Revista Portuguesa de Cirurgia

II Série • N.° 33 • Junho 2015

ISSN 1646-6918

Órgão Oficial da Sociedade Portuguesa de Cirurgia

Neutrophil-to-eosinophil ratio is predictor of surgery in acute diverticulitis

A relação neutrófilos/eosinófilos é preditiva de cirurgia na diverticulite aguda

Gisela Marcelino[1], Nuno Carvalho[2**], Gabriel Oliveira[3**], Celso Marialva[4**], Rafaela Campanha[5**], Diogo Albergaria[6**], Carlos Santos[2**], Rui Lebre[2**], João Corte-Real[7**]*

[1] Interna de Medicina Interna, [2] Assistente Graduado de Cirurgia Geral, [3] Assistente Hospitalar de Cirurgia Geral, [4] Interno de Urologia, [5] Interna de Pneumologia, [6] Interno de Cirurgia Geral, [7] Chefe de Serviço de Cirurgia Geral

[*] Service de Gériatrie, Hôpital des Trois-Chêne, Thônex, Suisse

[**] General Surgery Department, Hospital Garcia de Orta, Almada, Portugal

We, the authors, state that NC was in charge of the conception of the article, that GM was responsible for the statistical analysis, that GO, CM and RC were responsible for the data collection and that all authors scientifically reviewed the paper and made major modifications regarding its intellectual content and gave their final approval of the version to be submitted.

Abbreviations: CRP, C-reactive protein; CT, computed tomography; NER, neutrophil-to-eosinophil ratio; NLR, neutrophil-to-lymphocyte ratio; PER, platelet-to-eosinophil ratio; PLR, platelet-to-lymphocyte ratio

ABSTRACT

Background: Patients with acute diverticulitis (AD) and Hinchey<III may also need surgery. Therefore, as other markers are needed to help deciding which patients should be operated on, we tried to test the value of the C-reactive protein (CRP) and of blood cell count (and their ratios). **Methods:** Retrospective chart review of patients admitted to our surgical department between 2009 and 2011 with the diagnosis of AD. Only cases with a computed tomography confirmation were included in the study. **Results:** 174 patients (147 men, 27 women, age range 24-93 years) presented with AD. 161 patients had a modified Hinchey classification <III and 17 patients were submitted to surgery (7 had Hinchey III or IV and 10 had Hinchey<III). The neutrophil-to-eosinophil ratio (NER) had the best discriminant value in deciding for a surgical procedure in the ROC (receiver operating characteristics) curve. NER discriminated non-surgical and surgical treatment with an area under the ROC curve of 0.86 (95% confidence interval (CI), 0.79-0.92). The cut-off>244.25 yielded a sensitivity of 80% (95% CI, 44-98%), a specificity of 86% (95% CI, 79-92%), a positive likelihood ratio of 5.85 (95% CI, 3.40-10.10) and a negative likelihood ratio of 0.23 (95% CI, 0.07-0.80). In fact, NER>244.25 successfully predicted 15 out of 17 cases that were operated on in our sample. **Conclusions:** NER is a good marker in discriminating those that should be operated on regardless of the Hinchey category. However, more studies are needed to confirm these data.

Key words: *acute diverticulitis, C-reactive protein, neutrophil-to-eosinophil ratio, surgery.*

RESUMO

Objectivo: Doentes com diverticulite aguda e Hinchey <III podem também necessitar de cirurgia. Assim, como outros marcadores são necessários para ajudar a decidir quais os doentes que devem ser operados, tentámos avaliar o valor da proteína C reactiva (CRP) e da contagem de células sanguíneas (e os seus rácios). **Métodos:** Revisão retrospectiva do ficheiro clínico de doentes admitidos no nosso serviço de cirurgia entre 2009 e 2011 com o diagnóstico de diverticulite aguda. Apenas os casos que tiveram confirmação diagnóstica com tomografia computorizada foram incluídos no estudo. **Resultados:** 174 doentes (147 homens, 27 mulheres, amplitude de idade 24-93 anos) apresentaram diverticulite aguda. 161 doentes tinham uma classificação modificada de Hinchey<III e 17 doentes foram submetidos a cirurgia (7 tinham Hinchey III ou IV e 10 tinham Hinchey<III). O rácio neutrófilos-eosinófilos (NER) tinha o melhor valor discriminativo na tomada de decisão cirúrgica na curva ROC (receiver operating characteristics). NER discriminou não cirurgia de cirurgia com uma área abaixo da curva de 0,86 (intervalo de confiança a 95% (IC), 0,79-0,92). O ponto de corte >244,25 tinha uma sensibilidade de 80% (IC 95%, 44-98%), uma especificidade de 86% (IC 95%, 79-92%), um valor preditivo positivo de 5.85 (IC 95%, 3,40-10,10) e um valor preditivo negativo de 0,23 (IC 95%, 0,07-0,80). De facto, NER>244,5 conseguiu prever 15 dos 17 casos operados na nossa amostra. **Conclusão:** O NER é uma boa variável para discriminar os doentes que deveriam ser operados independentemente da categoria de Hinchey. No entanto, mais estudos são necessários para confirmar estes dados.

