Original Paper

Anastomotic Leakage after Colorectal Surgery: Risk Factors, Diagnosis and Therapeutic Options

MARIA MĂDĂLINA DENICU[1], DAN CÂRȚU[2], SANDU RÂMBOIU[2], MIHAI CIORBAGIU[3], VALERIU ȘURLIN[2], RĂDUCU NEMEȘ[2], LUMINIȚA CRISTINA CHIUȚU[4]

[1]*University of Medicine and Pharmacy of Craiova, Romania*

[2]*1st Surgery Clinic, County Emergency Hospital of Craiova, University of Medicine and Pharmacy of Craiova, Romania*

[3]*2nd Surgery Clinic, County Emergency Hospital of Craiova, University of Medicine and Pharmacy of Craiova, Romania*

[4]*ICU Department, County Emergency Hospital of Craiova, University of Medicine and Pharmacy of Craiova, Romania*

ABSTRACT: Anastomotic leakage (AL) is the most severe and devastating complication of colorectal surgery. The objectives of this study were to identify the risk factors involved in the development of AL, evaluate diagnostic methods and explore therapeutic options in case of colorectal cancer surgery. Material and Methods: we conducted a retrospective study on 28 AL recorded after 315 elective colorectal cancer surgeries performed in 1st Surgery Clinic of Craiova over an 8-year period (2014-2022). Results: The overall incidence of AL was 8.88%. The identified risk factors were rectal cancer (22.38%), low anterior rectal resection (50%), open approach, advanced age (82.15% over 60 years old), male sex (3:1), and the presence of two or more co-morbidities. Medical conservative treatment was the primary line of treatment in all cases. Leakage closure was achieved in 22 cases (78.56%), with exclusive conservative treatment in 15 cases (46.42%) and combined conservative and surgical treatment in 7 cases (25.0%). Overall morbidity was recorded at 64.28%, with 8 cases of general evolving complications and 10 cases of local complications. General mortality was reported at 6 (21.42%), with 3 (16.66%) occurring after conservative treatment and 3 after re-interventions (30%). Conclusions: our study identified advanced age, the presence of two or more co-morbidities, male sex, rectal surgery, and neoadjuvant chemoradiation as the most important risk factors for AL. Medical conservative treatment was the primary treatment modality, while reoperation was necessary in cases of uncontrollable sepsis and MODS. Mortality after re-intervention was nearly double compared to conservative treatment.

KEYWORDS: *Anastomotic leakage, colorectal surgery, reintervention.*

Introduction

Improvements in surgical technique due to technological advances and modern equipment (laparoscopic and robotic surgery, mechanical suturing with circular stapling) over the last 50 years, together with antibiotic prophylaxis and conceptual changes in preoperative preparation and postoperative management strategies have greatly increased the safety of colorectal cancer surgery [1-3].

However, complications after colorectal surgery are inevitable and continue to occur, ranging in severity from mild forms with minimal impact on the patient to severe forms with a potentially fatal outcome, as in the case of anastomotic fistulas.

Credited with an incidence of 2.8-30% [1,2,4] anastomotic leakage (AL) is the most serious and devastating complication of colorectal surgery, with negative impact on immediate and long-term outcome and burdened by increased morbidity and mortality due to sepsis and peritonitis, likelihood of reoperation and unintended permanent stoma, resulting in increased length of hospitalization, costs and resources used, and significantly decreased quality of life [4-8].

Anastomotic leakage increases the rate of local recurrence, decrease survival time and disease-free interval and are the leading cause of death after colorectal surgery [4,9-11].

A number of common risk factors are involved in the development of anastomotic leakage.

The occurrence of AL involves a number of risk factors pre-, intra- and postoperatively, as general patient factors that cannot be changed (age, gender, co-morbidities, emergency vs. elective surgery, etc.), disease-related factors (topography and morphological features of the tumour, TNM stage, etc.) and factors related to the operation itself (timing, approach, type of resection and anastomosis, etc.).

10.12865/CHSJ.49.03.05

Diagnosis is established clinically and by imaging, with CT-scan being the standard investigation.

Management is complex, medical-conservative and/or surgical, carried out according to an individualized algorithm for each patient depending on the patient's general condition, the type of primary operation, the site and size of the defect, the presence or absence of proximal stoma protecting the anastomosis.

The aims of the paper were to identify the risk factors involved in the occurrence of AL and to evaluate its diagnostic methods and therapeutic options.

Material and Method

The paper is a retrospective study of 28 (8.88%) ALs registered after 315 colorectal cancers operated in 1st Surgery Clinic of Craiova over an 8-year period (2014-2022).

Inclusion criteria were: patients over 18 years of age with colorectal cancer of various localization in whom the primary surgery was resection within oncological limits, with restoration of transit, the type of colectomy depending on the tumor topography.

Excluded from the study were: Miles abdomino-perineal resections, Hartmann resections and colostomies, regardless of type.

Pre-operative preparation was performed in all patients and consisted of: mechanical preparation with polyethilenglycol (4 packets in 4 l of water on the evening before surgery), chemical preparation (1 dose of 2nd generation cephalosporin 30 minutes before anesthetic induction repeated post-operatively if the procedure was longer than 3 hours) and thromboembolism prophylaxis with LMWH (low-molecular weight heparins) at least 12 hours before surgery.

The diagnosis of fistula was established clinically (fever, chills, prolonged ileus, abdominal guarding/tenderness, fecal leakage on the drain tube or through the wound, digital tact), and imaging (water-soluble contrast irigography, CT-scan).

