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ORIGINAL ARTICLE

Anastomotic Failure in Colorectal Surgery. Risk Factors and Therapeutic Management

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ABSTRACT
Introduction: *Anastomotic dehiscence (AD) is a complication of colorectal surgery that determines high morbidity and mortality and a worse oncological prognosis. The objective of this study is to analyze its relationship with risk factors and describe its therapeutic management.*
Material and Methods: *Retrospective, observational and analytical study. Colorectal resections with primary anastomosis for malignant neoplastic pathology performed between January 2015 and November 2018 were included.*
Results: *One hundred and twelve patients met the inclusion criteria. The AD rate was 17% and mortality 15%. Tumor size was statistically significantly associated with an increased risk of AF.*
Discussion: *Our results are similar to those reported in the literature, highlighting a high proportion of early AD and therefore of re-intervention and intestinal diversion.*
Conclusions: *The management of AD is a therapeutic challenge, and must be adjusted to many parameters, one of the most important being the surgeon's experience.*

Keywords: *Colorectal Surgery; Anastomotic Dehiscence; Risk factors*

INTRODUCTION

Surgical complications are events inherent to the treatment of some conditions with more or less invasive procedures. The importance of this issue encompasses multiple aspects, including those related to the increase in healthcare costs during the healthcare process.[1]
Colorectal surgery has a morbidity that ranges 10-30%.[2]
Among the different complications, AF (AF) plays a leading role due to its potential severity, being responsible for up to a third of postoperative deaths.[3] In addition, there is evidence that anastomotic dehiscence is also a factor of poor long-term oncological prognosis.[4]

Its global incidence according to the literature ranges 3-6%,[5] although it is highly variable since depends on the type and level of anastomosis,[6] as well as on the multiple definitions and lack of standardization in its diagnosis.[7] Several risk factors have been studied as predictors of complications for colorectal surgery,[8] but above all an attempt has been made to establish which are those that influence the appearance of an AF. The latter include male gender, nutritional status, anemia, tumor size, location below 12 cm from the anal margin, anastomosis below 10 cm, prolonged operative time, intraoperative bleeding, obesity and pelvic radiotherapy.[9-11]

On the other hand, the comprehensive treatment of this complication continues to being challenging, currently having a wide therapeutic arsenal: pharmacological, percutaneous, endoscopic, surgical therapies, or a combination of them. This is where the judgment and experience of the surgeon usually prevail. It is also important to recognize that when evaluating the treatment of a relatively low incidence complication, such as AF, the evidence necessarily arises from retrospective studies of large series of patients, given the difficulty of designing prospective studies for this purpose.[12]

The objective of this study is to determine the role of various risk factors for AF, and to describe its therapeutic management in the studied population.

PATIENTS AND METHODS

This is a multicenter, observational, retrospective and analytical study. All patients who underwent colon and/or rectal resection with primary anastomosis due to malignant neoplasia in the period January 2015- November 2018 at Surgical Clinic 2 (Hospital Maciel) and Canelones Medical Corporation (COMECA) were included were included. Other procedures such as colostomy closure or bowel transit reconstruction were excluded, since in these cases it is not possible to assess some of the risk factors. AF was defined by the presence of clinical (systemic inflammatory response syndrome, peritonitis), imaging (free intraperitoneal fluid, pneumoperitoneum, perianastomotic collection with or without gas) and intraoperative signs (verification of dehiscence at the anastomosis site).

The data were obtained from the medical records of the patients. The following variables were recorded (taking as a cut-off point the time of the collection of data): age

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(years), gender, previous abdominal surgery, renal failure (Creatininemia >1.2 mg/dl), heart failure, tumor location, tumor size (cm), preoperative hypoalbuminemia (<3,5 mg/dl), neoadjuvant treatment, preoperative anemia (Hb <10 mg/dl), laparoscopic or open approach, operative time (minutes), type of anastomosis (handsewn or stapled), height of the anastomosis (intra or extraperitoneal), anastomotic diversion , placement of drains, surgeon´s experience (senior vs. junior), early AF (before the 6th postoperative day) or late AF, therapeutic management and mortality.

