



Original Article

Procalcitonin as an early marker in the detection of anastomotic intestinal leak in a University Hospital of Bogotá



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ABSTRACT

Introduction: Anastomotic leakage is a complication of intestinal anastomosis, with an incidence of 2%–7% in centers of experience. To be able to achieve an early detection, serological markers such as Procalcitonin were included.

Methods: Descriptive retrospective cohort study of patients taken to colorectal surgery with intestinal anastomosis, the objective is to estimate association between procalcitonin (≥ 2 ng/dl) as an early inflammatory marker and anastomotic leakage in a Coloproctological Service of a highest level of health care hospital, between September 2017 and January 2019.

Results: Cohort of 237 patients, 51% women (18–89 years), with multiple comorbidities in 81% of patients, colon cancer was the most operated pathology (53.1%). Laparoscopic approach was the most applied 60.34%, colorectal anastomosis was the most frequently performed (47.26%). Ileocolic anastomosis presented a higher frequency (43.75%-n:7) of dehiscence. Anastomotic leakage was associated with a serum procalcitonin positive 3 days postoperatively (p-value <0.05). Patients with a positive result had 4.28 times higher risk of presenting an anastomotic leak, compared to this risk in those patients with negative results 3 days postoperatively, this association was statistically significant 95% CI (1.34–14.16); p value <0.05.

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Conclusion: Anastomotic leakage is a source of morbidity in patients taken to intestinal anastomosis. It's necessary to guarantee an early diagnosis of this complication, prevent abscesses and secondary peritonitis, providing adequate treatment and even reducing the associated mortality. We recommend including the procalcitonin in the assessment protocol on the third day of postoperative follow-up.

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Procalcitonina como um marcador precoce na detecção de vazamento anastomótico intestinal em um Hospital Universitário de Bogotá

R E S U M O

Palavras-chave:

Fístula anastomótica

Cirurgia colorretal

Procalcitonina

Deteção precoce

Introdução: O vazamento anastomótico é uma complicação da anastomose intestinal, com uma incidência de 2% a 7% em centros com experiência. Para conseguir uma detecção precoce, foram incluídos marcadores sorológicos como a Procalcitonina.

Métodos: Estudo de coorte descritivo e retrospectivo de pacientes submetidos a cirurgia colorretal com anastomose intestinal, cujo objetivo é estimar a associação entre os níveis de procalcitonina (≥ 2 ng/dL) como marcador inflamatório precoce e vazamento anastomótico em um Serviço de Coloproctologia de alto nível de atenção à saúde hospitalar, entre setembro de 2017 a janeiro de 2019.

Resultados: Coorte de 237 pacientes, 51% mulheres (18–9 anos), com múltiplas comorbidades em 81% dos pacientes, sendo o câncer de cólon a patologia mais operada (53,1%). A abordagem laparoscópica foi a mais utilizada, em 60,34%, e a anastomose colorretal foi a mais frequentemente realizada (47,26%). A anastomose ileocólica apresentou a maior frequência (43,75%, $n = 7$) de deiscências. O vazamento anastomótico foi associado a procalcitonina sérica positiva 3 dias após a cirurgia ($p < 0,05$). Pacientes com resultado positivo tinham um risco 4,28 vezes maior de apresentar vazamento anastomótico, em comparação com esse mesmo risco nos pacientes com resultado negativo 3 dias após a cirurgia, sendo essa associação estatisticamente significativa, (IC95%:1,34–14,16); $p < 0,05$.

Conclusão: O vazamento anastomótico é fonte de morbidade em pacientes encaminhados para anastomose intestinal. É necessário garantir o diagnóstico precoce desta complicação, prevenir abscessos e peritonites secundárias, proporcionando tratamento adequado e até mesmo reduzindo a mortalidade associada. Recomendamos incluir a procalcitonina no protocolo de avaliação no terceiro dia de seguimento pós-operatório.

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Introduction

Anastomotic leak is a complication of intestinal anastomoses that despite perioperative preventive measures, has an incidence of 2%–7% in experienced centers.¹ Several associated factors have been reported including factors related to anastomosis such as type of anastomosis, perfusion and tension of the suture. Others factors are associated with anastomotic leak are type of surgery (emergency surgery), administration of certain medication during the procedure the patient receives medications that can potentially affect the anastomosis, and factors associated with the patient such as diabetes, age, gender, cancer, preoperative chemotherapy and other comorbidities that affect the outcomes.²

The anastomotic leak is known like one of the most frequent complications in colorectal surgery. An early diagnosis is necessary to provide faster management and lower

impact on the morbidity and mortality of these patients.² The incidence of leakage varies between institutions and the anastomosed intestinal segment, literature reports the most susceptible anastomoses is the low colorectal anastomosis, occurring between 8%–14%,³ in some reports the morbidity of this complication reach the 34%.⁴

In order to achieve early detection of intestinal fistula, different diagnostic methods have been investigated, without achieving the expected efficacy. In recent years, the most commonly used serological markers for this purpose are C Reactive Protein (PCR) and Procalcitonin.⁵

Research question

Is the procalcitonin ≥ 2 ng/dL as an early inflammatory marker associated with the detection of intestinal anastomotic leakage, in patients with intestinal anastomoses, in the

Table 1 – Frequency of the clinic and laboratory variables of the patients with intestinal anastomosis between 2017 and 2019.

