ORIGINAL ARTICLE

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C-reactive protein as postoperative complications predictor of colorectal surgeries

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ABSTRACT - Background - The use of inflammatory markers in order to accurate the diagnosis, decrease the reoperation rate and enable earlier interventions during the postoperative period of a colorectal surgery is increasingly necessary, with the purpose of reducing morbimortality, nosocomial infections, costs and time of a readmission. Objective - To analyze C-reactive protein level on the third postoperative day of an elective colorectal surgery and compare the marks between reoperated and non-reoperated patients and to establish a cutoff value to predict or avoid surgical reoperations. Methods - Retrospective study based on the analysis of electronic charts of over 18-year-old patients who underwent an elective colorectal surgery with primary anastomoses during the period from January 2019 to May 2021 by the proctology team of Santa Marcelina Hospital Department of General Surgery with C-reactive protein (CRP) dosage taken on the third postoperative day. Results - We assessed 128 patients with a mean age of 59.22 years old and need of reoperation of 20.3% of patients, half of these due to dehiscence of colorectal anastomosis. Comparing CRP rates on the third postoperative day between non-reoperated and reoperated patients, it was noted that in the former group the average was of 153.8±76.2 mg/dL, whereas in reoperated patients it was 198.7±77.4 mg/dL (P<0.0001) and the best CRP cutoff value to predict or investigate reoperation risk was 184.8 mg/L with an accuracy of 68% and negative predictive value of 87.6%. Conclusion - CRP levels assessed on the third postoperative day of elective colorectal surgery were higher in patients who were reoperated and the cutoff value for intra-abdominal complication of 184.8mg/L presented a high negative predictive value.

Keywords – Colorectal surgery; reoperation; C-reactive protein; accuracy; negative predictive value.

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INTRODUCTION

The use of inflammatory markers in patients who underwent colorectal surgery as an early predictor of anastomotic dehiscence still challenges researchers and supporting staff.

Complications that demand invasive treatment, such as percutaneous drainage, reoperation or support of the intensive care unit (ICU) are reported to be up to 19% of the patients who underwent major abdominal surgery⁽¹⁻⁴⁾. Among the surgical complications, anastomotic leak and related complications, is one of the most feared one and, even with postoperative care (PC), its occurrence fluctuates between 2 and 14% and around 6 to 25% of the patients are reoperated within the first 30 days after the colorectal resection⁽⁵⁻⁹⁾.

Numerous researches in the literature elicit the risk factors, both clinical and surgical ones^(4,10-12), however, not unusually, the diagnosis of postoperative anastomotic leak not always happen in due time to achieve a satisfactory resolution^(2,13).

Thus, the use of blood markers to attempt to reach an accurate diagnosis, to reduce reoperation rate and to enable earlier interventions is increasingly necessary, in order to seek to reduce morbimortality, nosocomial infections, costs and time of a reoperation^(1,14). Among the blood markers, one can use C-reactive protein (CRP), a non-specific inflammatory marker of acute phase, synthesized by short-lived half-lives hepatocytes^(7,14-20) – around 19 hours –, that rapid normalizes in situations of favorable clinical evolution^(19,21,22).

Objective

To analyze CRP level on the third postoperative day of an elective colorectal surgery and compare the marks between non-reoperated and reoperated patients. Furthermore, this paper aims at establishing a cutoff value to predict or avoid surgical reinterventions.

METHODS

Retrospective study based on the analysis of electronic charts of over 18-year-old patients who underwent an elective colorectal surgery with primary anastomoses during the period from January 2019 to May 2021 by the coloproctology team of Santa Marcelina Hospital Department of General Surgery. Patients who did not have their dosage of CRP taken in this period postoperative day, who lacked anastomoses, who had emergency surgery and who had charts with incomplete data were excluded from this study.

The study evaluated data related to age, sex, type of surgery (right hemicolectomy, left hemicolectomy or rectosigmoidectomy), acess route (laparotomy or laparoscopy), use of surgical staples, anastomosis height (for rectal and sigmoid surgery), confection of protective stoma, the length of the surgery in minutes, use of vasoactive drugs, hemotransfusion during the intraoperatorive period, postoperatorive in the ICU, nutritional postoperative therapy, necessity of reoperation and CRP values on the third postoperative day. The information is stored under secrecy and confidentiality, it is presented in a cluster, not allowing the identification of patients, and utilized only and exclusively for the purposes of this research.

Statistical analysis

The software program GraphPad Prism 9 was used to establish the inferential analysis. The Shapiro-Wilk test was applied in order to verify the abnormality of quantitative variables. In order to compare two continuous variables the student *t* test was applied, whereas for non-parametric samples the Mann-Whitney test was applied.