Statistical analysis

The quantitative variables are expressed as mean and standard deviation (SD) and the qualitative variables as percentage relative frequency. As it was a retrospective study, the risk of each variable was estimated using Odds Ratio. Those that resulted in an individually significant OR were included in a multivariate model, considering as variables of increased risk those that continued to be so in the multivariate model. The data were processed using SPSS IBM statistical software (version 22.0). A value of p <0.05 is accepted as statistically significant.

Ethical aspects

Patient participation was anonymous. As it was a retrospective study, it did not imply an interference in the patient's care process, nor there was any risk for the study subjects, since they were not exposed to any change in management. The information was processed only by the authors of the research respecting professional secrecy, and each patient was assigned a self-generated number in order to preserve confidentiality. Informed consent was not requested as it was an observational study in which data were used anonymously and for statistical purposes. The work was approved by the hospital ethics committee. The authors declare no conflicts of interest or support from the industry.

RESULTS

A total of 112 patients (56 in each institution that participated in the study) met the inclusion criteria, 49 (43.8%) were female and 63 (56.2%) male, with a mean age of 66. 6± 11,74 (range, 30-89) years. The mean size of the lesions was 4.4 ± 2.51 (range, 0.7-16.1) cm and the mean operative time 160.7±60.94 min (range, 60-390). The approach was laparoscopic in 79.5% of patients and open in 20.5% (Table 1).

The distribution of tumors according to their location was as follows: ascending colon 33.9%, transverse colon 5.4%, splenic flexure 1.8%, descending colon 2.7%, sigmoid colon 22.3% and rectum 33,9% (Figure 1).

According to the experience of the acting surgeon, 59 procedures were performed by a junior surgeon and 53 by a senior surgeon.

The anastomosis was stapled In 68% of cases and intraperitoneal in 80.4%. Anastomotic diversion was performed in 10.7% of patients and drains were used in 46.4%.

Nineteen patients (17%) had an AF. According to the type of anastomosis, the AF distribution was as follows: ileocolic 20% (10/50), intraperitoneal colorectal 10.4% (5/48) and extraperitoneal colorectal 22.2% (4/18). Overall mortality was 15.2%.

The risk of each of these factors for AF, calculated with its 95% confidence interval (CI), is summarized in Table 2. The risk of some of these factors in relation to mortality was also calculated (Table 3). According to the time of presentation and therapeutic management of the AF, in 13 patients the diagnosis was in the early stage (before the 6th day), while in 6 it was in the late stage.

The treatment according to the type of failure was the following:

- Ileocolic AF:[10] anastomotic takedown and ileostomy in 7, antibiotic therapy in 1, percutaneous drainage in 1, and therapeutic abstention in 1 (stage IV).
- Colorectal AF:[9] anastomotic takedown and Hartmann´s procedure in 8, and transgluteal percutaneous drainage in 1.

DISCUSSION

The overall rate of anastomotic dehiscence was 17%, with early presentation in most cases.

The incidence of AF in colorectal surgery is variable, there are studies that report rates of 3 to 28%,[13] while series from high-volume centers report somewhat lower figures, between 1.6 and 9.9%.[14] Taking these data into account, the results of our series are within those indicated in the bibliography, although close to the upper limit usually accepted.

The risk of dehiscence increases the lower the anastomosis is.[6] Although in our series, in accordance with the aforementioned, the highest percentage of failures occurred in extraperitoneal colorectal anastomoses (22.2%), there was a percentage slightly lower of ileocolic anastomosis failure (20%), which may be explained by the low power of the study. However, we must point out some shortcomings in the research that constitute the current source of evidence.