Variables	N	Percentage	Missing data, n%
Female	122	51,48	0 (0%)
Comorbidities	192	81,01	0 (0%)
More than one comorbidity	94	48,96	0 (0%)
Active cancer (immunosuppression)	168	70,89	0 (0%)
Diabetes mellitus	37	19,27	0 (0%)
Arterial hypertension	87	45,31	0 (0%)
Chronic kidney disease	6	3,12	0 (0%)
Chronic Gastritis	17	8,85	0 (0%)
Familial Adenomatous Polyposis	3	1,56	0 (0%)
Normal Body mass index	98	41,35	4 (1.69%)
Program Surgery	202	85,23	0 (0%)
Laparoscopic assessment	143	60,34	0 (0%)
Positive for anastomotic leak in postoperative	16	6,75	0 (0%)
Procalcitonin positive at 3rd postoperative day	60	25,32	0 (0%)
Procalcitonin positive at 5th postoperative day*	11	29,73	0 (0%)
Intraoperative diagnostic of intestinal anastomotic leak	13	86,67	0 (0%)
Mortality	7	2,95	0 (0%)
Re-operation	27	11,39	0 (0%)
Out-patient control	227	95,78	0 (0%)
Hospital readmission	15	6,33	0 (0%)
Total	237	100,00	

Control procalcitonin in 37 patients^a, 1 case with HIV.

Coloproctological department of a highest-level University Hospital in Bogotá?

Objective

To estimate the association between procalcitonin (≥ 2 ng/dL) as an early inflammatory marker and intestinal anastomotic leakage in the Coloproctological Service of the Hospital Universitario Mayor – Mederi, between September 2017 and January 2019.

Methodological aspects

Type of study

This is an observational cross-sectional study, of patients surgically managed by the Coloproctological Service of the Hospital Universitario Mayor – Mederi.

Population and sample

Reference population

Patients undergoing intestinal anastomosis in the Coloproctological Service of the Hospital Universitario Mayor - Mederi, between September 2017 and January 2019.

Sampling frame

The selection of the sample was consecutive or sequential of the patients who met the selection criteria, between September 2017 and January 2019, until completing the appropriate minimum sample size.

Sample frame

The database of surgeries performed by the Coloproctology Service of the Hospital Universitario Mayor – Mederi was used, from which the patients in whom colorectal surgery with intestinal anastomosis was performed between September 2017 and January 2019 were selected.

Selection criteria

Patients 18 years old of age were included, those who underwent an intestinal anastomosis, performed by the Coloproctology Service of the Hospital Universitario Mayor – Mederi, during the period from September 1, 2017 to January 31, 2019 and patients with serum procalcitonin measurement on the third postoperative day.

Exclusion criteria were thus established for patients who underwent septic processes in organs outside the abdominal cavity at the time of the surgical procedure, pregnant patients, and patients with perforation of hollow viscus distal to the intestinal anastomosis.

Results

The studied population consisted of 237 patients treated surgically by the Coloproctological service at the Hospital Universitario Mayor – Méderi.

Demographic characteristics

In this cohort, the female gender predominated 51.4% ($n = 122$) and the patients with comorbidities (81%), with immunosuppression being more frequent; it was found active cancer in 167 patients and retrovirus (HIV+) infection in pharmacolog-

Table 2 – Preoperative diagnosis of patients with an intestinal anastomosis between 2017 and 2019.

Preoperative diagnosis	n	Percentage
Colon cancer	126	53,16
Rectum cancer	33	13,92
Ileostomy owner	28	11,81
Colostomy owner	8	3,38
Complicated diverticular disease treated with sigmoidectomy or colostomy	8	3,38
Colonic perforation by endoscopy	7	2,95
Colonic Volvulus	6	2,53
Gynecologic tumor	5	2,11
Fournier Gangrene	5	2,11
Familial adenomatous polyposis	3	1,27
Appendicular tumor	3	1,27
Ulcerative Colitis	2	0,84
Colonic inertia	1	0,42
Synchronic colon tumor	1	0,42
Un-resectable rectal polyp	1	0,42
Missing data	0	0,00
Total	237	100

ical management in 1 patient, followed by Diabetes Mellitus. 41% of patients were within range for a normal body mass index, followed by overweight (35%) and grade 2 obesity (13%). The Coloproctological service of this University Hospital handles a large volume of 85% scheduled surgery for oncological purposes, although they also perform emergency surgical management, including reoperations. A mortality of 9.95% (n=7) of the patients brought to intestinal anastomosis is reported.

The characteristics of this cohort are described in Table 1.