Palavras chave: *diverticulite aguda, proteína C reactiva, relação neutrófilos/eosinófilos, cirurgia*

INTRODUCTION

Colon diverticular disease is common in the Western population[1] affecting more than 50% of individuals over 60 years of age[2]. Up to 25% of these individuals will develop symptomatic diverticulitis, and 15–20% of these, will develop significant complications such as perforation, abscess, phlegmon, obstruction or bleeding[1].

Indication for surgery depends on several factors such as clinical presentation, physical examination, extent and severity of the disease or comorbidities[3-5]. The Hinchey's grading system describes the severity of acute diverticulitis and stratifies the risk of fatal events[6]. In the presence of purulent or faecal peritonitis (Hinchey stages III and IV), surgical indication is straightforward. On the other hand, management of Hinchey stages lower than III is generally conservative. However, there are cases with Hinchey lower than III where surgery is considered the best treatment[1]. Therefore, other markers of severity are still lacking.

Diverticulitis is an inflammatory and infectious disease with important local and systemic repercussions[2]. We also know that blood cells can signalize the gravity of very different distinct diseases and that they can also guide their treatment[7-8]. Eosinopenia has long been known as a marker of acute infection and has been used as a diagnostic marker of sepsis and mortality in newly admitted critically ill patients[8]. Likewise, in patients admitted to hospital with exacerbations of chronic obstructive pulmonary disease, eosinopenia was identified as a marker of mortality and length of hospital stay[7]. Additionally, neutrophil-to-lymphocyte ratio (NLR) has been considered as a prognostic factor in colorectal cancer[9-10]. As for acute diverticulitis, it seems that C-reactive protein (CRP) can predict more severe course of the disease[11].

Therefore, we tried to test the value of CRP and of blood cell count (and their ratios) at admission in the decision to operate on patients with acute diverticulitis.

MATERIAL AND METHODS

A retrospective study based on the chart review of patients admitted to a surgical department of a 600 hundred-bed general hospital with a diagnosis of acute sigmoid diverticulitis was performed from 2009 until 2011.

Patient's data were retrieved using the ICD-9 (International Classification of Diseases, 9^{th} Revision)[12] codes 562.13 and 562.11, referring to diverticulitis of the colon, with and without haemorrhage, respectively.

For this study, diverticulitis was defined by clinical presentation and required confirmation by computerized tomography (CT) [2]. Therefore, patients without a CT scan or with a negative CT scan were excluded. Modified Hinchey classification was used to stage disease severity[1].

Data collected included patients' age, gender, modified Hinchey classification (stage Ia: confined pericolic inflammation or phlegmon; stage Ib: pericolic or mesocolic abcess: stage II: pelvic, distant intraabdominal or retroperitoneal abscess, stage III: generalized purulent peritonitis; stage IV: generalized faecal peritonitis), other complications of diverticular disease (fistula, haemorrhage, stenosis or obstruction), length of hospital stay, treatment (conservative, percutaneous or surgery), comorbidities (considered as any condition that could induce an immunosuppressed state, like diabetes and leukopenia) and blood cell count (including platelets, leukocytes, neutrophils, lymphocytes, eosinophils, monocytes and basophiles). C-reactive protein (CRP) was also collected.

The study protocol was approved by the hospital ethics committee. Informed consent was not demanded because this observational study did not require any deviation from routine medical practice[13].

Statistical analyses were performed with parametric Student's T test for normal data, non-parametric Mann-Whitney and Kendall-Wallis Tests for non-normal quantitative variables, and Fisher Exact test and χ^2 test for qualitative variables. Correlations were performed using the Spearman's coefficient.