The following parameters were studied:

- Demographics: age, gender, occupation, background
- Comorbidities
- ASA score
- Neoadjuvant radio-chemotherapy
- Tumour data established by clinical examination (digital tact), colonoscopy with biopsy, barium enema
- Surgery data: preoperative preparation, timing of surgery (emergency vs. scheduled surgery), approach (classic vs. laparoscopic), type of operation: (right colectomy, left colectomy, sigmoidectomy, transverse segmental colectomy, anterior rectosigmoid resection with sphincter preservation), type of anastomosis (ileo-transverse, colo-colic, colo-rectal, ileo-rectal) and type of suture (mechanical or manual), presence of protective ileostomy
- Leakage data:
  - lekage characteristics (leakage type, topography, effluent characteristics, flow rate, etc.)
  - treatment: conservative vs. surgical
  - the rate of re-interventions and their type
  - Morbidity and mortality

The study was approved by the Ethics and Academic and Scientific Deontology Commission of UMF Craiova No. 228/20.12.2021.

Results

The overall incidence of anastomotic leakage (AL) after colorectal surgery was 8.88% (28 AL out of 315 operated cases), with different values depending on tumor topography, type of primary surgery, approach route, type of anastomosis and suture, and presence or absence of protective ileostomy (Table 1 and 2).

Thus, the highest incidence of AL was found after resections performed for rectal cancer (12.38%), followed in order by left colon cancer (7.93%), right colon cancer (3.75%).

2 AL were recorded after total/subtotal colectomies performed for synchronous cancers or polyposis from 8 cases with synchronous tumours or rectocolonic polyposis (Table 1).

Table 1. Incidence of AL by tumor topography.

Topography	No of cases	Anastomotic fistula	%
Rectum	104	16	15.38
Left colon (including sigmoid)	63	5	7.93
Right colon	140	5	3.75
Polyposis/ Synchronous Cancer	8	2	25.0
Total	315	28	8.88

In terms of primary surgery, most AL were encountered in 17 (60.71%) cases after rectal surgery, of which 14 cases after low anterior resections (LAR), followed in order by left colectomy 5 cases, right colectomy 5 cases, respectively reintegration after Hartmann, total rectocolectomy and subtotal rectocolectomy 1 case. Conventional surgery was the approach

10.12865/CHSJ.49.03.05

in 20 cases; 8 cases were operated laparoscopically.

AL was recorded after colorectal anastomosis in 20 cases, ileo-transverse in 5 cases and transverse-sigmoid, ileo-sigmoid and ileo-rectal in 1 case.

In 18 cases AL occurred after manual suturing and in 10 cases after mechanical suturing. 11 patients received ileostomy (Table 2).

Table 2. Incidence of AL by type of operation, approach, type of anastomosis and suture and presence of protective ileostomy.

Type of operation	No of cases	Approach		Type of anastomosis					Mechanical	Ileostomy
		Laparoscopic	Classic	Colorectal	Ileo-transverse	Transverse-sigmidian	Ileosigmoidian	Ileorectal		
Rectum	17	7	10	16				1	10	11
-Low anterior resection (LAR)	14									
-Reintegration after Hartmann	2									
-Total Rectocolectomy	1									
Left colon (including sigmoid colon)	5	1	4	4		1				
-Left colectomy	2									
-sigmoidectomy	3									
Right colon	6	0	6		5		1			
-Right colectomy	5									
-Subtotal colectomy	1									
Total	28	8	20	20	5	1	1	1	10	11

Risk factors recorded pre- and intraoperatively were:

-Old age and male sex: 82.14% elderly (over 60 years), net predominance of male sex (21 males vs. 7 females).

Table. 3 Comorbidities.

Comorbidities	Cases	%
Cardiovascular	**19**	**67.85**
- Hypertension	14	
- Atrial fibrillation	1	
- Myocardial infarction/ischemic cardiomyopathy	4	
- Heart failure	3	
- Valvular lesions	4	
- Peripheral arterial disease	2	
Respiratory	**7**	**25.0**
- Pulmonary fibrosis	5	
- CPOD	2	
- Asthma	1	
- Pulmonary emphysema	1	
- Pahipleuritis	1	
Diabetes	**8**	**18.57**
Obesity	**5**	**17.85**
Digestive	**9**	**32.14**
- recto-colic polyposis	3	
- cholecystitis	3	
- hiatal hernia/reflux oesophagitis	1	
- chronic hepatitis	1	
- hepatic steatosis	2	
Renal	**7**	**25.0**
- renal lithiasis	3	
- renal cysts	2	
- chronic kidney disease	1	
Abdominal operations in the past	**6**	**21.42**
- colorectal neoplasm operated	2	
- appendectomy	1	
- duodenal ulcer operated	1	
- incisional hernia	1	
- adnexectomy for ectopic pregnancy	1	
C**ashexia**	1	**3.57**

-Comorbidities (Table 3): 27 patients had two or more associated comorbidities, cardiovascular diseases being the most common, present in 67.85%, followed in order by digestive 32.14% respiratory 25.0%, renal 25%, diabetes 18.57%, obesity 17.85%, malnutrition 3.5%. 6 patients had previous abdominal surgery, including 2 cases for colorectal cancer. No comorbidities were recorded in only one case.

Preoperative biological assessment revealed hypoproteinemia in 17 cases, anemia in 14 cases (moderate 10, and severe in 4 cases respectively), hypoelectrolytemia in 12 cases and hyperazothoraemia in 5 cases. 18 cases were assessed on admission with ASA score 3 and 10 cases with ASA score 2.

Neoadjuvant radio-chemotherapy was performed in all patients with rectal cancer, of whom 16 AL were recorded.

Intraoperatively the following risk factors were recorded: difficult viscerolysis 4 cases, parietal edema 3 cases, stricture with stenosis with significant dilatation of the proximal colon 3 cases, bulky mesenteric adenopathy with mesenteric retraction 1 case and iatrogenic ileum injury 1 case.