Colon cancer was the most frequent oncological pathology managed surgically (53.1%), followed by rectal cancer (13.9%), cancer of gynecological origin (2.1%) that required intestinal resection due to compromise and appendicular tumors (1.2%). 15.19% (n=36) of the patients were taken to surgery for stomal closure, in the context of treated colon cancer, post neoadjuvant rectal cancer and benign pathology such as diverticular disease, among others described in Table 2.

The sigmoid colon (27.6%) was the intestinal segment most frequently affected by gastrointestinal tumor pathology, followed by the ascending colon and rectum. Tumors in the appendix and ileocecal valve, among others described in Table 3, occurred less frequently.

The most widely applied surgical approach was the laparoscopic 60.34% (n=143), with right hemicolectomy being the most frequent procedure performed in this way in 19.83% (n=47) of the cases and in the open approach, it corresponded to ileostomy closure in 21.52% (n=51) of cases. 46.84% (n=111) of the patients were taken to surgery to close ostomies in the context of treated colon cancer, post neoadjuvant rectal cancer and benign pathology such as diverticular disease, among others.

Anastomotic leak according to the type of intestinal anastomosis

Colorectal anastomosis was the most frequently performed in 47.26% (n=112) of patients in this cohort, the others are

Table 3 – Surgical procedure in patients with intestinal anastomosis between 2017 and 2019.

Surgical procedure	N	Percentage
Open closure of ileostomy	51	21,52
Laparoscopic right hemicolectomy	47	19,83
Open closure of colostomy	32	13,50
Laparoscopic sigmoidectomy	28	11,81
Laparoscopic closure of colostomy	27	11,39
Laparoscopic anterior rectal resection	15	6,33
Laparoscopic left hemicolectomy	7	2,95
Laparoscopic low/ultralow rectal resection	6	2,53
Others	5	2,11
Total colectomy + ileocecal anastomosis + protective ileostomy	5	2,11
Open right hemicolectomy	5	2,11
Open left hemicolectomy	2	0,84
Open low/ultralow rectal resection	2	0,84
Open sigmoidectomy	2	0,84
Laparoscopic closure of ileostomy	1	0,42
Open anterior rectal resection	1	0,42
Open Total colectomy + ileocecal anastomosis + distal pancreatectomy + splenectomy	1	0,42
Missing data	0	0,0
Total	237	100

described in Table 7. However, ileocolic anastomosis was the one with the highest frequency 43, 75% (n = 7) of dehiscence, within the group of patients with anastomotic leakage (Fig. 1).

The median age of presentation of patients undergoing intestinal anastomosis was 66 years, with a minimum of 18 years and a maximum of 89 years. All patients underwent procalcitonin test on the third postoperative day, reporting a median of 0.71 (0.04–65.7), this top value is not explained by chronic renal failure, which can generate false positives (only 1 patient presented positive procalcitonin – value of 16 – without anastomotic leak) and one of them in terminal stage presented anastomotic leak, the rest (4) were negative. It should be noted that 5 of 6 patients with this pathology were in stage 3 to 5 for chronic kidney failure. This top value was presented in a patient without anastomotic leak or kidney disease.

Control serum procalcitonin at 5 days was conditioned to the patient's clinical evolution; where in the context of an initial positive procalcitonin with an asymptomatic and clinically stable patient, it was not taken. However, if the patient had a stationary evolution or clinical deterioration, a sample was taken for analysis in the laboratory.

Control serum procalcitonin at 5 days was taken in 37 patients, reporting a median of 1 (0.22–15), with a positive persistence in 11/37 patients, of whom additional behaviors were taken (TAC [n=3] and/or Surgery [n=3]), confirming intra-operatively the anastomotic leak in 1 patient. In the remaining 5 patients, the postoperative evolution was satisfactory (Table 4).

The diagnosis of anastomotic leak was made with a median on the sixth postoperative day. The median length of stay was 4 days, with a minimum of 2 days, giving discharge for a satisfactory postoperative evolution and a maximum

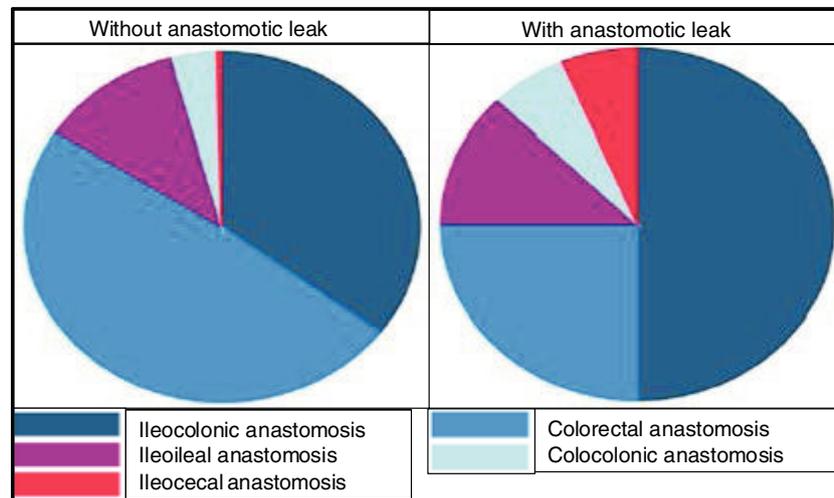


Fig. 1 – Frequencies of anastomotic leaks grouped by type of intestinal anastomosis.

