

# Risk factors associated to intestinal anastomotic leakage in elective surgery

## *Factores de riesgo asociados a fuga anastomótica intestinal en cirugía electiva*

Martín A. Bolívar-Rodríguez<sup>1\*</sup>, Francisco Magaña-Olivas<sup>1</sup>, Marcel A. Cázarez-Aguilar<sup>1</sup>, Adrián Pamanes-Lozano<sup>1</sup>, Benny A. Osuna-Wong<sup>2</sup> and Felipe de J. Peraza-Garay<sup>3</sup>

<sup>1</sup>General Surgery Service; <sup>2</sup>Coloproctology Service; <sup>3</sup>Statistics Department. Research and Teaching Centre of Health Sciences, Autonomous University of Sinaloa, Civil Hospital of Culiacán, Culiacán, Sinaloa, Mexico

### Abstract

**Background:** The intestinal anastomotic leakage is the most feared surgical complication of a digestive surgery and is associated with a significant increase of morbidity, mortality and hospital stay. **Objective:** Analyze the risk factors to the intestinal anastomotic leakage in elective surgery. **Method:** Observational and retrospective study in which we include patients with intestinal anastomosis, in elective surgery at the second level hospital from January 2007 to January 2017. **Results:** 64 patients were included in the study, in which 7 presented anastomotic leakage. The statistically significant risk factors associated with anastomotic leakage were, cocaine use ( $p = 0.030$ ), neoplasia as a primary pathology ( $p = 0.008$ ), neoadjuvant treatment for neoplasia ( $p = 0.003$ ), and end-to-end anastomosis ( $p = 0.037$ ). Patients with a leakage had a longer hospital stay and a mortality of 14.3%. **Conclusions:** The risk factors associated with the presence of anastomotic leakage found in this study are consistent with the reported worldwide literature. However, in our results, it is worth highlighting the use of cocaine as a risk factor, with statistical significance.

**Keywords:** Anastomosis. Risk factors. Anastomotic leakage. Elective surgery.

### Resumen

**Antecedentes:** La fuga de una anastomosis intestinal es la complicación quirúrgica más temida de la cirugía digestiva y se asocia con un aumento significativo de la morbimortalidad y de la estancia hospitalaria. **Objetivo:** Analizar los factores de riesgo asociados a la fuga de anastomosis intestinal en cirugía electiva. **Método:** Estudio observacional y retrospectivo en el que se recabaron los expedientes de los pacientes operados de anastomosis intestinal en forma electiva en un hospital de segundo nivel de enero de 2007 a enero de 2017. **Resultados:** Se incluyeron 64 pacientes, de los cuales siete presentaron fuga de la anastomosis. Los factores de riesgo asociados a fuga anastomótica estadísticamente significativos fueron consumo de cocaína ( $p = 0.030$ ), neoplasia como patología primaria ( $p = 0.008$ ), tratamiento con neoadyuvantes para neoplasia ( $p = 0.003$ ) y anastomosis término-terminal ( $p = 0.037$ ). Los pacientes con fuga tuvieron una estancia intrahospitalaria más prolongada y una mortalidad del 14.3%. **Conclusiones:** Los factores de riesgo asociados con la presencia de fuga anastomótica encontrados en este estudio son consistentes con los reportados en la literatura mundial. Sin embargo, en nuestros resultados cabe destacar el uso de cocaína como factor de riesgo, con significancia estadística.

**Palabras clave:** Anastomosis. Factores de riesgo. Fuga anastomótica. Cirugía electiva.

### \*Correspondence:

Martín A. Bolívar-Rodríguez

E-mail: bolivarmartin64@hotmail.com

2444-0507/© 2020 Academia Mexicana de Cirugía. Published by Permanyer. This is an open access article under license CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Date of reception: 01-12-2020

Date of acceptance: 16-12-2020

DOI: 10.24875/CIRUE.M20000296

Cir Cir (Eng). 2022;90(1):82-86

Contents available at PubMed

[www.cirugiaycirujanos.com](http://www.cirugiaycirujanos.com)

## Introduction

Anastomotic leakage (AL) is one of the most feared complications of digestive surgery. Despite the advances in anastomotic techniques, post-surgery monitoring, and diagnosis, its incidence and consequences have not changed in the last 50 years. AL can have repercussions in the mortality and morbidity of the patients in the short- and long-term. Many surgeons believe that AL is the biggest challenge in digestive surgery<sup>1</sup>.

