

RISK FACTORS FOR ANASTOMOSIS LEAKAGE IN LOWER ANTERIOR RESECTION: OUR EXPERIENCE

FATORES DE RISCO PARA DEISCÊNCIA DA ANASTOMOSE NA RESSECÇÃO ANTERIOR DO RETO: NOSSA EXPERIÊNCIA

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ABSTRACT

Introduction: Anastomotic leakage is a complication of anterior rectum resection, with an incidence up to 20%. Although there's no consensus about risk factors for anastomotic leakage, they can be divided into patient/disease/surgery related. We analyze risk factors in our experience for colorectal anastomosis leakage. **Material and Methods:** Retrospective review of 105 patients with rectal cancer submitted to anterior rectum resection in the General Surgery Department of a tertiary referral center from 1/1/2018 to 31/12/2019. Statistical analysis was performed using the SPSS, version 25.0. **Results:** We found an anastomotic leakage incidence of 10.5%. A statistically significant association between anastomotic leakage and previous abdominal surgery and usage of intraabdominal drain was seen, and a tendency to statically significance with intraoperatively red blood cells transfusion. We didn't found association with age, sex, cardiovascular risk factors, use of NSAIDs, corticoids, radio chemotherapy, open or laparoscopic surgery, surgeon experience, rectum tumor location and time of surgery. **Discussion:** Risk factors for anastomotic leakage vary between different studies but it is consensual that it has a multifactorial cause. As there are preoperative factors that increase the risk of anastomotic leakage, an extensive study of the patient previous to the surgery is mandatory in order to minimize the complications. Unlike current literature, we didn't find any risk factors related to the surgery and the surgeon, and only one risk factor related to the patient (previous abdominal surgery). The association between anastomotic leak and use of pelvic drain is difficult to explain and needs additional studies. **Conclusion:** In our experience previous abdominal surgery is the only risk factor for anastomotic leakage development in anterior rectum resection for rectal cancer

Key words: *Colorectal surgery; rectal neoplasms; anastomotic leak.*

RESUMO

Introdução: A fístula anastomótica é uma complicação da ressecção anterior do reto, com incidência de até 20%. Embora não haja consenso sobre os fatores de risco para a deiscência da anastomose, estes podem estar relacionados com o doente, com a doença, ou com a cirurgia. Analisámos os fatores de risco para a deiscência da anastomose colorretal na nossa série. **Material e Métodos:** Realizámos uma revisão retrospectiva de 105 doentes com cancro retal submetidos a ressecção anterior do reto no Departamento de Cirurgia Geral de um centro terciário de referência no período de 01/01/2018 a 31/12/2019. A análise estatística foi realizada com recurso ao programa SPSS, versão 25.0.



Resultados: Encontramos uma incidência de deiscência da anastomose de 10,5%. Observou-se associação estatisticamente significativa entre deiscência da anastomose e antecedentes de cirurgia abdominal e a necessidade de colocação de dreno intra-abdominal, observámos uma associação sem significância estatística com a transfusão intraoperatória de eritrócitos. Não encontramos associação com a idade, sexo, fatores de risco cardiovascular, uso de AINEs, corticóides, radioquimioterapia, cirurgia aberta ou laparoscópica, experiência do cirurgião, localização do tumor de reto e a duração da cirurgia. **Discussão:** Os fatores de risco para fístula anastomótica variam entre os diferentes estudos, mas é consensual que tem uma causa multifatorial. Como existem fatores pré-operatórios que claramente aumentam o risco de deiscência da anastomose, é mandatório o estudo das morbidades do doente antes da cirurgia, a fim de as mitigar e minimizar as complicações. Ao contrário da literatura, não encontramos nenhum fator de risco relacionado com a técnica cirúrgica e com o cirurgião, apenas a história de cirurgia abdominal prévia revelou uma associação estatisticamente significativa. A associação entre a deiscência da anastomose e uso de dreno pélvico é difícil de explicar e necessita, por esse motivo de estudos adicionais. **Conclusão:** Na nossa série, a cirurgia abdominal prévia foi o único fator de risco para o desenvolvimento de deiscência da anastomose na ressecção anterior do reto por cancro do reto.