Table 4 – Frequency of anastomotic leak grouped by type of intestinal anastomosis.

	Anastomotic leak				Total	
	(+)		(-)		N	Percentage
	N	Percentage	N	Percentage		
Ileocolic anastomosis	8	50,00	78	35,29	86	36,29
Colorectal anastomosis	4	25,00	108	48,87	112	47,26
Ileoileal anastomosis	2	12,50	26	11,76	28	11,81
Colocolonic anastomosis	1	6,25	8	3,62	9	3,80
Ileocecal anastomosis	1	6,25	1	0,45	2	0,84
Total	16	100,00	221	100,00	237	100,00

of 77 days, this outrank value being explained by the management of anastomotic leak and subsequent reoperations in specific cases.

Regarding follow-up, given by the number of days the patient attended his postoperative control from the date of surgery, a median of 7.5 days, a minimum of 2 and a maximum of 86 days, was reported. Follow-up time corresponds to a median of 4 postoperative outpatient visits with a range (1–14), which correspond to patients who had a postoperative complication and required stricter long-term control or oncological follow-up based on their surgically treated disease, which explains this extreme value.

Taking into account that all the quantitative variables have a non-normal distribution (Shapiro Wilk Test < 0.05), in Table 5 they are described by medians and percentiles. The medical conduct in the hospital follow-up carried out by the treatment service in patients undergoing intestinal anastomosis, was variable considering the patient's clinical status and diagnostic suspicion according to their postoperative evolution; where surgical management predominated 11.39% (n = 27) in case of clinical or images based suspicion of anastomotic leak, these patients were re-operated. In 13 patients, the anastomotic dehiscence was documented and the corresponding surgical management was performed. In the remaining cases, the intraoperative findings correspond to mechanical intestinal obstruction secondary to adhesions and intra-abdominal collections with undamaged anastomosis.

In two patients, anastomotic leak was confirmed by contrast Computerized Tomography (CT), leading to reoperation, and finally, in 1 patient, partial dehiscence of an ultralow colorectal anastomosis was evidenced by recto-sigmoidoscopy, performing local drainage of the perianastomotic collection and clinical surveillance with a satisfactory evolution without reintervention.

The association between procalcitonin (≥ 2 ng/dL) as an early inflammatory marker and intestinal anastomotic leakage was described as follows, the presence of anastomotic leakage is associated with a positive serum procalcitonin 3 days postoperatively p-value < 0.05, this association being statistically significant (Table 6).

Patients in whom a positive serum procalcitonin was documented 3 days postoperatively have a 4.28 fold risk of presenting an anastomotic leak, compared to the risk of those patients with negative serum procalcitonin on the third postoperative day, this association is statistically significant with a 95% Confidence Interval (1.34–14.16) and a p-value < 0.05. The 56.25% of the patients with anastomotic leak had a positive procalcitonin 3 days after the initial surgery and 76.92% of the patients without anastomotic leak had a negative procalcitonin. The distribution of procalcitonin values between these two groups is presented in Fig. 2.

The other dichotomous variables and their association or absence with the presentation of anastomotic leakage are described in Table 7, identifying as significant: laparo-

Table 5 – Measures of central tendency and dispersion of clinical and laboratory variables of the patients with intestinal anastomosis between 2017 and 2019.

Variables	N	Minimum	P25	P50	P75	Maximum	Media	DE	Missing data n (%)	Test shapiro-wilk
Age (years)	237	18	56	66	74	89	63,67	14,52	0 (0%)	0,00
BMI (Kg/m2)	233	15	22	25	28	41	25,26	4,45	4(1,69%)	0,00
PCT value at 3rd POP day	237	0,04	0,25	0,71	1,97	65,70	2,61	6,76	0 (0%)	0,00
PCT value at 5th POP day	37	0,22	0,82	1	2	15	2,20	3,01	0 (0%)	0,00
POP day of diagnosis of anastomosis leak	16	3	4	6	9	15	6,75	3,66	0 (0%)	0,04
Length of hospital stay (days)										
Number of out-patient consult	237	2	3	4	6	77	6,14	8	0 (0%)	0,00
Days of Postoperative follow-up	225	1	3	4	5	14	4,1	2	2(0,88%)	0,00
	226	2	6	7,5	10	86	10,12	10,02	1(0,44%)	0,00

Table 6 – Association between serum procalcitonin and intestinal anastomotic leak.