Since 1991, more than 50 definitions of anastomotic leakage (dehiscence) have been introduced, but none of them has been widely accepted. In 2015, an international group of experts in gastrointestinal surgery called International Multispecialty Anastomotic Leak Global Improvement Exchange (IMAGInE), reached a consensus on the following definition for anastomotic leakage anywhere along the digestive tract: "a defect in the integrity of surgical connection between two hollow viscera, resulting in communication between the intraluminal and extraluminal compartments", classifying it as A, B, or C, according to the therapeutic needs of the AL<sup>1,2</sup>.

AL incidence is variable (1-24%), depending on the type of anastomosis performed and at what level of the digestive tract<sup>3</sup>.

When it comes to its pathophysiology, a decrease in blood flow is frequently mentioned since it causes a deficient intestinal perfusion, though there is no proof of this as it is complicated to detect an inadequate perfusion during surgery<sup>4</sup>.

The diagnosis is simple when observing the presence of intestinal material through the drainage or coming out from the surgical wound. However, this could be a late sign. It is very important to have an early diagnosis for the treatment to be successful, thus decreasing the morbidity and mortality rates<sup>5</sup>. The surgeon's ability to predict a leakage before or shortly after the surgery is very low (38-62% sensitivity and 46-52% specificity)<sup>6</sup>. For this reason, biochemical markers have been sought for its early diagnosis, before the onset of systemic signs in the patient, even before leukocytosis, such as C-reactive protein and procalcitonin. However, they have high negative predictive values (89-97%), low sensitivity and low positive predictive values<sup>2</sup>.

A CAT scan contrasted with a water-soluble medium is the most commonly used imaging study for the diagnosis of AL, but the literature is inconclusive as to whether it is the most appropriate one (74.3% sensitivity vs. 68% without contrast)<sup>7</sup>.

There are studies, the vast majority in patients with colorectal surgery, that have described multiple risk factors for the development of AL, such as those related to the patient, the hospital environment, the surgeon's experience and the surgical technique, among others<sup>8</sup>.

The purpose of this study was to analyze the risk factors that led patients to develop AL in elective surgery in our hospital center.

## Method

An observational and retrospective study was conducted in which we collected the records of patients who underwent intestinal anastomosis in elective surgery at a second level hospital over a 10-year period, from January 2007 to January 2017. All patients aged 18 years and older, regardless of their sex, who underwent mechanical or manual intestinal anastomosis, with or without AL, and who had a complete clinical record for the extraction of the variables of interest were consequently included. Patients under 18 years of age who had emergency surgeries, and those who underwent intestinal anastomosis with clinical records that did not show all the variables of interest were excluded.

Two groups were formed, one with patients who did not present AL and the other with those who did. We followed the definition for AL provided by the IMAGInE group. The categorical variables and their definitions were the patient's age in years from birth to the time of the surgery; sex, in terms of external sexual characteristics for phenotypic traits as male or female; drug addictions, as the patient referenced being a user of chemical compounds that are addictive and damaging to their health (specifically tobacco, alcohol or drugs like cocaine and others); comorbidity, by the presence of other conditions that could induce or worsen the pathology (lung disease, nephropathy, liver disease, heart disease, neoplasia, diabetes or hypertension); the cause, determined by the pathology that originated the intervention to perform anastomosis (trauma, neoplasia or benign abdominal pathology); the location, with regard to the anatomical situation where the anastomosis was conducted, considered as high or low; the technique, manual or mechanical, implemented in the surgical procedure to perform anastomosis; bowel preparation, determined by the use of Macrogol/NaHCO<sub>3</sub>/HCl/KCl, sodium phosphate enema, soapsuds enema, sodium picosulfate or unknown; and drainage, conditioned by its use at the end of the surgery of Penrose anastomosis, low

negative-pressure silicone drainage, high negative-pressure plastic drainage or none.

In order to compare categorical variables,  $\chi^2$  test was used and odds ratio (OR) was estimated, with a 95% confidence interval. Student's t-test was used for numerical variables.