In order to compare qualitative variables the chi-squared test was applied. The CRP cutoff in the third postoperative day to predict reoperation was obtained by the Bioestat software through ROC curve. To all the analyses it was considered statistically significant P<0.05.

RESULTS

We assessed 128 patients who underwent elective colorectal surgery with intestinal anastomoses confection during the period from January 2019 to May 2021 by the coloproctology medical residency team of Santa Marcelina Hospital Department of General Surgery.

General data

The mean age was 59.22 years old (20–85 years) and 50.8% were female. Fifty-five patients (43%) underwent rectosigmoidectomy, 32 underwent bowel transit reconstruction (25%) – 65.5% colostomy and 34.5% loop ileostomy – 31 patients underwent right hemicolectomy (24.2%) and ten left hemicolectomy (7.8%). Also, 89.3% of the cases had laparotomy surgery.

During the preoperative period nutritional therapy was necessary for 15.6% of the patients. Surgical staples were used in the suture in 87 (68%) cases and a protective stoma was used in 16 (12.5%). Twenty patients (15.6%) needed vasoactive drugs during the postoperative period, 5.5% needed hemotransfusion and 17.2% needed recovering in the intensive care unit.

Comparison between non-reoperated and reoperated patients

Twenty and six (20.3%) patients needed reoperation during the same hospitalization, from this group 50% were reoperated due to dehiscence with overall rate of 10.15% of enteric fistula complications. From those patients who were reoperated for reasons that are not dehiscence, 5 (38.5%) of them were because of abdominal wall eventration, 4 (30.1%) of them because of intracavitary collection, 3 (23.1%) of them due to bands, and 1 (8.3%) of them because of bleeding.

When comparing the groups – reoperated and non-reoperated – no statistic difference was observed among the sex, suture with or without the use of surgical staples, confection or not of protective stoma, use of vasoactive drugs or the need for hemotransfusion, permanence in the ICU and preoperative nutritional therapy, as demonstrated in TABLE 1.

Comparing the percentage of reoperation to the initial surgery, it was noticed this intercurrence in 25.8% of the patients who underwent a right hemicolectomy, 24.1% of rectosigmoidectomy, 12.5% of those who had a bowel transit reconstruction and 10% left hemicolectomy.

TABLE 1. Comparison between reoperated and non-reoperated patients.
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		Non-reoperated	Reoperated	Total	Р
	Male	47 (37%)	16 (12%)	63	
Sex	Female	55 (43%)	10 (08%)	65	0.159
	Total	102	26	128	
	Yes	70 (55%)	17 (13%)	87	
Staples	No	32 (25%)	09 (07%)	41	0.751
	Total	102	26	128	
	Yes	14 (11%)	05 (04%)	19	
Stoma	No	88 (69%)	21 (16%)	109	0.468
	Total	102	26	128	
	Yes	13 (10%)	07 (05%)	20	
DVA use	No	89 (70%)	19 (15%)	108	0.075
	Total	102	26	128	
	Yes	05 (04%)	02 (1%)	7	
Hemotransfusion	No	97 (76%)	24 (19%)	121	0.576
	Total	102	26	128	
	Yes	19 (16%)	08 (06%)	27	
Postoperative ICU	No	80 (64%)	18 (14%)	98	0.202
	Total	99	26	125	
	Yes	14 (11%)	06 (04%)	20	
Preoperative nutritional therapy	No	88 (69%)	20 (16%)	108	0.241
	Total	102	26	128	

Analysis of rates of C-reactive protein in the third postoperative day

Comparing the rates of CRP on the third postoperative day between non-reoperated and reoperated patients, it was noted that in the former group the average was of 153.8 ± 76.2 mg/dL, whereas in reoperated patients it was 198.7 ± 77.4 mg/dL (*P*<0.0001) – FIGURE 1 and TABLE 2.

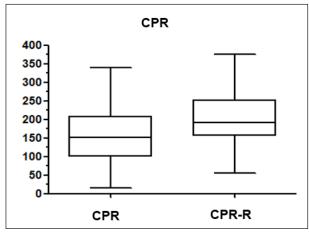


FIGURE 1. CRP values of non-reoperated patients to the left and reoperated patients to the right (*P*<0.0001). CRP: C-reactive protein.

TABLE 2. Data comparision between non-reoperated and reoperated patients.

Variables ·	Non-reoperated	Reoperated	P-value
variables –	Average	<i>P</i> -value	
CRP	153.8±76.2	198.7±77.4	<0.0001
AGE (years)	58.9±13.8	60.6±11.9	0.742
Surgical time (min)	217±79.2	209±58.05	0.972

SD: standard deviation.