Leakage data:

-onset was immediate (first 24 hours post-op) in 2 cases, early (first 2-7 days) in 12 cases and late (after 7 days) in 14 cases.

-the diagnosis has been clinically established, the main sign being the exteriorization of intestinal contents on the drainage tube, through the wound or both, preceded or accompanied by fever, tachycardia, dyspnea, altered general

condition, oligo-anuria, localized or generalized abdominal pain, maintenance or increase of naso-gastric suction, peritoneal or bowel obstruction syndrome (Table 4).

Table 4. Clinical signs in case of anastomotic leakage.

Clinical signs	Cases	%
Fever	17	60.7
Tahycardia	18	64.3
Dyspnea	6	21.4
Altered general condition	10	35.7
Oligo-anuria	8	28.6
Abdominal pain	21	75
-Diffuse	10	
-Localised	11	
• **inferior abdomen**	10	
• **mezogastric**	1	
Peritonitis	17	60.7
Bowel obstruction syndrome	4	14.3
Incresed naso-gastric aspirate	7	25
Diarrhea	3	10.7
Pus	17	60.7
-On the drainage tube	13	
-Through the surgical wound	4	

Imaging: water-soluble contrast enema confirmed leakage in 5 cases and CT scan identified localized fluid collections in 4 cases (subphrenic, right parieto-colic, left parieto-colic and pelvic in 1 case).

Leakage characteristics: all cases were external anastomotic leakages, simple, with direct tracts in 18 cases and complex, with multiple tracts or open through a localized collection in 10 cases, exteriorized on the drainage tube in 6 cases, through the wound in 13 cases and both in 9 cases.

The source of the leakage was at the colorectal anastomosis in 19 cases, ileo-transverse in 5 cases, and transverse-sigmoid, colo-colic, ileo-rectal and entero-enteric in 1 case respectively.

The contents of the leakage were intestinal in 8 cases, fecaloid in 9 cases and purulent, later becoming fecaloid in 11 cases. 19 AL had low flow (<200ml/day), 7 medium (200-500ml/day) and 2 high flow (>500ml/day). Skin around the leakage site were normal in 14 cases, the remaining 14 cases presented with erythematous lesions in 12 cases and ulcerative lesions in 2,

-biological assessment after the onset of leakage showed hypoproteinemia in 22 cases, moderate anemia in 9 cases, hyperazotemia in 6 cases and hypoelectrolyteuria in 8 cases.

Treatment was complex, medically conservative and/or surgical.

Conservative medical treatment was the first-line treatment applied in all cases. 12 cases were initially admitted and treated in the ICU (2 days on average, with limits between 2-22 days) where aggressive volemic and electrolyte rebalancing therapy with saline administered intravenously and broad-spectrum antibiotics was started (23 cases).

Blood transfusion was indicated in 7 cases. Effluent control required complete cessation of oral food intake and total parenteral nutrition in 2 cases, for the remaining 26 cases nutrition was mixed, with oral food intake decreasing in 14 cases until the flow ouptput of leakage decreased.

For drug control of effluent, we used H2-receptor antagonists in 20 cases and somatostatin in one case.

For protection of the tegument sprays were used in 5 cases, creams/other topics in 12 cases and collection bags in 6 cases.

Compressive dressings with elastic balloon were used in 9 cases, of which in 3 cases combined with suction.

For the remaining 19 cases the protection of the tegument and wound care was done with simple or absorbent dressings, changed on average once a day.

Surgical treatment. 10 (35.71%) cases required reoperation, with the operative time being more than 7 days after the primary operation. The indication for reintervention, intraoperative lesion assessment and surgical management are shown in Table 5.

Table 5. Anastomotic leakage reoperations: indications, intraoperative assessment, type of operation.

Primary surgery	Anastomosis (type)	No.	Indication	No.	Intraoperative findings	Reoperation
- Left colectomy	Colo-colic	1	Unfavorable outcome	2	Peritoneal abscesses:	Evacuation of the
- Subtotal colectomy	Ileocolic	1	Increase in flow	1	mesogastric -1; right	peritoneal abscess,
- Dixon procedure					subphrenic-1; pelvic-1; left	drainage
- Right extended	Colorectal	1	Localized peritonitis		parietocolic- 1.	
colectomy	Ileotransverse	1	Deep wound infection	1		
- Hartmann procedure				1		
reversal	colorectal	1				
-Sigmoidectomy	Colorectal	1	Diffuse peritonitis	2	Total (2) or partial (7)	- Take-down anastomosis
- left colectomy	Colo-colic	1	Increse in AL flow	1	anastomotic dehiscence	and colostomy (5);
- Dixon procedure	Colorectal	4	Unfavorable outcome	5	Ileum fistula	- Take down anastomosis
- Extended right						and ileostomy (1);
colectomy	Ileosigmoid	1				- enteroenterostomy (1);
- Total colectomy	ileorectal	1				Ileosigmoidostomy (1).

10.12865/CHSJ.49.03.05

Fistula closure was achieved in 22 cases (78.56%), of which 15 (46.42%) cases by conservative treatment alone and 7 (25.0%) cases after conservative and surgical treatment.

Overall morbidity 64.28%. 18 cases had progressive complications: general 8 cases (sepsis 2, cachexia 2, COVID 1, bilateral pleural effussion 1, gastrointestinal bleeding in 2cases) and 10 locals (parietal suppuration of which 2 with fixed evisceration).

Overall mortality 21.42%-6 deaths, of which 3 (16.66%) after conservative treatment and 3 after re-interventions (30%), the causes of death being multiple organ and system failure in 3 cases, respectively sepsis, COVID and acute respiratory failure (pulmonary fibrosis and bilateral pleural effussion) 1 case.

Days in hospital: 33.35 average, with limits between 12 and 122 days.