First, the definition of what is considered an "anastomotic leak", which can be extremely variable in terms of the stage of clinical presentation, imaging and/or intraoperative findings, such as the degree or extent of dehiscence at

the suture line, which undoubtedly determines the lack of a standardized definition.[15]

In fact, a systematic review of 97 studies found a total of 56 different definitions for AF,[16] thus clearly demonstrating the scope and complexity of the problem to which we refer. Our study does not exclude from the definition of AF those cases in which the presentation was late, generally in the form of abscess, regardless of the treatment prescribed, knowing that if we did not do so, we would be underestimating the true incidence of this complication. In 2010, the International Study Group of Rectal Cancer, in an attempt to unify diagnostic and therapeutic criteria, defined AF as any defect at the level of the anastomosis (including the suture lines of the rectal reservoirs) that produces a communication between the endoluminal and extraluminal compartments.[17]

Second, the rate of anastomotic dehiscence also varies according to the type of anastomosis considered (ileocolic, colocolic, ileoanal),[18] which invariably tend to coexist in the majority of the studies that investigate the problem, as occurres with ours.

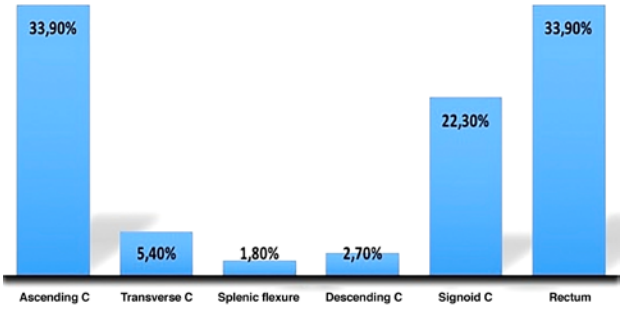
Currently, two patterns of AF are recognized according to the time of presentation: early and late, before and after the 6th postoperative day. Early failures are usually associated with risk factors that translate a difficult procedure, especially at the time of making the anastomosis (intraoperative bleeding, obesity, prolonged operative time),[19] while late failures are associated with various factors related in some way to tissue repair and healing (neoadjuvant therapy, hypoalbuminemia, etc). In our series, most failures occurred at an early stage, and the form of presentation in these cases was acute peritonitis. In contrast, the late presentation was mainly in the form of intra-abdominal abscesses.

However, not all investigations agree in their results when trying to determine the association and/or magnitude of risk factors with AF.[22] Among theserisk factors, the following stand out: male gender, body mass index (BMI), anemia/hypoalbuminemia, neoadjuvant therapy, number of stapled firings, temporary ostomy, prolonged operative time, use of drains, preoperative bowel preparation, anastomosis height less than 10 cm from the anal margin, and the experience of the surgeon/annual volume of the institution.[23-29]

One objective of this study was to analyze the association between some of the risk factors and AF, and also between them and mortality. As can be seen in Tables 2 and 3, only tumor size was statistically significantly associated with the risk of AF (OR 1.018; p = 0.045). Likewise, only splenic flexure location and heart failure were statistically significantly associated with mortality (OR 7.333, 95% CI 1.848-29.107). Despite this, we must take

TABLE 1: DEMOGRAPHIC DATA, TUMOR SIZE, OPERATIVE TIME AND APPROACH

n	112
Female, n (%)	49 (43,8)
Male, n (%)	63 (53,2)
Age (yrs), mean±SD	66,6 ± 11,74
Tumor size (cm), mean±SD	4,4 ± 2,51
Operative time (min), mean±SD	160,7 ± 60,94
Laparoscopic approach	79,50%
Open approach	20,50%



Graphic 1: Distribution of colorectal tumors according to their location.

into account that the small sample size and low power of the study should lead to a careful interpretation of our results. In the same sense, it is to be assumed that the experience factor of the acting surgeon /annual volume of the institution affect the results even more than we have been able to demonstrate in our study. To this must also be added that in the hands of young surgeons who have not completed their learning curve surgery is generally performed in a longer operative time.