Palavras-Chave: *cirurgia colorretal; neoplasias retais; deiscência da anastomose.*

INTRODUCTION

The standard treatment with curative intent in rectal cancer is the anterior resection of the rectum (ARR)^{1,2}. In this surgery, an anastomosis is made after the tumor is removed, most commonly a terminoterminal colorectal anastomosis, in order to reconstruct the intestinal transit. Anastomotic leakage (AL) is a serious complication of anterior rectum resection, having an incidence of up to 20%, and one of the most life threatening, with a mortality between 6-22%.^{3,4}

Although there's no consensus in the literature about the risk factors for AL, they can be divided into patient/disease related and surgery related.³

Several studies have found that men undergoing rectal resection have a higher AL probability due to other risk factors patient-related include malnutrition, immunosuppression, diabetes, nonsteroidal anti-inflammatory drug (NSAID) use and preoperative chemoradiation therapy.⁵

The main causes for surgery related failure are insufficient blood supply at the proximal or distal ends of the anastomosis, tension on anastomosis and insufficient integrity of anastomosis.⁶ Also, the location of the anastomosis highly relates with AL, being the higher the anastomosis, the lesser the risk

of AL, with resection of a distal rectal cancer having almost a five-fold increased risk of anastomotic leak compared with resection for colon cancer.⁵ AL also increases mortality rates, health care costs and local recurrence during long term follow up.⁷

Therefore, it is of uttermost relevance to study the risk factors in order to correct them, if possible, and to score the patients based on the risk of having complications.

The aim of this study was to determine risk factors for post-operative anastomosis leaks in our academical tertiary center.

METHODS

Retrospective medical record review of patients with rectal cancer that were submitted to an anterior rectum resection in the general surgery department of a Portuguese tertiary referral center, from 1st January 2018 to 31st December 2019.

From a total of 122 patients, we excluded 17 patients of other primary disease rather than neoplasm or incomplete medical records. The remaining 105 patients were included for retrospective analysis.

Al is defined as a defect at the anastomotic site leading to a communication between intraluminal



and extraluminal compartments⁸. Demographic data relative to the patients and variables related to the surgery and tumor were also analyzed. Related to the tumor localization, we considered low rectum at less than 5cm from the anal margin, medium from 5-10cm and high >10cm.

Related to the surgical experience, we considered experienced surgeon the ones that had at least 10 years as colorectal surgeons.

The option between open surgery /laparoscopic surgery and the use of prophylactic pelvic drainage is it depends on the surgeon's individual option.

Statistical analysis was performed using the Statistical Package for the social Sciences (SPSS, version 25.0 for windows / MacOS) program. Continuous variables with normal distribution were expressed through the mean and standard deviation and the rest by median and interquartile amplitude. The categorical variables were described by frequency

and percentage. Patients were categorized with the presence or absence of anastomosis dehiscence. The Chi-square test and Fisher's exact test were used to assess the statistical association between categorical variables and the presence of dehiscence. The continuous variables were evaluated with the t-test of independent samples or Mann-Whitney U test according to the normality of the distribution. The normality of the distribution of variables was assessed using the Kolmogorov-Smirnov test or skewness and kurtosis. The level of statistical significance adopted was $p < 0.005$.

RESULTS

In this study, the AL incidence is 10.5%.

Relative to patients related variables (table 1) 60% of the patients were men, the mean age was

TABLE 1 – Characteristics related to the patients

	All (n = 105)	With leakage (n = 11)	Without (n = 94)	p value
Age (years) – mean±SD	67.3 ± 13.36	70.1 ± 10.8	67.0 ± 13.0	0.472
Sex – n (%)				0.193
Men	63 (60)	9	54	
Women	42 (40)	2	40	
Cardiovascular Risk Factors – n (%)				0.751
With	57 (54.3)	7	50	
Without	48 (45.7)	4	44	
Previous abdominal Surgery – n (%)				0.046
With	23 (21.9)	6	18	
Without	82 (78.1)	5	76	
NSAIDs* – n (%)				0.787
With	14 (13.3)	1	13	
Without	90 (86.5)	10	80	
Corticoids* – n (%)				
With	7 (6.8)	0	7	
Without	96 (93.2)	11	85	
Hemoglobin (g/dL)* – median (IQR)	13.2 (2.2)	12.2 (4.7)	13.2 (2.1)	0.142
Chemotherapy – n (%)				
With	25 (23.8)	4	21	0.288
Without	80 (76.2)	7	73	
Radiotherapy- n (%)				
With	20 (19)	4	16	0.215
Without	85 (81)	7	78	