Discussions

Anastomotic fistulas are the most serious and devastating complication of colorectal surgery, with negative impact on immediate and long-term outcome and progression, burdened by increased morbidity and mortality, likelihood of reoperation and unintended permanent stoma, increased length of hospital stay, increased costs and resources used, and significantly decreased quality of life [4-8].

The average incidence of anastomotic leakage after colorectal cancer surgery is 11%, with limits ranging from 2.8 to 30%, depending on the author, diagnostic criteria, clinical form at admission, topography and stage of the tumor, operative timing, type of surgery and duration of follow-up [1-3,11].

The overall incidence of anastomotic fistulas in our study was 8.8%, the majority (60.71%) occurring after rectal cancer surgery and 71.45% after colorectal anastomoses (Tables 1 and 2), confirming literature data that considers tumor topography and anastomotic level from anal verge one of the determinants in the occurrence of anastomotic leakage and reports 5 times higher incidence of AL after rectal resections than after those performed for other topographic forms of colon cancer [10,12-14].

Among 74 rectosigmoid resections with sphincter preservation and colorectal anastomosis in our study, the incidence of AL was 22.97% (17 cases). The etiopathogenesis of anastomotic leakage is multifactorial and includes a wide range of potential risk factors related to the patient, the disease and the primary operation, covering the pre-, intra- and postoperative periods and divided in the literature of recent years into non-alterable risk factors and alterable risk factors [2].

Potential non-changeable risk factors identified in the present study were: net predominance of elderly patients (82.14% patients over 60 years) of male sex (21 males vs. 7 females), body mass index (morbid obesity 17.85%), 64.28% ASA 3 score, malnutrition (21.42%), comorbidities (96.42%, cardiovascular 67.75%, renal 25%), emergency surgery (28.57%), anaemia and preoperative blood transfusions (21.42%), tumour topography and anastomotic height (14 rectal tumours, 6 left colon tumours, 20 colorectal anastomoses, of which 14 low) (Tables 2,3).

Potential risk factors that can be modified include:

-preoperative: mechanical colon preparation and neoadjuvant radio-chemotherapy;

-intraoperatively: open vs. laparoscopic surgery, manual vs. mechanical suturing, prophylactic anastomotic drainage and temporary diversion stomas;

-postoperatively: nasogastric decompression tube and early enteral nutrition.

Mechanical colon preparation promoted as a method to prevent infectious complications and AL routinely practiced for nearly a century has raised many questions in recent decades, with numerous studies comparing the potential protection of the method with the inconvenience to the patient and the side effects of dehydration, hydroelectrolyte imbalances and inflammation.

Thus, the French GRECCAR III multicentre randomized trial found no significant differences in AL incidence and morbidity rates between patients with and without mechanical preparation, and the Cochrane systematic review of 4633 patients found no significant differences in mortality, reoperation rates, wound infection and extra-abdominal infectious or non-infectious complications [15-17].

Preoperative colon preparation in our study was complex, which in addition to mechanical preparation with Fortrans® included chemical preparation (1 dose of 2nd generation cephalosporins administered 30min before anesthetic induction and repeated postoperatively if the procedure lasted more than 3h) and thromboembolism prophylaxis with LMWH at least 12h before surgery. This preparation was performed only in electively operated patients targeted only electively operated colorectal cancer patients and the anastomotic AL rate of 8.88% recorded by us

cannot be compared with any other type of preparation or lack of it, as this was the attitude in our clinic throughout the duration included in the study.

Neoadjuvant radiotherapy is almost unanimously accepted as one of the important risk factors in the development of AL due to its negative impact on inflamed tissues by decreasing blood flow at the anastomosis and its toxic effect on the rectal mucosa [18,19].

Down-staging and decreasing tumor size making resection easier and allowing excision of even initially unresectable tumors with increased R0 resection rates [20-22] were the main arguments that led us to include neoadjuvant radio-chemotherapy in the standard rectal cancer protocol in electively operated patients (104), in whom we recorded 14 AL (13.46%).

Laparoscopic surgery tends today to become the surgery of choice for colorectal cancer, both for simple and complex forms due to its known advantages: reduced morbidity, rapid resumption of oral feeding, shorter hospital stay and lower costs. With these caveats, the Cochrane study comparing laparoscopic to conventional resection found no significant differences in disease-free interval, tumour recurrence, morbidity and mortality, including AL rate [24-25].

We performed laparoscopic anterior rectal resection in 22 cases (21.15%) with an AL rate of 36.36% (8 AL), compared to classical surgery 82 cases (79.85%) with an AL rate of 24.39% (20 cases), with the note that the data refer only to rectal and sigmoid cancer surgery, for the other topographic forms the number of laparoscopic operations is too small to make a real comparison.

Regarding mechanical vs. manual suturing, the literature does not clearly show the superiority of mechanical suturing in terms of AL rate, which is also revealed by our study, in which the incidence of AL was approximately equal for the two types of suturing (10 mechanical vs. 11 manual suturing) [25,26].

However, mechanical suture is preferred by most authors due to lower complication rate and shorter operative time [27].

Prophylactic drainage of the anastomosis to prevent abscess formation and early identification of bleeding and infectious processes by the bloody, purulent or fecaloid character of the drained fluids has on the other hand a number of disadvantages: it increases fluid production (ascites), offers the possibility of contamination of the peritoneum with germs from outside, causes foreign body reaction and may cause mechanical erosion of the anastomosis. We used systematic perianastomotic drainage, but like other authors [28] we could not identify any relationship between the incidence of AL and the presence or absence of drainage.

Temporary diversion stomas have been introduced as a way of protecting the anastomosis by keeping it out of fecal transit with the aim of reducing the incidence of clinically overt colorectal AL and decreasing the severity of reinterventions [17,29,30].