Regarding the treatment of AF, as occurs with its definition and scope, the first problem that arises is to standardize its therapeutic management. To this end, multiple attempts have been made, such as those of the aforementioned International Anastomotic Leak Study Group,[18] the International Study Group of Rectal Cancer[30] and the study by Blumetti et al.[31] In any case, the following aspects should be taken into account: timing of presentation (early vs. late), clinical severity, intra/extraperitoneal (with or without diversion for the latter), degree of dehiscence and contamination (free fluid vs. abscess).[32] Furthermore, we believe that should also be considered other key elements such as the experience and judgment of the acting surgeon and the resources available. Septic patients, with a significant degree of abdominal and pelvic contamination, has a formal indication for a diverting ostomy, probably associated with take-down of the anastomosis, since they are not usually good candidates for repair or re-do anastomosis. If we consider

TABLE 2: RISK FACTORS AND ANASTOMOTIC FAILURE

Factor	Odds Ratio (OR)	95% Confidence Interval	p
Gender	0,825	0,319 - 2,137	
Previous surgery	1,280	0,438 - 3,738	
Renal failure	1,059	0,314 - 3,574	
Heart failure	1,952	0,460 - 8,286	
Hypoalbuminemia	0,565	0,150 - 2,127	
Neoadjuvant therapy	1,113	0,122 - 10,162	
Anemia	1,056	0,369 - 3,026	
Operative approach	1,122	0,338 - 3,727	
Anastomosis (handsewn/stapled)	0,722	0,269 - 1,938	
Anastomosis height	1,360	0,428 - 4,228	
Intestinal diversion	0,472	0,057 - 3,913	
Drainage	1,061	0,410 - 2,743	
Age	0,994		0,764
Tumor size	1,018		0,045
Operative time	1,004		0,336
Surgeon experience (junior/senior)	1,590	0,601	4,201
Topography			
Ascending colon	0,226		0,313
Transverse colon	0,200		0,368
Splenic flexure			
Descending colon	0,500		0,711
Sigmoid colon	0,250		0,355
Rectum	0,188		0,259

the moment of presentation, early failures usually require reoperation during the first postoperative week, when the inflammatory adhesions are still lax and allow it with no major inconveniences. However, the late presentation, generally as abscesses, allows a less aggressive management with minimally invasive techniques. In abscesses up to 3-4 cm, antibiotic therapy as the only treatment is feasible[33] and in larger collections percutaneous drainage has also shown good results.[6]

Whether or not the height of the anastomosis and the ostomy in situ is considered, different alternatives arise. Free cavity (intraperitoneal) AF is usually treated by taking down the ileocolic, colocolic, or colorectal anastomosis and performing a proximal-end ostomy, and a distal-end mucous fistula or, alternatively distal-end closure (Hartmann´s procedure). Less frequently, the finding of a small defect generally smaller than 1/3 of the circumference, extrapolating the concepts of colorectal trauma, allows repair associated with proximal diversion.[34] In the case of extraperitoneal AF, if the patient has a diverting ostomy and do not present serious local or systemic signs, he or she can be periodically evaluated by contrast imaging, waiting for spontaneous resolution and take down the ostomy afterwards. If this is not possible, it may be necessary to re-do the anastomosis. The use of sponges connected to the suction system is currently under investigation in order to reduce and close the existence of these "blind sinuses" that persist after failure.[35]

TABLE 3: RISK FACTORS AND MORTALITY

Risk factor	Odds Ratio (OR)	95% Confidence Interval
Gender	1,546	0,528 - 4,526
Previous surgery	0,35	0,074 - 1,647
Renal failure	1,442	0,416 - 5,003
Heart failure	7,333	1,848 - 29,107
Hypoalbuminemia	1,574	0,491 - 5,049
Neoadjuvant therapy	1,113	0,122 - 10,162
Anemia	0,532	0,141 - 2,000
Operative approach	1,261	0,330 - 4,823
Anastomosis (hand-sewn/stapled)	0,637	0,281 - 1,840
Anastomosis height	1,887	0,587 - 6,069
Diverting ostoma	0,472	0,057 - 3,913
Drainage	0,762	0,267 - 2,172
Surgeon experience	0,590	0,207 - 1,683