Footnote: IQR – Interquartile Range. SD – Standard deviation. * 1 missing values for NSAIDs; 2 missing value for corticoids; * 14 missing values for hemoglobin.



67,33 +- 13,36 years. It was not seen any association between sex and AL and neither between age and AL.

54,3% had at least one cardiovascular risk factor (Diabetes mellitus and/or Hypertension and/or Dyslipidemia). However, we didn't found any association with cardiovascular risk factors neither with preoperative use of NSAIDs, corticoids or radiochemotherapy.

Moreover, 21,9% of the patients had previous abdominal surgery. We found a statistically significant association between previous abdominal surgery and AL development ($p=0,046$), meaning that patients with previous abdominal surgery have

higher risk of developing AL.

Median preoperative hemoglobin value was 13,2 g/dL with an interquartile range of 2,2 g/dL. There was no statistically significant difference in median hemoglobin value between the group with AL and the group without.

Relative to surgical /tumor variables (table 2) 38.2% of surgeries were performed by experienced surgeons. 59,6% were performed laparoscopically and 40,4% were open surgery; In addition, 58,4% of the tumors were considered low/medium rectum and 41,6% were high, 41,3% had terminolateral (TL) anastomosis and 58,7% had a terminoterminal (TT)

TABLE 2 – Characteristics related to the surgery

	All (n = 105)	With leakage (n = 11)	Without (n = 94)	p value
Surgery* - n (%)				0.517
Laparoscopic	59 (59.6)	8	51	
Open	40 (40.4)	3	37	
Surgical experience -				0.602
> = 10 years	39 (38.2)	5	34	
< 10 years	63 (61.8)	6	57	
Tumor localization*- n (%)				0.180
Low/Medium	45 (58.4)	8	37	
High	32 (41.6)	2	30	
Type of anastomosis* - n (%)				0.342
Termino-terminal (TT)	54 (58.7)	5	49	
Termino-lateral (TL)	38 (41.3)	6	32	
Anastomosis Test - n (%)				
Yes	93 (88.6)	11	82	
No	12 (11.4)	0	12	
Surgery Time (hours) - mean±SD	3.4 +- 1.0	3.5+- 1.0	3.5+-0.9	0.714
Hospital Stay (days) - median (IQR)	6 (3)	9 (9)	6 (2)	0.04
Drain- n (%)				0.025
Yes	42 (40)	8	34	
No	63 (60)	3	60	
Protective ileostomy* - n (%)				0.969
Yes	54 (54)	6	48	
No	46 (46)	5	41	
Transfusion* - n (%)				0.061
Yes	4 (4.1)	2	2	
No	94 (95.9)	9	85	

Footnote: IQR – Interquartile Range. SD – Standard deviation. *6 missing values for Surgery; 28 missing values for Local of cancer; 13 missing values for Type of anastomosis; 5 missing values for ostomy; 7 missing values for transfusion.



anastomosis. The surgical experience, the approach used to perform the surgery, the local of the tumor and the kind of anastomosis used had no statistically significant association with AL.

In 40% of surgeries, an intraabdominal drain was used. We found a statistically significant association between the use of intrabdominal drains and AL ($p=0,025$), possibly because drains were used in the most difficult and challenging surgeries.

Therewithal, the mean surgical time was 3,4+/-1,0 hours. 3,4 +/-1,1h in the group without AL and 3,5+/-0,9 h in the group with AL – There was no relevant difference between this groups.