However, diversion stomas are characterized by high morbidity, patient inconvenience and increased hospitalization costs, and in addition, difficulties in their care can lead to patient isolation and deterioration of quality of life [31,32].

Therefore, many authors recommend the use of diversion stomas only in cases with increased risk of AL: LAR, poor general condition, neoadjuvant radiochemotherapy, intraoperative technical difficulties or prolonged operative time [33,34].

Cochrane systematic review on 648 patients showed superiority of diversion stomas in terms of clinically manifest AL and reoperation rate, but no significant difference in overall mortality.

In our study, on 74 LARs of which 47 with protective ileostomy and 27 without, we recorded 17 AL (22.97%) with 11 AL (23.40%) in the ileostomy group, respectively 6 (22.22%) in the group without ileostomy and a mortality rate of 0 in patients with ileostomy and 7.40% in those without.

The positive diagnosis of anastomotic fistula is usually not problematic, being clinically established in most cases, the sign of certainty being the appearance of purulent discharge or intestinal contents through the wound, on the drainage tubes or both [36,37,39].

However, the diagnosis is not obvious from the beginning in some patients or very difficult to establish in others [38] on the one hand due to the fact that many of the clinical signs associated with AL are non-specific to them, and on the other hand temporary diversion stomas associated with sphincter-preserving rectal resections may mask the true extent and severity of AL [12].

There are, however, a number of premonitory signs that may raise suspicion of fistula and are encountered during the pre-fistula stage (Table 4) [36,37,39,40]:

-Localized then generalized pain,

 10.12865/CHSJ.49.03.05

-Unfavorable, persistent clinical course,

-Unexplained signs of sepsis (fever, chills, hyperleukocytosis, asthenia, fatigability, altered general condition, etc.) that may progress to septic shock,

-Cellulitis, with the formation of an abscess in the wound, after evacuation of which the intestinal contents are externalized through the wound,

-Peritoneal syndrome with abdominal pain, defense or abdominal rigidity, initially localized, then generalized,

-Occlusive/subocclusive syndrome: prolonged postoperative ileus with significant meteorism, increased volume of digestive aspiration or need for re-installation

In general, the diagnosis of AL is established in the first 2 weeks postoperatively, on average between the 5th and 8th postoperative day, the onset being a particularly important element in assessing the severity and establishing the management of AL, depending on which, AL can be early or late, each with different etiopathogenic characters and therapeutic options. Early leakage usually attributed to technical errors (poor vascularization of anastomotic ends, anastomoses in tension, etc.), associated with postoperative peritonitis, early reoperations and increased mortality. Late AL, due to tissue fragility mainly due to pre-existing risk factors: obesity, malnutrition, immunosuppressants, neoadjuvant radiotherapy, with insidious onset with subfebrile, prolonged ileus and other non-specific signs that can be attributed to other postoperative infectious complications; they represent 1/3 of all AL and up to 60% of them respond to conservative treatment. [1,4,42,43].

In our study group, the proportion of the two types of fistulae was equal (14 cases each).

Computed tomography is today the standard of medical imaging for diagnosis, evaluation of morphological features of the fistula and choice of therapeutic management; rated with specificity of 84% and sensitivity of 68-71%, associated or not with enema with water-soluble contrast agent can show the following signs indicating the existence of AL: extravasation of contrast agent, perianastomotic fluid levels and presence of fluid and perianastomotic inflammatory infiltrate. [4,12,44-47].

Computed tomography allowed us to identify localized fluid collections in 7 cases (1 left parieto-colic, 1 left subphrenic, 1 right parieto-colic, 1 right subphrenic and 1 pelvic) and irigography with water-soluble contrast identified fistula in 5 cases by externalizing the contrast substance perianastomotic and/or on the drainage tube.

Evaluation of the morphological characters of the leakage showed us: all fistulas were postoperative external fistulas, simple (direct tract) in 18 cases and complex (multiple tracts, open in a collection drained to the outside through the drain tube or through the wound, fistula in the eviscerated) 10 cases, with colorectal anastomosis as source in 19 cases, ileo-transverse anastomosis in 5 cases, respectively transverse-sigmoid, ileo-rectal, colo-colic and entero-enteric anastomosis in 1 case, with exteriorisation at the drain tube in 6 cases, through a wound in 13 cases and both in 9 cases: effluent content was intestinal in 8 cases, fecaloid in 9 cases and initially pus then transformed to fecaloid content in 11 cases, and the fistula flow rate was low (<200ml/24 hours) in 19 cases, medium (200-500ml/24 hours) in 7 cases and high (<500ml/24 hours) in 2 cases.

With a wide range of therapeutic methods, medical-conservative and/or surgical, the primary goal of AL treatment is to close the fistula and restore digestive transit, with minimal morbidity and mortality and to correct metabolic and nutritional deficits, with the intention of restoring the patient's independence and tolerance for oral feeding [48,50].

The fundamental principles of initial care of anastomotic fistulae stated by Chapman in 1964 have been supplemented over time with new techniques and principles of care, so that today there is a consensus on the main stages that make up the algorithm of postoperative anastomotic fistula management, each stage with well established goals and priorities: leakage identification, patient stabilization (resuscitation), sepsis control, effluent control and skin protection, nutritional support and definitive (surgical) treatment [48-52].

The management of AL after colorectal surgery must take into account the clinical course of the patient, since there is a wide range of clinical and evolutionary forms, from asymptomatic to life-threatening, requiring emergency re-intervention. In this regard, the International Study Group of Rectal Cancer has proposed a three-grade classification of AL according to clinical course and severity as a guideline for the choice of therapeutic options [12,53]:

-Grade A-diagnosed radiologically (identification of a fluid collection or extravasation of the contrast agent) or clinically

(appearance of intestinal contents on the tube or through the fistula, without other clinical manifestations), in which the therapeutic attitude is conservative treatment and follow-up of the evolution.