Data were analyzed with SPSS v25 statistical package and a value of  $p < 0.05$  was considered statistically significant.

## Results

64 patients who met the criteria were included, of whom 7 (10.9%) had AL, with a mean age of  $49.3 \pm 9$  years, and 57 (89.1%) had no leakage, with a mean age of  $44.2 \pm 18$  years. No significant difference was found regarding sex ( $p = 0.109$ ) and age ( $p = 0.463$ ).

Risk factors associated with anastomotic leakage were cocaine use (OR: 22.4;  $p = 0.030$ ), alcohol (OR: 0.19;  $p = 0.096$ ), neoplasia (OR: 20.63;  $p = 0.008$ ) and neoadjuvant therapy with chemotherapy and radiotherapy for rectal cancer (OR: 42;  $p = 0.003$ ). Regarding mechanical bowel preparation, the use of sodium picosulfate with citric acid and magnesium oxide was statistically significant (OR: 89.4;  $p = 0.001$ ). The location of low colorectal anastomosis (when performed 8 cm or less from the anal margin) proved to be a risk factor (OR: 2.47;  $p = 0.410$ ), but not significant; the type of end-to-end anastomosis was a greater risk factor (OR: 9.55;  $p = 0.037$ ). The use of closed mild aspiration drainage was also considered a risk factor, although not significant (OR: 2.55;  $p = 0.662$ ) (Table 1).

Patients who presented AL spent on average 8.2 more days at the hospital, with a statistically significant difference ( $p < 0.001$ ).

As for mortality, one patient (14.3%) with AL died (OR: 26.54;  $p = 0.109$ ) and none of those without AL.

## Discussion

Intestinal anastomosis is a surgical procedure often performed by a surgeon, and AL is one of the most feared complications for its high morbidity and mortality rates. It usually happens during the first 7 days post-surgery, but it has been reported that it can occur up to 30 days after having anastomosis<sup>2</sup>.

In our study, out of the 64 patients who had intestinal anastomosis, 7 (10.9%) presented AL, similar results to those of the study by Pacheco et al.<sup>9</sup>, where they found an AL rate of 10.7%. However, they differ from the study by Konishi et al.<sup>10</sup>, who report a leakage

percentage of 2.8%. In our review of the literature, we notice these percentages vary from 1% to 24%<sup>3</sup>.

With regard to risk factors, neoplasia was the common etiology associated with AL ( $p = 0.008$ ), and even more so when patients underwent neoadjuvant therapy ( $p = 0.003$ ). Unfortunately, the time elapsed between the completion of this treatment and the performance of the surgery was not documented in this study. Our results coincided with those of the study by Konishi et al.<sup>10</sup>, who mentioned that surgical oncology is directly related both to the outcome of AL and the prognosis of the patients presenting this complication with this pathology as the primary etiology in terms of local recurrence of the tumoral disease.

With respect to drug addictions as a risk factor, 2 patients (28.6%) with AL were smokers, a result that agrees with the study by Midura et al.<sup>11</sup>, in which out of 13,684 patients, 520 (3.8%) had AL, and of these, 27.3% were chronic smokers. When discussing drug addictions as a risk factor, our study found that 2 patients (28.6%) with AL were cocaine users. In our review of the literature, we did not find any study that links it as a risk factor. However, it has been proven that cocaine can cause alteration in the mesenteric circulation, such as visceral infarcts, intestinal ischemia, and ischemic colitis from 3 to 48 hours after its use, in addition to the effects of the vasoconstriction in the endothelial membranes and the increase in platelet aggregation that leads to the formation of arteriolar thrombi in the intestinal circulation<sup>12</sup>. Given this claim, there is no doubt that chronic cocaine use can be considered a risk factor due to the decrease of blood supply at the site of the anastomosis, producing alterations in scarring and, consequently, anastomotic leakage. Now, if we focus on the study by Peacock et al.<sup>13</sup>, we see they found an overall prevalence of 0.35% (0.27-0.46) of people aged between 15 and 64 years old who used cocaine during the 12 months prior to the study being conducted. This represents a considerable number, taking into account that, since it is illegal, it means not all people report using it, which makes it an under-reported prevalence. Therefore, emphasis should be placed on this information.