In TABLE 2, beyond these data, it was noticed that the average age between the groups was similar (58.9 years (\pm 13.8 years) x 60.6 years (\pm 11.9 years) *P*=0.742). Similarly, the surgical time in the procedures of patients who did not have to be reoperated was similar to the ones who needed reoperation (217 minutes (\pm 79.2 minutes) x 209 minutes (\pm 58.05 minutes) *P*=0.972).

When analyzing the best CRP cutoff value in order to foretell or investigate the risk of reoperation, it was obtained 184.8 mg/dL with an accuracy of 61.5%, specificity of 69.9%, positive predictive value of 34% and negative predictive value of 87.6% as it is shown in FIGURE 2 and TABLE 3.

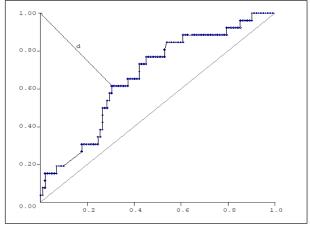


FIGURE 2. ROC curve of CRP. The point in which line d connects correspond the CRP cutoff value. CRP: C-reactive protein.

TABLE 3. CRP data analysis.

	ACC (95%Cl)	Cutoff value				NPV (%)
CRP	68	184.8	61.5	69.9	34	87.6

ACC: accuracy; CRP: C-reactive protein; sens: sensitivity; spec: specificity; PPV: positive predictive value; NPV: negative predictive value.

Among the patients with CRP higher than 184.8 mg/dL non-reoperated, 51.5% of them had other infectious complications, such as surgical site infection (64.7%), intestinal sub-occlusion (17.6%), pelvic abscess – lower than 4 cm – treated conservatively (11.8%) and bronchopneumonia (5.9%). TABLE 4, it is demonstrated the demographic characteristics of these patients.

DISCUSSION

This paper aims at analyzing the CRP values on the third postoperative day of elective colorectal surgery and verifying the correlation between these values and the readmission for surgery in a teaching hospital. According to the literature it is noted that CRP values during the postoperative period are considered an important tool in the early assessment of the main complications during this period^(5,7,8), complications that can lead to a delay in the adjuvant therapies and/or increase the morbidity to patients^(16,21,23).

The knowledge of specific risk factors of complications or anastomotic dehiscence certainly implies better prevention and intensive postoperative follow-up of high risk patients.

Sex	Mean age	CRP average value	Necessity of preoperative nutritional therapy	Necessity of ICU during the postoperative period	Identification of infection
54.5% women	60.3 years old	247.9 mg/dL	15.2%	33.3%	51.5%

TABLE 4. Demographic characteristics of patients with CRP higher than 184.8 mg/dL non-reoperated.

CRP: C-reactive protein; ICU: intensive care unit.

General data

The mean age of this study is similar to other studies, as well as the sex percentage^(6,17,24). Regarding the surgical procedures executed, most of our patients were submitted to rectosigmoidectomy, followed by a bowel transit reconstruction and right hemicolectomy. Pantel et al.⁽¹⁷⁾, on the other hand, indicate a higher number of left hemicolectomy.

Garcia-Granero and co-authors⁽⁶⁾, similarly to this study, have also observed a higher percentage of patients who underwent left colon surgery or rectal surgery with procedures related to benign pathology in 26,8%, likewise the cases presented in this study (25%).

Pantel et al.⁽¹⁷⁾ after analyzing the CRP levels on the third postoperative day in 752 patients performed a minimally invasive surgery in 74% of cases, whereas we only used this access route in 10.7%. Besides that, it was shown that the levels of general CRP are higher in laparotomy surgery statistically significant (*P*=0.0000002), what might explain, among other factors, the higher cutoff level of this marker in our study and perhaps the lower values of sensibility and specificity of inflammatory marker as well.

Comparison between non-reoperated and reoperated patients

The percentage of reoperation for anastomotic dehiscence in this current study was higher than the average of other studies, in which one finds an overall rate between 2 to 8.3 $\%^{(6,17)}$, while we observed this occurrence in 10.15%. However, the literature indicates an incidence up to 20% of complications with colonic anastomoses with mortality rate of about 22% in these cases^(23,25).

Faron et al.⁽²⁴⁾, likewise our study, have demonstrated 21.6% of postoperative intra-abdominal complication after a colorectal surgery and, besides that, performed laparotomy surgery in a higher percentage (37% of cases). They also noticed that the construction of a protective stoma was a factor associated to a greater incidence of intra-abdominal complications (P<0.0001). We, on the other hand, did not observe such correlation (P=0.468).

Regarding the CRP level on the third postoperative day, when comparing patients who needed reoperation to those who did not have to be reoperated, this study observed a meaningful difference in the values of this inflammatory marker (P<0.0001). Pantel and contributors⁽¹⁷⁾ also registered this difference between reoperated or non-operated patients (P=0.00000002), the same way as Garcia-Granero did it (P<0.0001)⁽⁶⁾.