In our series, stands out the high percentage of patients treated by re-intervention (85.7%), and within this group the large proportion of cases in which taking down the anastomosis was chosen as the definitive procedure (17/18 patients). In principle, this is consistent with the high percentage of early failures observed, where the link with technical problems makes a reoperation more likely in the immediate postoperative period. On the contrary, those

patients with late failures, usually related to ischemia of the intestinal ends or small defects, have a greater chance of obtaining good results through conservative or minimally invasive treatment, as has also been demonstrated in our experience (Figures 1 and 2).

Regarding the tactic used in reoperated patients, taking down the anastomosis as opposed to repairing it is fully justified, since the last technique is very risky and will only lead in most cases to an increase in the defect size.[36]

Regarding the approach almost all reoperations were performed by laparotomy, except for 2 cases in which the Hartmann´s procedure was done by laparoscopy (Fig. 3).

The laparoscopic treatment of this complication remains controversial, since to the aforementioned factors is added the complexity in the management of distended thin loops, increased bleeding, and the need for an exhaustive peritoneal debridement and toilette that is sometimes difficult to carry out in this way.[37,38] Even so, there is also evidence that supports the choice of a laparoscopic approach, based above all on the lower systemic stress and wall aggression.[39,40] In any case, it is to be assumed that as surgeons gain experience in the laparoscopic approach to colorectal surgery, they will also do so in the management of its complications through this approach.

Overall mortality in the series reached 15.2% (17 patients), although in only 7 cases it was a direct consequence of AF. The rest of the cases died from other causes, such as disease progression, bowel obstruction by adhesions, and cardiovascular disease.

Finally, we must point out the main limitations of this study. Some of them are characteristic of its retrospective nature, which makes it impossible to standardize preoperative (bowel preparation) and intraoperative (surgeon's experience, techniques, approach, systematic diversion of low anastomoses) aspects, and determines the loss of data in some cases. Second, and as previously analyzed, the small sample size may be responsible for the absence of statistical significance in the analysis of some of the risk factors studied due to lack of power. This is due to the low caseload of both institutions.

CONCLUSIONS

Anastomotic dehiscence constitutes a therapeutic challenge in colorectal surgery, and its management often falls on the judgment and experience of the surgeon. In our series there was a somewhat high incidence but still within what is accepted according to the literature analyzed. Likewise, a statistically significant risk association was found only for tumor size. The moment of presentation of the AF and the general condition of the patient are those that usually determine the therapeutic possibilities.

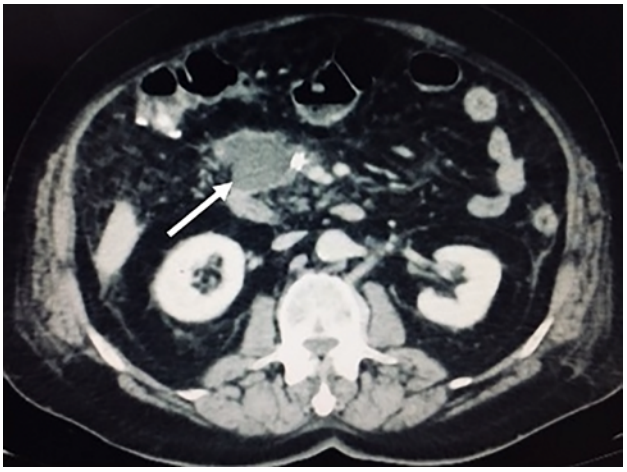


Figure 1: Intraperitoneal abscess (arrow) after laparoscopic right colectomy, conservative management. Source: author.

Figure 2: Pelvic abscess after laparoscopic anterior resection (transgluteal percutaneous drainage). Source: author.

Figure 3: Laparoscopic re-intervention with anastomotic take-down and Hartmann´s procedure. Source: author.

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