Bowel preparation as a statistically significant risk factor ( $p = 0.001$  with sodium picosulfate) is similar to what was published by Kumar et al.<sup>14</sup>, who also comment that mechanical preparation of the colon has a direct impact on the anastomosis as it is done with osmotic agents that accumulate liquid in the area, causing edema of the intestinal loops, which is why they only recommend a preparation with intraluminal antibiotics.

**Table 1. Risk factors associated with anastomotic leakage**

|                                         | Total (n = 64)          |      |                     |      | p     | OR    | CI95%       |
|-----------------------------------------|-------------------------|------|---------------------|------|-------|-------|-------------|
|                                         | Without AL n = 57 (89%) |      | With AL n = 7 (11%) |      |       |       |             |
|                                         | n                       | %    | n                   | %    |       |       |             |
| Drug addictions                         |                         |      |                     |      |       |       |             |
| Tobacco                                 | 27                      | 47.4 | 2                   | 28.6 | 0.125 | 0.44  | 0.08-2.48   |
| Alcohol                                 | 27                      | 47.4 | 1                   | 14.3 | 0.096 | 0.19  | 0.02-1.64   |
| Cocaine                                 | 1                       | 1.8  | 2                   | 28.6 | 0.030 | 22.4  | 1.72-292.36 |
| Other                                   | 1                       | 1.8  | 1                   | 14.3 | 0.208 | 9.33  | 0.52-169.10 |
| Comorbidity                             |                         |      |                     |      |       |       |             |
| Pneumopathy                             | 0                       | 0.0  | 1                   | 14.3 | 0.109 | -     |             |
| HTN                                     | 8                       | 14.0 | 1                   | 14.3 | 1.000 | 1.02  | 0.11-9.64   |
| DM                                      | 4                       | 7.0  | 0                   | 0.0  | 1.000 | -     |             |
| Cardiopathy                             | 2                       | 3.5  | 0                   | 0.0  | 1.000 | -     |             |
| Neoadjuvant therapy                     | 1                       | 1.8  | 3                   | 42.9 | 0.003 | 42    | 3.52-501.61 |
| Type of surgery                         |                         |      |                     |      |       |       |             |
| Oncology                                | 2                       | 3.5  | 3                   | 42.9 | 0.008 | 20.63 | 2.64-162.35 |
| Bowel preparation                       |                         |      |                     |      |       |       |             |
| Macrogol/NaHCO <sub>3</sub> /HCl/KCl    | 42                      | 73.7 | 4                   | 57.1 | 0.391 | 0.48  | 0.10-2.38   |
| Sodium phosphate enema                  | 4                       | 7.0  | 0                   | 0.0  | -     |       |             |
| Soapsuds enema                          | 3                       | 5.3  | 0                   | 0.0  | -     |       |             |
| Unknown                                 | 8                       | 14.0 | 0                   | 0.0  | -     |       |             |
| Sodium picosulfate                      | 0                       | 0.0  | 3                   | 42.9 | 0.001 | 89.4  | 3.97-201.4  |
| Anastomosis                             |                         |      |                     |      |       |       |             |
| Side-to-side                            | 32                      | 56.1 | 1                   | 14.3 | 0.050 | 0.13  | 0.01-1.15   |
| End-to-end                              | 22                      | 38.6 | 6                   | 85.7 | 0.037 | 9.55  | 1.08-84.7   |
| End-to-side                             | 2                       | 3.5  | 0                   | 0.0  | -     |       |             |
| Ileoanal (J-pouch)                      | 1                       | 1.8  | 0                   | 0.0  | -     |       |             |
| Location                                |                         |      |                     |      |       |       |             |
| Low                                     | 20                      | 35.1 | 4                   | 57.1 | 0.410 | 2.47  | 0.50-12.13  |
| Technique                               |                         |      |                     |      |       |       |             |
| Mechanical                              | 34                      | 59.6 | 5                   | 71.4 | 0.695 | 1.69  | 0.30-9.47   |
| Drainage                                |                         |      |                     |      |       |       |             |
| None                                    | 8                       | 14.0 | 0                   | 0.0  | 0.773 | 1.02  | 0.28-22.83  |
| Penrose                                 | 5                       | 8.8  | 1                   | 14.3 | 0.516 | 2.55  | 0.11-9.64   |
| Low negative-pressure silicone drainage | 40                      | 70.2 | 6                   | 85.7 | 0.662 |       |             |
| High negative-pressure plastic drainage | 4                       | 7.0  | 0                   | 0.0  | -     |       |             |
| Cause of surgery                        |                         |      |                     |      |       |       |             |
| Trauma                                  | 18                      | 31.6 | 1                   | 14.3 | 0.664 | 0.36  | 0.04-3.22   |
| Neoplasia                               | 2                       | 3.5  | 3                   | 43.0 | 0.008 | 20.63 | 2.64-161.35 |
| Abdominal pathology                     | 19                      | 33.3 | 1                   | 14.3 | 0.419 | 0.33  | 0.04-2.97   |