Analysis of CRP levels on the third postoperative day

Measuring the CRP between the third and the fifth postoperative day of colorectal surgery is considered to present a higher sensitivity and negative predictive value possible⁽²⁶⁾. Thus, collecting the CRP level on the third postoperative day was adopted as a method. Besides that, this study corroborates the literature that considers CRP levels during the postoperative period as an important early assessment tool of postoperative complications, mainly in non-symptomatic patients^(5,8,9).

According to some papers, after elective colorectal surgery, CRP level on the third postoperative day higher than 140 mg/L presents 25% of chance of forewarning serious complication^(18,20,23). Moreover, patients who got discharged with CRP level superior to 100 mg/L presented higher risk of developing intra-abdominal complications at home, leading to readmission (P=0.0008)⁽²¹⁾.

Pantel and contributors⁽¹⁷⁾ analyzed 752 patients who underwent colorectal surgery and verified that, for hospital readmission, CRP accuracy was 59%, using a cutoff value of 145 mg/L and negative predictive value of 93%. In the same way, the accuracy value for dehiscence of anastomosis was 76% with a cutoff value of 147 mg/L and a negative predictive value of 99%. In this study, it was observed 68% of accuracy (confidence interval of 95%) with CRP cutoff value, for reoperation, of 184.8 mg/L and negative predictive value of 87.6%.

Similarly to this study, these authors⁽¹⁷⁾ demonstrated, using CRP cutoff value of 145 mg/L, low sensitivity and specificity for both hospital readmission (52% and 66%, respectively) and dehiscence of anastomosis (82% and 66%, respectively).

Critical appraisal

This paper is a retrospective study conducted in only one standard CRP collection center on the third postoperative day of elective colorectal surgery that has shown a statistically meaningful difference in the value of this marker between reoperated and non-reoperated patients. Besides that, it has been possible to obtain a cutoff value based on our data.

Study limitations

The analysis of CRP value only on the third postoperative day might present a confusion factor, notably in patients with colorectal neoplasia, once their baseline values might be higher, specially due to inflammatory alterations observed in these patients. Therefore, the assessment of the difference between the values of this marker before and after the surgery may have a greater clinical relevance as well as the categorization of these data between laparoscopy and laparotomy surgeries.

CONCLUSION

The CRP levels assessed on the third postoperative day of elective colorectal surgery were higher in reoperated patients and the cutoff value for intra-abdominal complications of 184.8 mg/L presented a high negative predictive value.

Authors' contribution

Theis C, Schelle G, Robles AG: data collecting. Nishiyama VKG: statitics analysis. Correa Neto IJF: writing the paper. Robles L: reviewing and final comments.

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RESUMO – Contexto – O uso de marcadores sanguíneos para tentar acurar o diagnóstico, reduzir a taxa de readmissão e possibilitar intervenções mais precoces no pós operatório de cirurgia colorretal é cada vez mais necessário, a fim de almejar reduzir a morbimortalidade, infecções nosocomiais, custos e tempo de uma reinternação. Objetivo – Analisar o nível da proteíne C reativa (PCR) no terceiro dia de pós-operatório de cirurgia colorretal eletiva e comparar os valores entre pacientes reoperados e não reoperados e estabelecer um valor de corte para prever ou afastar re-intervenção cirúrgica. Metodos – Estudo retrospectivo através da análise de prontuários eletrônicos de pacientes maiores que 18 anos submetidos a cirurgia colorretal de forma eletiva com anastomoses primárias no período de janeiro de 2019 a maio de 2021 pelo serviço de Coloproctologia do Departamento de Cirurgia Geral do Hospital Santa Marcelina com dosagem da PCR no 3º pós-operatório. Resultados – Foram avaliados 128 pacientes com média de idade de 59,22 anos e necessidade de reoperação em 20,3% dos pacientes, sendo metade desses por deiscência de anastomose colorretal. Ao se comparar os valores de PCR no 3º pós operatório entre os pacientes não reoperados e os reoperados, observou-se que nos primeiros a média foi de 153,8±76,2 mg/dL, enquanto nos pacientes reoperados foi de 198,7±77,4 mg/dL (*P*<0,0001) e, o melhor valor de corte de PCR para predizer ou investigar o risco de reoperação, foi 184,8 mg/ dL com uma acurácia de 68% e valor preditivo negativo de 87,6%. Conclusão – Os níveis de PCR avaliados no 3º pós-operatório de cirurgia colorretal eletiva foram maiores em pacientes reoperados e o valor de corte para complicações intra-abdominal de 184,8 mg/L apresentou elevado valor preditivo negativo.

Palavras chaves - Cirurgia colorretal; reoperação; proteína C reativa; acurácia; valor preditivo negativo.

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