The median hospital stay was 6 vs 9 days, having the group with AL a statistically longer length of stay ($p=0,004$). (Table 2)

DISCUSSION

AL is a severe complication that colorectal surgeons face during his career when doing an oncologic anterior rectal resection. AL is a life threatening complication and, even if it is managed properly, it can result in prolonged hospital stay, increased costs, dead or poor oncologic outcomes. This complication has been studied since decades ago but it hasn't had any significant reduction of the incidence in the last years.⁴

Risk factors for AL vary between different studies but it is consensual by most that it has a multifactorial cause, possibly with some unknown risk factors.⁸

It is described that patient-related factors increasing AL include: male sex (may present technical difficulties due to their narrow pelvises¹⁰), which can be as 13,2 times higher, age > 70years, previous abdominal surgery, steroid use and cardiovascular risk factors.^{9,10,11} In our study, we didn't find any association with sex, age, cardiovascular risk factors or preoperative use of NSAIDs, corticoids or radiochemotherapy. We found a relation between AL and previous abdominal surgery which can reflect technical difficulties.

Anemia is another preoperative potent risk factor for AL^{12,13,14,15} and the literature recommends a preoperative hemoglobin >8 g/dL before surgery. [6] In our study, median preoperative hemoglobin value in the group with AL was lower than the group without AL (12,2 vs 13,2), however our patients have normal hemoglobin levels and this difference was not statistically significant.

Surgical techniques and technologies have greatly evolved over the past years and laparoscopic surgery for rectal cancer is associated with less blood loss and improved short-term postoperative results with no detrimental on oncological outcomes. The laparoscopic approach appears to be beneficial compared with open approach^{16,17,18} and became the gold standard, although it has not been associated with a reduction in AL incidence¹⁰. In our serie, 37% of the cases were laparotomy but we didn't find any statically significance between AL and the two surgical approaches.

Surgeon experience and hospital volume is associated with few AL in some reports^{19,20,21}, however others refer that there are no differences in AL between experts and experts supervised trainees²². In our study, a team exclusively dedicated to colorectal surgery was used but we didn't found a significant statistical relation between surgeons with more than 10 years of experience and the less experienced ones. This might be due to the fact that the most experienced surgeons usually perform the most complex cases.

Prolonged operations may reflect intraoperative difficulties, something that can be especially important in critically ill patients. Silva-Velazco et al²⁵ refers an increasing odd ratio of 1.03 for every 30 minutes of surgical duration. We didn't find any association with AL and the operative time.

In our series, 88,6% of the surgeries had an anastomosis test done intraoperatively. Testing systematically the mechanical integrity (by air-leak and/or methylene blue), the blood supply (with ICG fluorescence transabdominally and transanal) and testing for tension of the anastomosis



may lead to decreased rate of AL²³. In fact, intraoperative assessment of anastomoses integrity is very important as they allow for the immediate identification of leaks with immediate repair, reanastomosis or derivation, but in our series there was no statistically between testing or not.

Routine prophylactic pelvic drainage is debatable. There are studies reporting no differences in terms of pelvic sepsis between drained and non-drained patients²⁷ and others estimating a clear benefit of pelvic drainage²⁸. In our study, we observed the opposite: a positive relation between AL and prophylactic pelvic drainage. This is difficult to explain since the use of drains was not protocolled, being dependent of the experience of the surgeon and how he assesses the difficulty and complexity of the surgery⁸.

Prolonged surgery is associated with intra and post-operative complications, including AL²⁴, something we didn't found in our series.

We see a tendency to statically significance relation between red blood cells transfusion and AL, which is in accordance with other studies that showed that blood loss during surgery was associated with AL^{25,26}.

Another predictable risk factor associated with AL described is the level of the anastomosis/location of the tumor, having an AL rate 10 times higher when the anastomotic region is located within 5cm of the anal verge³². **This factor was not observed in our series.**

We also found a positive statistical relation between AL and hospital stay, having longer hospital stays those with AL, as expected.

A reduction in the rate of AL must be included in the department's clinical quality improvement program.

CONCLUSION

AL is still one of the most concerning complications while performing rectal anterior resection for rectal malignity and therefore should continue to be studied.

In our series, previous abdominal surgeries were the only risk factor associated with AL and should be considered previously to the surgery. The role of prophylactic pelvic drainage needs further investigation to explain this association with AL.

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