-Grade B-requiring modification of treatment but not necessarily re-intervention, with antibiotic therapy and percutaneous drainage of the collection being the main therapeutic interventions.

-Grade C-requiring relaparotomy to control major life-threatening sepsis.

18 (64.28%) of our cases were grade B leakages and 10 (25.72%) grade C leakages; we had no grade A fistulas identified only radiologically clinically asymptomatic.

Conservative medical treatment was the first-line treatment in all our cases, following the standard therapeutic algorithm, adapted to the specific features of AL after colorectal surgery:

-The majority (92.85%) being low (19 cases) or medium (7 cases) output flow in which hypovolaemia, dehydration and hydroelectrolyte imbalances at onset are attributed to sepsis (septic shock) rather than fluid and electrolyte loss through the fistula, so resuscitation must be carried out concurrently with sepsis control. For volemic and hydroelectrolytic rebalancing we used saline administered as an intravenous infusion according to the balance initially every 4 hours, then daily. 12 cases required admission to the ICU for 2 days on average (limits 2-22 days). 7 cases with severe anaemia required blood transfusion.

-Sepsis control consisted of antibiotic therapy and drainage of collections; broad-spectrum antibiotics covering the full range of gram-negative and anaerobic germs were used in all cases (10) where local and general signs of sepsis were present. We have no experience with CT-guided percutaneous drainage of collections, all 5 CT-identified collections were drained by relaparotomy.

-Effluent control was achieved by total cessation of intake in 2 cases and partial abatement in 14 cases. In the other 12 cases, the low flow of the fistula did not require special measures to control the inflow. Antacid medication (histamine receptor blockers) was used in 20 cases, less for reducing fistula flow than for its beneficial effect in decreasing gastric acidity and secretion and thus the corrosive action of the effluent on the tegument, preventing gastritis and stress ulcers [40,48,54-56]. Somatostatin was used in only one case.

-Nutrient intake was provided by mixed nutrition in 26 cases, except in 2 cases where total parenteral nutrition was used in conjunction with total withdrawal of nutrition.

-The protection of the skin, a priority objective in high output leakages, in AL after colorectal surgery has some particularities related to the characteristics of the effluent; of semi-liquid or pasty consistency, with low or absent proteolytic enzyme concentration, it is much less irritating to the skin. The skin lesions were erythematous in 12 cases, and ulcerative in one case, the rest being free of the disease. Absorbent dressings were used, on average 1-2/day, and for skin protection sprays were used in 5 cases and zinc oxide creams/pastes in 12 cases and collecting bags in 6 cases; simple elastic balloon compression/contention (6 cases) or associated with intermittent suction drainage (3 cases) was used in eviscerating or superficial short-tract fistulas.

10 cases required re-intervention, with a re-intervention rate of 35,.71% similar to literature data [30].

All re-interventions were performed more than 7 days after primary surgery, the main indications for re-intervention being unfavorable evolution under conservative treatment with increased fistula flow, clinically detected and CT confirmed intra-abdominal fluid collections and generalized peritonitis. Intraoperative lesional assessment showed purulent collections in 4 cases and anastomosis dehiscence in 6 cases, and the type of reintervention was evacuation, toileting and drainage of the abscess in 4 cases, anastomosis dissection and terminal left-side colostomy (3 cases) and terminal ileostomy (1 case), entero-enteroanastomosis (1 case) and ileo-sigmoidoanastomosis (1 case) (Table 5)

Fistula closure rate was 78.57% (22 cases) of which 15 (46.42%) cases closed after conservative treatment only and 7 (25.0%) cases closed after re-intervention.

The morbidity rate recorded by us was 64, 28%, close to that reported by Kube et al (62.7%) [57]; complications recorded in our study were general complications 8 cases (sepsis 2, cachexia 2, upper/lower gastrointestinal hemorrhage with hemorrhagic shock 2, COVID infection 1 and bilateral pleurisy 1).

There were 6 deaths, with an overall mortality rate of 21, 42% comparable to the literature between 2.8 and 30% [1]; 3 of the 6 deaths were after conservative treatment (mortality 16.66%) and 3 after reintervention (mortality 30.0%), the causes of death were MODS (multiple organic dysfunction) 3 cases, respectively sepsis, COVID infection and bilateral pleurisy with acute respiratory failure 1 case.

The average number of days spent in hospital was 35.35 days, ranging from 12 to 122 days.

10.12865/CHSJ.49.03.05

Conclusions

Our retrospective study upon a series of cases of anastomotic dehiscence and leakage after colorectal cancer elective surgery, by laparoscopic or open approach identified as the most important risk factors advanced age, presence of 2 or more co-morbidities, male sex, rectal surgery, neoadjuvant chemoradiation. Diagnosis of the leakage was made by a combination of clinical observation and imagery with iv and enema contrast enhanced CT. Medical conservative treatment was the ground treatment, reoperation was mandated by incontrollable sepsis and ODS. Mortality after reintervention was almost double compared with the conservative treatment.

Conflict of interests

None to declare.