DM: diabetes mellitus; AL: anastomotic leakage; HTN: hypertension; CI95%: confidence interval of 95%; OR: odds ratio.

Additionally, in our study it was evidenced that patients with AL show a clear statistically significant difference in terms of prolongation of hospital stay ( $p < 0.001$ ), increasing patient costs, as well as the risk for infections. These results are similar to those found in the study by Gessler et al.<sup>15</sup>, who state that patients with AL had a longer hospital stay, thus increasing the associated mortality to 5%, in comparison with 0.6% of patients without AL.

No statistically significant differences were found in terms of sex, age, and location of the anastomosis,

although low anastomoses were more likely to present AL: on the one hand, out of 24 patients who underwent low anastomosis, 4 had AL, representing 57.1% of the 7 who had AL. On the other hand, out of 28 patients who underwent end-to-end anastomosis, 6 had AL, representing the great majority (85.7%) with statistical significance ( $p = 0.037$ ). These data are related to the results of the studies by Trencheva et al.<sup>16</sup> and Bannura et al.<sup>17</sup>, who reported that the location of the anastomoses, mainly low and end-to-end anastomoses, is a risk factor for dehiscence. In their study, Park et al.<sup>18</sup> obtained

similar results to ours, although they found that the male sex had a higher risk of AL with statistical significance, which they attribute to the difficulty in bowel management due to pelvic narrowing in this sex. Therefore, they propose to perform selective defunctionalization in certain patients with a protective ostomy, which has been established in recent years as an independent risk factor for AL, and added it in their preoperative predictive *score* for colorectal AL.

In our study, the nutritional status of the patient was not evaluated as a risk factor as the study universe included patients scheduled for elective surgery, so all patients had a nutritional profile within normal parameters. However, studies such as that of Silva-Godínez et al.<sup>3</sup> and Gutiérrez-Rangel et al.<sup>19</sup> have shown that hypoalbuminemia and a low body mass index are not statistically significantly associated with the development of AL.

Our study, despite its 10-year period, had its limitations due to its retrospective and single-center nature. Nevertheless, the results obtained are comparable with those of the international literature, with cocaine use being a statistically significant risk factor.

## Conclusions

The risk factors associated with the presence of AL found in this study are consistent with the reported worldwide literature, where surgical oncology, neoadjuvant treatment, and mechanical preparation stand out. Subsequent studies, preferably prospective and multicenter studies, should take into account cocaine use as a risk factor because, even though the number of cases in our study was small, it was statistically significant, and the number of cocaine users around the world is considerable.

## Funding

The authors declare they have not received any funding for the article.

## Conflicts of interest

The authors declare that they have no conflicts of interest.

## Ethical disclosures

**Protection of people and animals.** The authors declare that no experiments have been made on human beings or animals for this research.

**Data confidentiality.** The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

**Right to privacy and informed consent.** The authors have received an informed consent from the patients and/or subjects referred to in this article. This document is in possession of the corresponding author.