	Patients with intestinal anastomosis Yes	With anastomotic leak in the postoperative	
		No	Total
Serum procalcitonin at 3rd POP day	Positive	9	51
	Negative	7	170
	total	16	221
			60
			177
			237

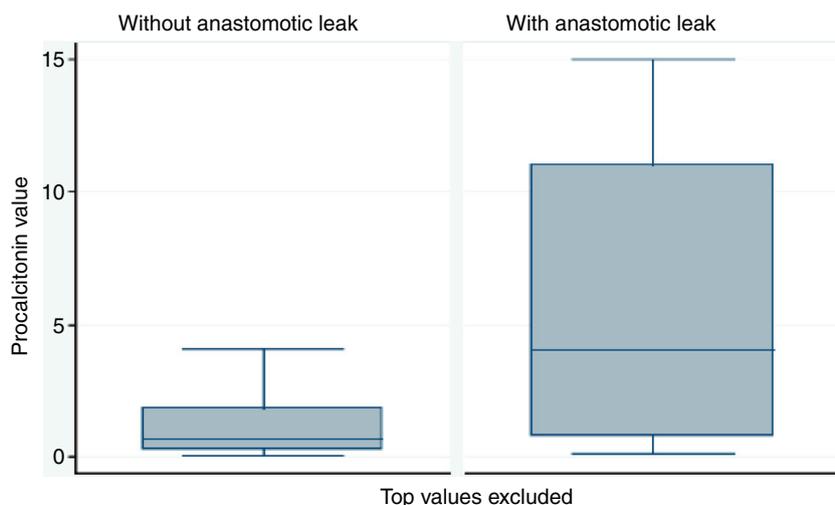


Fig. 2 – Distribution of procalcitonin value on the third postoperative day.

scopic surgical approach ($p = 0.02$), being explained as the most commonly performed approach in this cohort and mortality ($p = 0.00$), reoperation ($p = 0.00$), postoperative control ($p = 0.00$) and hospital readmission ($p = 0.00$) that are conditioned by this type of surgical complication.

Hospital stay of patients with intestinal anastomosis

The length of stay in patients who presented anastomotic leak was longer (median of 10 days) compared to those who did not present it, this difference being statistically significant ($p < 0.05$) (Table 8, Fig. 3).

The length of stay in patients with negative serum procalcitonin (< 2 ng/dL) at 3 postoperative days was shorter (median of 3 days) compared to those who presented a positive serum procalcitonin (≥ 2 ng/dL), this difference was statistically significant ($p < 0.05$), as described in Table 9.

Additionally, an early reoperation (median of 4 days) was evident in the patients with positive procalcitonin, compared to those who had negative procalcitonin on the third postoperative day. Despite not being a statistically significant difference ($p = 0.20$), it is important in the context of the patient with anastomotic leak, since it positively influences the morbidity and mortality associated with this pathology, where it is not usual to re-operate before the fifth postoperative day.

Discussion

Anastomotic leakage is one of the most morbid complications of intestinal anastomoses, with an incidence between 2%–7% reported in world experience centers,¹ being in the range described (6.75%) in our cohort. Until now there is no knowledge of the exact pathophysiology of the generation of the anastomotic leak, multiple theories try to explain this phe-

Table 7 – Association between anastomotic leak and other independent variables with the Fisher test or X² test.

Variables	N	Percentage	OR	Exact Fisher Test
Male	6	2,53	0,62	p 0,36
Comorbidities	13	5,49		1,00
More than one comorbidity	8	3,38		0,39
Active cancer ^a (immunosuppression)	12	5,06		0,70
Diabetes mellitus	1	0,42		0,47
Arterial hypertension	6	2,53	1,04	0,94
Chronic kidney disease	1	0,42		0,35
Chronic Gastritis	2	0,84		0,32
Familial Adenomatous Polyposis	1	0,42		0,29
Urgent surgery	5	2,11		0,07
Laparoscopic assessment	5	2,11		0,02
Procalcitonin positive at 3rd postoperative day*	9	3,80	4,29	0,003
Procalcitonin positive at 5th postoperative day	1	0,42		0,51
Mortality	4	1,69		0,00
Re-operation	15	6,33		0,00
Out-patient control	12	5,06		0,00
Hospital readmission	5	2,11		0,00

^a X² Test with a grade of liberty: 0,83 OR 0,62 [IC 95% 0,18 – 1,95] p 0,36.

* X² Test with a grade of liberty: 8,68 OR 4,29 [IC 95% 1,34 – 14,16] p 0,003.

Table 8 – Association between intestinal anastomotic leak and other quantitative variables by U Mann–Whitney.

Variables	Anastomotic leak		p value
	(+) ^a	(-)	
Age (years)	66,5	66,0	0,29
BMI (Kg/m ²)	23,5	25,0	0,08
PCT value at 3rd POP day	4,1	0,7	0,00
Length of hospital stay (days)	10,0	3,0	0,00
Number of out-patient consult	5,0	4,0	0,18
Days of Postoperative follow-up	17,0	3,0	0,07

^a 16 patients with anastomotic leak in the studied cohort, with a median of 5,5 days for postoperative diagnosis.

