent that was inserted through the orifice of the fistula (between the peritoneal cavity and the lumen of the colon or rectum). It should be noted that the double-pigtail stent never sticks out through the anus but always remains in the rectal lumen. The researchers found that double-pigtail stent placement under endoscopic control is associated with AL healing, good clinical tolerance, and the ability to undergo chemotherapy. It's also an alternative to repeat laparotomy when radiological drainage is unfeasible or inefficient [23].

Zhou provided a case of chronic anastomotic sinus that was successfully managed by endoscopic needle knife therapy with endoscopic

clips [17]. The detail was that endoscopy with a GIFH180 upper endoscope confirmed the presence of a 6-cm-long sinus with a narrowed orifice and a septum. The orifice was enlarged by cutting through the septum between the sinus and the adjacent bowel lumen using an Olympus Triple Lumen Needle Knife (Olympus) at a setting of endoscopic retrograde cholangiopancreatography 'Endocut' on ERBE (USA Incorporated Surgical Systems, Marietta, Georgia, USA). However, owing to the small number of cases, the efficacy of this technique is uncertain and it needs to be evaluated further.

There was a retrospective study of fibrin glue application in the treatment of AL following colorectal resection [20]. The application of fibrin glue was performed with a double injection system "Duploject" only after rinsing the insufficiency/fistulae with sterile NaCl 0.9%. The syringe with fibrin glue and the thrombin solution can be applied through this system. The results showed that endoscopic therapy cured 55.7% of the patients, and 36.5% were cured with fibrin glue as the sole endoscopic option. Therefore, endoscopic therapy with fibrin glue is a valuable option for the treatment of AL and deserves further study.

### *Surgical treatment of AL*

Although many patients with AL have been successfully treated conservatively, most patients should undergo re-operation. There was a series of studies to explore the surgical treatment to cure AL following colorectal resection. These studies are summarized in **Table 2**. Basilio et al. [24] reported their experience with the surgical treatment of AL after colorectal resection. They found that 46.1% of AL cases healed with conservative treatment, but in the remaining 53.8%, reoperation was necessary. The choice of surgical procedure depended on the type of anastomosis, the size of the leak, and the presence of ischemia at the site of the anastomosis. Generally, for minor leaks, they adopted anastomotic salvage and loop ileostomy; for major leaks, they adopted anastomotic take-down and terminal stoma [24]. Similarly, Khan et al. found that 70.8% of patients with AL should undergo re-operation. Their opinion on the treatment on AL included the defunctioning of anastomosis, anastomosis taken down, and so on [35].

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There are studies showing that if an anastomosis is taken down following an anastomotic leak after anterior resection, this will usually result in a 'permanent' stoma [35]. So, many approaches have tried to cure AL through anastomotic salvage. Krarup et al. showed that patients with small anastomotic defects were safely managed by anastomotic salvage, and anastomotic salvage is a viable option for patients with AL [28]. In salvage patients, 73% had a loop-ostomy (loop ileostomy or loop-transversostomy); 27.0% of the salvage patients underwent an anastomotic repair or redo without a loop-ostomy. Some other studies reached the same conclusion [29, 30]. Moreover, Uzun et al. reported a case of salvage repair of anastomotic dehiscence following colon surgery using an expanded polytetrafluoroethylene graft [31]. An expanded polytetrafluoroethylene graft is an inert biomaterial that is impermeable to secretions and is not destroyed, hydrolyzed or weakened by tissue enzymes or microorganisms. This approach proved successful and could be confirmed further.

There was a study showing that the transanal repair of a persistent low colorectal or coloanal anastomotic leakage was feasible in selected cases [25]. This study involved five patients who underwent transanal repair of the AL. Transanal repair consisted of a simple suture, curettage or a flap procedure. The opening in the anastomosis was identified and excised. A broad, U-shaped flap was raised and the opening of the cavity was closed with an absorbable suture. To allow for a tension-free anastomosis, a small portion of anoderm was mobilized distally and the flap was secured with an absorbable suture [25]. Another study showed that transanal repair of the defect was feasible [26]. However, owing to the number of cases in which this has been applied, the effects of transanal repair should be evaluated further.

The surgical treatment of AL has often brought more trauma to patients owing to reoperations. Therefore, the reoperations should be effective and minimally invasive. Many studies report on experiments that tried to treat AL through a laparoscopic approach. Jung et al. evaluated the feasibility and safety of a re-laparoscopic approach to managing AL. They concluded that compared with the conventional open treatment of anastomotic leakage, the laparoscopic

approach resulted in fewer wound complications and the tendency of early recovery of bowel movement without an increase in adverse outcomes. Using a laparoscopic approach, all the advantages of minimally invasive surgery can be realized in patients who develop AL after minimally invasive surgery [32]. Similar to this, Cimitan et al. concluded that laparoscopic reoperation can be performed in most cases of AL occurring after minimally invasive colorectal resection for cancer. Stephen et al. also showed that AL can be managed with laparoscopy in a majority of cases [33].

### Prospective

With the advance of ERAS, patients who underwent colorectal resection could be discharged before the AL appears. So, the diagnosis and treatment of AL is important and significant. This paper has summarized the studies about the diagnosis and treatment of AL. Generally, the treatments included conservative treatment, endoscopic treatment, and surgical intervention. Clinically, we should select the proper strategy to manage the defects according to the grade of AL. Most cases of AL were cured through comprehensive therapy. So, departments of medicine and surgery should work hand in glove to treat AL. In our opinion, we should focus on the study of endoscopic treatment, which is often effective and minimally invasive. This review summarized many endoscopic strategies to treat AL. However, owing to the limited number of application cases, these methods have not been widely used in clinical practice. So, we should pay more attention to the endoscopic approach in treating AL. Besides, the laparoscopic approach in treating AL is also important. Nowadays, the laparoscopic approach is widely used in initial surgical operations. We should actively apply the laparoscopic approach to reoperations to manage AL following colorectal resection.

### Disclosure of conflict of interest

None.

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