References

1. Chiarella MM, Fransvea P, Variati M, Adms NJ, Bianchi V, Brisinda G. Anastomotic leakage in colorectal cancer surgery. Surg Oncol, 2022, 40:101708.
2. Wallace B, Schuepbach F, Gaukel S, Marwan AI, Staerkle RF, Vuille-dit-Bille RN. Evidence according to Cochrane Systematic Reviews on Alterable Risk Factors for Anastomotic Leakage in Colorectal Surgery. Gastroenterol Res Prac, 2020, 2020:9057963.
3. Oki E, Ando K, Saeki H, Nakashima Y, Kimura Y, Hiyoshi Y, Imamura Y, Ohgaki K, Ito S, Morita M, Ikeda T, Maehara Y. The Use of a Circular Side Stapling Technique in Laparoscopic Low Anterior Resection for Rectal Cancer: Experience of 30 Serial Cases. Int Surg, 2015, 100(6):979-83.
4. Yuan-Yao Tsai, William Tzu-Liang Chen. Management of anastomotic leakage after rectal surgery: a review article. J Gastrointest Oncol, 2019, 10(6):1229-1237.
5. Paun BC, Cassie S, MacLean AR, Dixon E, Buie WD. Postoperative complications following surgery for rectal cancer. Ann Surg, 2010, 251(5):807-818.
6. Turrentine FE, Denlinger CE, Simpson VB, et al. Morbidity, mortality, cost, and survival estimates of gastrointestinal anastomotic leaks. J Am Coll Surg, 2015, 220(2):195-206.
7. Lindgren R, Hallböök O, Rutegård J, Sjödahl R, Matthiessen P. What is the risk for a permanent stoma after low anterior resection of the rectum for cancer? A six-year follow-up of a multicenter trial. Dis Colon Rectum, 2011, 54(1):41-47.
8. Nesbakken A, Nygaard K, Lunde OC. Outcome and late functional results after anastomotic leakage following mesorectal excision for rectal cancer. Br J Surg, 2001, 88(3):400-404.
9. McArdle CS, McMillan DC, Hole DJ. Impact of anastomotic leakage on long-term survival of patients undergoing curative resection for colorectal cancer. Br J Surg, 2005, 92(9):1150-1154.
10. Mirnezami A, Mirnezami R, Chandrakumaran K, Sasapu K, Sagar P, Finan P. Increased local recurrence and reduced survival from colorectal cancer following anastomotic leak: systematic review and meta-analysis. Ann Surg, 2011, 253(5):890-899.
11. Moghadamyeghaneh Z, Hanna MH, Alizadeh RF, et al. Contemporary management of anastomotic leak after colon surgery: assessing the need for reoperation. Am J Surg, 2016, 211(6):1005-1013.
12. Thomas MS, Margolin DA. Management of Colorectal Anastomotic Leak. Clin Colon Rectal Surg, 2016, 29(2):138-44.
13. Kingham TP, Pachter HL. Colonic anastomotic leak: risk factors, diagnosis, and treatment. J Am Coll Surg, 2009, 208(2):269-278.
14. Boccola MA, Buettner PG, Rozen WM, et al. Risk factors and outcomes for anastomotic leakage in colorectal surgery: a single-institution analysis of 1576 patients. World J Surg, 2011, 35(1):186-195.
15. Jung B, Påhlman L, Nyström PO, Nilsson E; Mechanical Bowel Preparation Study Group. Multicentre randomized clinical trial of mechanical bowel preparation in elective colonic resection. Br J Surg, 2007, 94(6):689-695.
16. Bretagnol F, Panis Y, Rullier E, et al. Rectal cancer surgery with or without bowel preparation: The French GRECCAR III multicenter single-blinded randomized trial. Ann Surg, 2010, 252(5):863-868.
17. Güenaga KF, Matos D, Wille-Jørgensen P. Mechanical bowel preparation for elective colorectal surgery. Cochrane Database Syst Rev, 2011, 7;2011(9):CD001544.
18. Buchs NC, Gervaz P, Secic M, Bucher P, Mugnier-Konrad B, Morel P. Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. Int J Colorectal Dis, 2008, 23(3):265-270.
19. Phillips BR, Harris LJ, Maxwell PJ, Isenberg GA, Goldstein SD. Anastomotic leak rate after low anterior resection for rectal cancer after chemoradiation therapy. Am Surg, 2010, 76(8):869-871.
20. Glimelius B. Radiotherapy in rectal cancer. British Medical Bulletin, 2002, 64(1):141-157.
21. Minsky BD, Cohen AM, Enker WE, et al. Preoperative 5-FU, low-dose leucovorin, and radiation therapy for locally advanced and unresectable rectal cancer. Int J Radiat Oncol Biol Phys, 1997, 37(2):289-295.
22. Nagtegaal ID, Marijnen CA, Kranenbarg EK, et al. Circumferential margin involvement is still an important predictor of local recurrence in rectal carcinoma: not one millimeter but two millimeters is the limit. Am J Surg Pathol, 2002, 26(3):350-357.
23. Kapiteijn E, Marijnen CA, Nagtegaal ID, et al. Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. N Engl J Med, 2001, 345(9):638-646.
24. Vennix, S., Pelzers, L., Bouvy, N., Beets, G. L., Pierie, J-P., Wiggers, T., Breukink, S. Laparoscopic versus open total mesorectal excision for rectal cancer. Cochrane Database of Systematic Reviews, 2014, 4:CD005200.