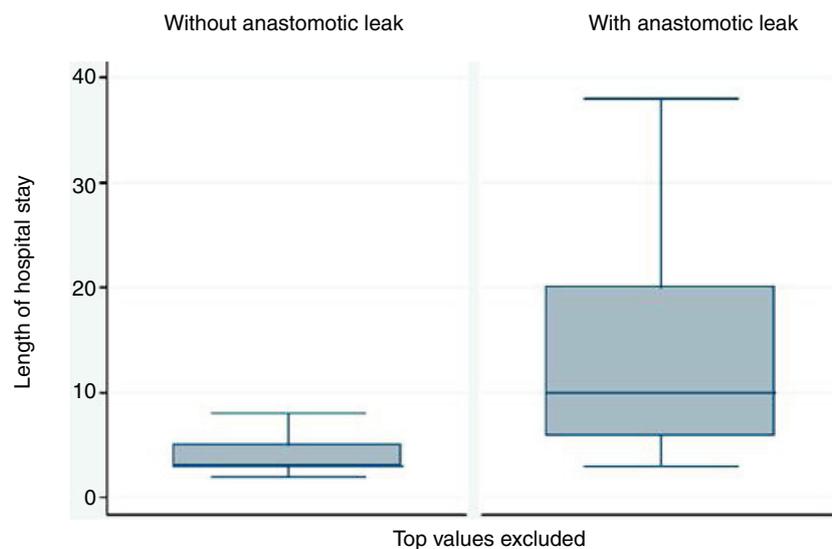
**Fig. 3 – Distribution of hospital stay according to the presence of anastomotic leak.**

Table 9 – Association between intestinal anastomotic leak and other quantitative variables by U Mann-Whitney.

Variables	Procalcitonin at 3rd postoperative day (Median)		p value
	(+) ^a	(-)	
Age (years)	69,0	64,0	0,04
BMI (Kg/m ²)	25,0	25,0	0,78
PCT value at 3rd POP day	4,2	0,4	0,00
POP day of diagnosis of anastomosis leak	5,0	6,0	0,59
Postoperative reintervention day ^b			
Length of hospital stay (days)	4,0	6,5	0,20
Number of out-patient consult	7,0	3,0	0,00
Days of postoperative follow-up	4,0	4,0	0,19
	8,0	7,0	0,31

^a 16 patients with anastomotic leak in the studied cohort.
^b 19 patients re-operated with positive procalcitonin at 3rd postoperative day.

nomenon, determining that the submucosa layer is in charge of generating the tensile force of the anastomosis. It has also been identified that the Bacteria lodged between the layers of the anastomosed intestinal wall play a fundamental role and are involved in the healing process after performing an intestinal anastomosis.⁶

In different studies, risk factors that may be determining for the presentation or not of intestinal anastomotic leak have also been identified, including anastomosis less than 6 cm from the anal border, preoperative radiation, presence of intraoperative adverse events and male gender,⁷ in other studies it was identified that adult patients, malnourished, with a long operative time,⁶ obesity, tobacco use, alcohol consumption, ischemia, use of Steroids are the patient's own factors that determine the presence of an intestinal anastomotic leak.⁸ In this study it was possible to show that within the risk factors for this population include advanced age, body mass index, immunosuppression from cancer, ingestion of corticosteroids or immunomodulators were determining factors for anastomotic leakage in intestinal anastomoses.

Other important issue is the time of diagnosis, it shows that a delay in diagnosis is reflected in major risk of death,^{9,10} that is reported in 24-39%.¹¹ In Colombia one study report that the incidence of anastomotic leak its 10.8%.¹² In this study it was possible to show that within the risk factors for this population include advanced age, body mass index, immunosuppression from cancer, ingestion of corticosteroids or immunomodulators were determining factors for anastomotic leakage in intestinal anastomoses.

Takakura et al. compare procalcitonin, with other inflammatory markers, as predictors of infection at the surgical site, finding that procalcitonin is a more reliable biomarker for early diagnosis.¹³ Additionally Di Filippo et al. 2003 establishes that 24 h after the surgical procedure, there is a significant increase in procalcitonin values in patients with anastomotic leak compared to those without it.¹⁴

Anastomotic leakage generates an increase in the reoperation rate, length of hospital stay, increased costs and worse long-term oncological results.¹⁵ The course of this entity can be insidious and difficult to recognize, manifesting as intra-abdominal sepsis.¹⁶ This creates diagnostic difficulties for the

surgeon, Karliczek et al. Reports that the predictive precision of the specialist surgeon to make the diagnosis of anastomotic leakage is about 50% of the cases.¹⁷

Recently, many studies have focused on the use of procalcitonin as specific and especially early biomarker in systemic inflammation, sepsis and infection.¹⁸ Procalcitonin is a protein with a very low concentrations in healthy individuals.¹⁹ Hyperprocalcitoninemia manifests itself in systemic inflammation or infection.^{18,19}