## References

- Vallance A, Wexner S, Berho M, Cahill R, Coleman M, Haboubi N, et al. A collaborative review of the current concepts and challenges of anastomotic leaks in colorectal surgery. *Colorectal Dis.* 2017;19:01-12.
- Chadi SA, Fingerhut A, Bertho M, DeMeester SR, Fleshman JW, Hyman NH, et al. Emerging trends in the etiology, prevention, and treatment of gastrointestinal anastomotic leakage. *J Gastrointest Surg.* 2016;20:2035-51.
- Silva-Godínez JC, Vázquez-Ciriaco S, Jarquín-Arremilla A, Vela Maqueda P. El estado nutricional no influye en el desarrollo de dehiscencia de anastomosis en una población mexicana. *Cir Gen.* 2013;35:9-15.
- Tavy ALM, de Bruin AFJ, Smits AB, Boerma EC, Ince C, Noordzij PG, et al. Intestinal mucosal and serosal microcirculation at the planned anastomosis during abdominal surgery. *Eur Surg Res.* 2019;60:248-56.
- Den Dulk M, Noter SL, Hendriks ER, Brouwers MA, van der Vlies CH, Oostenbroek RJ, et al. Improved diagnosis and treatment of anastomotic leakage after colorectal surgery. *Eur J Surg Oncol.* 2009;35:420-6.
- Karliczek A, Harlaar NJ, Zeebregts CJ, Wiggers T, Baas PC, van Dam GM. Surgeons lack predictive accuracy for anastomotic leakage in gastrointestinal surgery. *Int J Colorectal Dis.* 2009;24:569-76.
- Samji KB, Kielar AZ, Connolly M, Fasih N, Doherty G, Chung A, et al. Anastomotic leaks after small- and large-bowel surgery: diagnostic performance of CT and the importance of intraluminal contrast administration. *AJR Am J Roentgenol.* 2018;210:1259-65.
- Sánchez-Guillén L, Frasson M, García-Granero A, Pellino G, Flor-Lorenzte B, Álvarez-Sarrado E, et al. Risk factors for leak, complications and mortality after ileocolic anastomosis: comparison of two anastomotic techniques. *Ann R Coll Surg Engl.* 2019;101:571-8.
- Pacheco MA, Aldana GE, Martínez LE, Forero JC, Gómez CA, Coral EM, et al. Incidencia de falla anastomótica en intestino delgado, colon y recto. *Rev Colomb Cir.* 2017;32:269-76.
- Konishi T, Watanabe T, Kishimoto J, Nagawa H. Risk factors for anastomotic leakage after surgery for colorectal cancer: results of prospective surveillance. *J Am Coll Surg.* 2006;202:439-44.
- Midura EF, Hanseman D, Davis BR, Atkinson SJ, Abbott DE, Shah SA, et al. Risk factors and consequences of anastomotic leak after colectomy: a national analysis. *Dis Colon Rectum.* 2015;58:333-8.
- Martínez-Vieira A, Camacho-Ramírez A, Díaz-Godoy A, Calvo-Durán A, Pérez-Alberca CM, de la Vega-Olías C, et al. Isquemia intestinal y consumo de cocaína; presentación de un caso y revisión de la literatura. *Rev Esp Enferm Dig.* 2014;106:354-8.
- Peacock A, Leung J, Larney S, Colledge S, Hickman M, Rehm J, et al. Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. *Addiction.* 2018;113:1905-26.
- Kumar AS, Kelleher DC, Sigle GW. Bowel preparation before elective surgery. *Clin Colon Rectal Surg.* 2013;26:146-52.
- Gessler B, Eriksson O, Angenete E. Diagnosis, treatment, and consequences of anastomotic leakage in colorectal surgery. *Int J Colorectal Dis.* 2017;32:549-56.
- Trencheva K, Morrissey KP, Wells M, Mancuso CA, Lee SW, Sonoda T, et al. Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. *Ann Surg.* 2013;257:108-13.
- Bannura CG, Cumsille GMA, Barrera EA, Contreras PJ, Melo IC, Soto CD, et al. Factores asociados a la dehiscencia clínica de una anastomosis intestinal grapada: análisis multivariado de 610 pacientes consecutivos. *Rev Chil Cir.* 2006;58:341-6.
- Park JS, Huh JW, Park YA, Cho YB, Yun SH, Kim HC, et al. Risk factors of anastomotic leakage and long-term survival after colorectal surgery. *Medicine.* 2016;95:e2890.
- Gutiérrez-Rangel A, Reyna-Sepúlveda F, Salinas-Domínguez R, Muñoz-Maldonado G. Evaluación del estado nutricional y su impacto en pacientes post operados de anastomosis intestinal. *Nutrición y fuga anastomosis.* *Nutr Clin Diet Hosp.* 2016;36:82-8.