25. Abraha I, Binda GA, Montedori A, Arezzo A, Cirocchi R. Laparoscopic versus open resection for sigmoid diverticulitis. Cochrane Database Syst Rev, 2017, 11(11):CD009277.
26. 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.
27. 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.
28. Korolija D. The current evidence on stapled versus hand-sewn anastomoses in the digestive tract. Minim Invasive Ther Allied Technol, 2008, 17(3):151-154.
29. Jesus EC, Karliczek A, Matos D, Castro AA, Atallah AN. Prophylactic anastomotic drainage for colorectal surgery. Cochrane Database Syst Rev, 2004, (4):CD002100.
30. Matthiessen P, Hallböök O, Rutegård J, Simert G, Sjödahl R. Defunctioning stoma reduces symptomatic anastomotic leakage after low anterior resection of the rectum for cancer: a randomized multicenter trial. Ann Surg, 2007, 246(2):207-214.
31. Marusch F, Koch A, Schmidt U, et al. Value of a protective stoma in low anterior resections for rectal cancer. Dis Colon Rectum, 2002, 45(9):1164-1171.
32. Edwards DP, Leppington-Clarke A, Sexton R, Heald RJ, Moran BJ. Stoma-related complications are more frequent after transverse colostomy than loop ileostomy: a prospective randomized clinical trial. Br J Surg, 2001, 88(3):360-363.
33. Gooszen AW, Geelkerken RH, Hermans J, Lagaay MB, Gooszen HG. Temporary decompression after colorectal surgery: randomized comparison of loop ileostomy and loop colostomy. Br J Surg, 1998, 85(1):76-79.
34. Wong NY, Eu KW. A defunctioning ileostomy does not prevent clinical anastomotic leak after a low anterior resection: a prospective, comparative study. Dis Colon Rectum, 2005, 48(11):2076-2079.
35. Laxamana A, Solomon MJ, Cohen Z, Feinberg SM, Stern HS, McLeod RS. Long-term results of anterior resection using the double-stapling technique. Dis Colon Rectum, 1995, 38:1246-1250.
36. Galie KL, Whitlow CB. Postoperative enterocutaneous fistula: when to reoperate and how to succeed. Clin Colon Rectal Surg, 2006, 19(4):237-246.
37. Falconi M, Pederzoli P. The relevance of gastrointestinal fistulae in clinical practice: a review. Gut, 2001, 49 Suppl 4(Suppl 4):iv2-iv10.
38. Filho IA, Rego ACM, Pinheiro FI. Digestive fistulas: The challenge continues. Transl Biomed, 2016, 7:2.
39. Tuma F, Crespi Z, Wolff CJ, Daniel DT, Nassar AK. Enterocutaneous Fistula: A Simplified Clinical Approach. Cureus, 2020,12(4):e7789.
40. Dumas RP, Moore SA, Sims CA. Enterocutaneous Fistula: Evidencebased Management. Clin Surg, 2017, 2:1435.
41. Hoedema RE, Suryadevara S. Enterostomal therapy and wound care of the enterocutaneous fistula patient. Clin Colon Rectal Surg, 2010, 23(3):161-168.
42. Morks AN, Ploeg RJ, Sijbrand Hofker H, Wiggers T, Havenga K. Late anastomotic leakage in colorectal surgery: a significant problem. Colorectal Dis, 2013, 15(5):271-275.
43. Li YW, Lian P, Huang B, Zheng HT, Wang MH, Gu WL, Li XX, Xu Y, Cai SJ. Very Early Colorectal Anastomotic Leakage within 5 Post-operative Days: a More Severe Subtype Needs Relaparatomy. Sci Rep, 2017, 13;7:39936.
44. Kornmann VN, Treskes N, Hoonhout LH, Bollen TL, van Ramshorst B, Boerma D. Systematic review on the value of CT scanning in the diagnosis of anastomotic leakage after colorectal surgery. Int J Colorectal Dis, 2013, 28(4):437-445.
45. Kauv P, Benadjaoud S, Curis E, Boulay-Coletta I, Loriau J, Zins M. Anastomotic leakage after colorectal surgery: diagnostic accuracy of CT. Eur Radiol, 2015, 25(12):3543-3551.
46. Huiberts AA, Dijksman LM, Boer SA, Krul EJ, Peringa J, Donkervoort SC. Contrast medium at the site of the anastomosis is crucial in detecting anastomotic leakage with CT imaging after colorectal surgery. Int J Colorectal Dis, 2015, 30(6):843-848.
47. Nicksa GA, Dring RV, Johnson KH, Sardella WV, Vignati PV, Cohen JL. Anastomotic leaks: what is the best diagnostic imaging study? Dis Colon Rectum, 2007, 50(2):197-203.
48. Weledji EP. Perspective on enterocutaneous fistula: a review article. Medical and Clinical Reviews, 2017, 3(25):1-7.
49. Evenson AR, Fischer JE. Current management of enterocutaneous fistula. J Gastrointest Surg, 2006, 10(3):455-464.
50. Lloyd DA, Gabe SM, Windsor AC. Nutrition and management of enterocutaneous fistula. Br J Surg, 2006, 93(9):1045-1055.
51. Heimroth J, Chen E, Sutton E. Management Approach for Enterocutaneous Fistula. The American Surgeon, 2018, 84:326-333.
52. Gribovskaja-Rupp I, Melton GB. Enterocutaneous Fistula: Proven Strategies and Updates. Clin Colon Rectal Surg, 2016, 29(2):130-7.
53. den Dulk M, Noter SL, Hendriks ER, et al. Improved diagnosis and treatment of anastomotic leakage after colorectal surgery. Eur J Surg Oncol, 2009, 35(4):420-426.
54. Haack CI, Galloway JR, Srinivasan J: „Enterocutaneous Fistulas: A Look at Causes and Management". Curr. Surg. Rep, 2014, 2:71
55. Draus JM Jr, Huss SA, Harty NJ, Cheadle WG, Larson GM. Enterocutaneous fistula: are treatments improving? Surgery, 2006, 140(4):570-578.
56. Hwang RF, Schwartz RW. Enterocutaneous fistulas: current diagnosis and management. Curr Surg, 2000, 57(5):443-445.
57. Kube R, Mroczkowski P, Granowski D, et al. Anastomotic leakage after colon cancer surgery: a predictor of significant morbidity and hospital mortality, and diminished tumour-free survival. Eur J Surg Oncol, 2010, 36(2):120-124.

Corresponding Author: Sandu Râmboiu, 1st Surgery Clinic, County Emergency Hospital of Craiova, University of Medicine and Pharmacy of Craiova, 2-4 Petru Rares Street, 200392, Craiova, Dolj, e-mail: sandu_r@yahoo.com

 10.12865/CHSJ.49.03.05