Takakura et al. Reports that procalcitonin is the most reliable biomarker for the early diagnosis of anastomotic leak.²⁰ Oberhofer et. al. In 2012, established that procalcitonin on day 2 has a better predictive value for the diagnosis of infectious complications after colorectal surgery.²¹ Zawadzki M et al. Establishes that in the postoperative period of colorectal surgery, procalcitonin increases on days 1-3 in all patients and the measurement of procalcitonin on postoperative day 3 presented a sensitivity of 75% and a specificity of 100% for patients with anastomotic leak.²²

The latter presented a statistically significant relationship with the presence of anastomotic leak in the immediate postoperative, it is of great importance to report that, like other studies, neither diabetes mellitus, nor chronic kidney disease, nor emergency surgery presented a statistically significant relationship with the presence of anastomotic leakage.²³

In this study, the presence of anastomotic leak was evidenced in 6.75% of the patients corresponding to 16 patients. In the general consolidated data, it was found that procalcitonin was positive on the third day in 25% of all included patients, mortality was evidenced in 2.95% of patients and a total 11.39% of patients underwent surgery.

Within our study, it was evident that the most performed anastomosis during the study time was the colorectal anastomosis, with a total percentage of 44.3%. Among all of the anastomosis performed, the one that presented the highest tendency to anastomotic leak was the ileocolic with 43.7%, which contrasts the globally known fact that colorectal anastomosis is a determining factor for the presence of anastomotic leakage.⁷ Among the results that we obtained, the colorectal anastomosis presented 25% of anastomotic leak, placing it in the second place of anastomotic leak incidence.

In this study, the length of stay was determined for patients with positive procalcitonin and those with a negative result, showing that those with anastomotic leak had a median hospital stay of 10 days, finding a statistically significant difference with respect to those who did not leak. Those patients with a negative procalcitonin and no other symptoms received medical discharge at 3 day of postoperative management, which contrasts with a previous result obtained by this same service, they documented a length of stay of 8.2 days.²⁴ This result impacts in the literature and the protocols that can be established in this institution, all of this with the aim of improving the management of patients, the diagnostic of complications and aiming reducing hospital total costs.

In this group of studied patients, the use of procalcitonin allowed to perform an early reoperation with a median of 4 days, without a statistically significant difference, but in the context of a patient with anastomotic leak, it can positively influence the patient's clinical-surgical outcomes.

When the analysis of central trends and dispersion of the clinical variables of the study was carried out, it was evidenced that age, value of procalcitonin on the third day and hospital stay are related to the presence of anastomotic leak. The average day of anastomotic leak diagnosis is 8.16 days with a minimum of 3 and a maximum of 36 days. When the association analysis between procalcitonin and anastomotic leakage was performed, it was shown that for procalcitonin values greater than 2 ng/dL, there is an increase in 4.28 fold risk of presenting anastomotic leak compared to patients with negative procalcitonin, with a statistically significant difference for the diagnosis of anastomotic leak. This confirms and establishes in agreement with the world literature that it is an adequate early marker of anastomotic leakage.

Conclusion

Anastomotic leakage continues to be an important source of morbidity in patients undergoing intestinal anastomoses. It is necessary to guarantee an early diagnosis of this postoperative complication to prevent local abscesses and subsequent secondary peritonitis, providing adequate and timely treatment, and even reducing related mortality, our results showed it to be a useful tool for this purpose.

We recommend including procalcitonin in the assessment protocol on the third day of postoperative follow-up given the association reported by this study.

Ethical aspect

This work follows the legal and ethical guidelines of the country, also those referred to in the Declaration of Helsinki of the World Medical Association (Principles Ethics for Research Involving Human Subjects, Last Modified Edinburgh, Scotland, October 2000).

Additionally, it is classified as Research without Risk, since it is a study that employs retrospective documentary research techniques and methods in which there is no performs any intentional intervention or modification of biological variables, physiological, psychological or social of the individuals

participating in the study, among the considered: review of medical records, databases and others, in which there is no identify or treat sensitive aspects of their behavior in accordance with the provisions of Art. 11 of Resolution No. 008430 of 1993 of the Ministry of Health of the Republic of Colombia (Scientific, technical and administrative standards for health research).

Conflict of interest

The authors declare no conflicts of interest.

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REFERENCES

1. Giaccaglia V, Salvi PF, Cunsolo GV, Sparagna A, Antonelli MS, Nigri G, et al. Procalcitonin, as an early biomarker of colorectal anastomotic leak, facilitates enhanced recovery after surgery. *J Crit Care*. 2014;29:528–32.
2. Giaccaglia V, Salvi PF, Antonelli MS, Nigri G, Pirozzi F, Casagrande B, et al. Procalcitonin reveals early dehiscence in colorectal surgery: the PREDICS study. *Ann Surg*. 2016;263:967–72.
3. Ramos Fernández M, Rivas Ruiz F, Fernández López A, Loinaz Seguro C, Fernández Cebrián JM, de la Portilla de Juan F. Proteína C reactiva como predictor de fuga anastomótica en cirugía colorrectal. Comparación entre cirugía abierta y laparoscópica. *Cirugía Española*. 2017;95:529–35.
4. 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;253:890–9.
5. Lagoutte N, Facy O, Ravoire A, Chalumeau C, Jonval L, Rat P, et al. C-reactive protein and procalcitonin for the early detection of anastomotic leakage after elective colorectal surgery: Pilot study in 100 patients. *J Visceral Surg*. 2012;149:e345–9.
6. Bosmans JWAM, Jongen ACHM, Bouvy ND, Derikx JPM. Colorectal anastomotic healing: why the biological processes that lead to anastomotic leakage should be revealed prior to conducting intervention studies. *BMC Gastroenterol* [Internet]. 2015. Dec [cited 2019 Nov 20];15(1). Available from: <http://www.biomedcentral.com/1471-230X/15/180>
7. Hayati F, Mohd Azman ZA, Nasuruddin DN, Mazlan L, Zakaria AD, Sagap I. Serum procalcitonin predicts anastomotic leaks in colorectal surgery. *Asian Pac J Cancer Prev*. 2017;18:1821–5.
8. Garcia-Granero A, Frasson M, Flor-Lorente B, Blanco F, Puga R, Carratalá A, et al. Procalcitonin and C-reactive protein as early predictors of anastomotic leak in colorectal surgery: a prospective observational study. *Dis Colon Rectum*. 2013;56:475–83.
9. Levy MM, Evans LE, Rhodes A. The surviving sepsis campaign bundle: 2018 update. *Crit Care Med*. 2018;46:997–1000.
10. Skandalakis JE. *Skandalakis' cirugía: bases de la anatomía quirúrgica*. Madrid: Marbán; 2015.

11. Hirst NA, Tiernan JP, Millner PA, Jayne DG. Systematic review of methods to predict and detect anastomotic leakage in colorectal surgery. *Colorectal Dis.* 2014;16:95–109.
12. Pacheco MA, Aldana GE, Martínez LE, Forero JC, Gómez CA, Coral EM, et al. Incidencia de falla anastomótica en intestino delgado, colon y recto, Bogotá, Colombia. *Rev colomb cir.* 2017;32:269–76.
13. Reith HB, Mittelkötter U, Wagner R, Thiede A. Procalcitonin (PCT) in patients with abdominal sepsis. *Intensive Care Medicine.* 2000;26:S165–9.
14. Di Filippo A, Lombardi A, Ognibene A, Messeri G, Tonelli F. Procalcitonin as an early marker of postoperative infectious complications. *Minerva Chir.* 2002;57:59–62.
15. Reisinger KW, Poeze M, Hulsewé KWE, van Acker BA, van Bijnen AA, Hoofwijk AGM, et al. Accurate prediction of anastomotic leakage after colorectal surgery using plasma markers for intestinal damage and inflammation. *J Am Coll Surg.* 2014;219:744–51.
16. Su'a BU, Mikaere HL, Rahiri JL, Bissett IB, Hill AG. Systematic review of the role of biomarkers in diagnosing anastomotic leakage following colorectal surgery. *Brit J Surg.* 2017;104:503–12.
17. 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.
18. Nargis W, Ahamed B, Ibrahim M. Procalcitonin versus C-reactive protein: usefulness as biomarker of sepsis in ICU patient. *Int J Crit Illness Injury Sci.* 2014;4:195.
19. Maruna P, Nedelniková K, Gürlich R. Physiology and genetics of procalcitonin. *Physiol Res.* 2000;49 Suppl 1:S57–61.
20. Takakura Y, Hinoi T, Egi H, Shimomura M, Adachi T, Saito Y, et al. Procalcitonin as a predictive marker for surgical site infection in elective colorectal cancer surgery. *Langenbeck's Arch Surg.* 2013;398:833–9.
21. Oberhofer D, Juras J, Pavčić AM, Rancić Zurić I, Rumenjak V. Comparison of C-reactive protein and procalcitonin as predictors of postoperative infectious complications after elective colorectal surgery. *Croat Med J.* 2012;53:612–9.
22. Zawadzki M, Czarnecki R, Rzaca M, Obuszko Z, Velchuru VR, Witkiewicz W. C-reactive protein and procalcitonin predict anastomotic leaks following colorectal cancer resections – a prospective study. *Videosurge Other Miniinvasive Tech.* 2015;4:567–73.
23. Nam HO, Kim Jong. Outcomes and risk factors affecting mortality in patients who underwent colorectal emergency surgery. *Ann Coloproctol.* 2016;32:133–8.
24. Agudelo L, Figueroa C, Isaza-Restrepo A, Monroy A, Padrón J. <http://repository.urosario.edu.co/handle/10336/11811>, 2015.