The best cut-off value was chosen using Youden's index. Receiver operating characteristic (ROC) curves and the respective areas under the curves were calculated for all blood parameters. The sensitivity, specificity, and positive and negative likelihood ratios (with 95% confidence intervals (CIs)) were calculated at the best cut-off value. The required sample size was also calculated for an area under the curve of 0.80, an α-level of 0.05 and a β-level of 0.10. Hence, the minimum number of positive and negative cases required was 8 and 73, respectively.

P-value was considered significant when <0.05. The majority of the statistical analyses were carried out using SPSS version 20.0 (SPSS, Inc., Chicago, USA). The ROC curves were performed using the MedCalc Software, version 13.0.0.0 for Windows.

RESULTS

Characteristics of the study sample

A total of 174 patients were admitted with acute diverticulitis, being 147 (84.5%) males and 27 (15.5%) females, average age 58.2 ± 13.8. Twenty (11.5%) had comorbidities. Most of the patients (n=161, 95.3%) had a modified Hinchey classification of 0-II and only 8 (4.7%) had Hinchey stage of III or IV (*see* table 1). Fifteen (8.6%) had other complications associated with acute diverticulitis like intestinal stenosis/obstruction (5.8%), fistulous tract (2.3%) or haemorrhage (1.1%). Conservative therapy was successful in most of the patients (87.2%, *see* table 1), and in those patients submitted to surgery (n=17), Hartmann procedure was the most frequently performed (data not shown). Finally, the median (interquartile range) of length of stay for all patients was 6.0 (IQR 3.0) days.

Diagnostic accuracy

No differences were detected between Hinchey stages 0-II and III-IV regarding gender distribution, age, comorbidities or number of past admissions with acute diverticulitis (*see* table 1). Still, length of stay was superior for the more severe stages as expected: patients with Hinchey III or IV and those submitted to surgery had medians of hospital stay of 13.5 and 11.0 days, respectively, comparing to the 4.0 days of median for the 0-II or conservative management group.

Table 1 – **Patients' characteristics are shown according to the modified Hinchey classification and need of surgery.**

	Modified Hinchey classification			**Surgery**		
	0-II	**III-IV**	*Test*	**No**	**Yes**	*Test*
Gender						
Male	138 (85.7)	7 (87.5)	$0.02^{\S\ \text{ns}}$	131 (84.5)	14 (82.4)	$0.05^{\S\ \text{ns}}$
Female	23 (14.3) (n=161)	1 (12.5) (n=8)		24 (15.5) (n=155)	3 (17.6) (n=17)	
Age (years)	58.1 ± 1.1	63.8 ± 4.4	0.16^{ns}			
Range	[24-93] (n=161)	[49-83] (n=8)		57.6 ± 1.1 [24-86] (n=155)	64.2 ± 3.0 (n=17) [45-93]	1.36^{ns}
Comorbidities	18 (11.2) (n=161)	2 (25.0) (n=8)	$1.40^{\S\ \text{ns}}$	18 (11.6) (n=155)	1 (5.9) (n=17)	$0.51^{\S\ \text{ns}}$
Other complications						
Fistula	4 (28.6)	–	NA	1 (11.1)	3 (42.9)	NA
Haemorrhage	1 (7.1)	–		2 (22.2)	–	
Stenosis or obstruction	9 (64.3) (n=14)	1 (100.0) (n=1)		6 (66.7) (n=9)	4 (57.1) (n=7)	
Treatment						
Conservative	147 (91.9)	–	NA	150 (96.8)	–	NA
Drainage of abscess	3 (1.9)	–		5 (3.2)	–	
Surgery	10 (6.3) (n=160)	7 (100.0) (n=7)		– (n=155)	17 (100.0) (n=17)	
Length of stay (days)	4.0 (3.0)	13.5 (21.2)	**119.0*****	4.0 (2.0)	11.0 (16.5)	
Range	[1-66] (n=161)	[5-35] (n=8)		[1-19] (n=155)	[5-66] (n=17)	**213.5*****
Nr of past admissions due to acute diverticulitis	0 (n=146)	0 (n=8)	528.0^{ns}	0 (n=141)	0 (n=16)	549.0^{ns}

Results are expressed as number (valid percentage) of individuals, mean ± standard deviation, or median (interquartile range). Range [minimum-maximum] is also presented for quantitative variables. Comparisons were performed with chi-square or Fisher's exact test (§) for qualitative variables, and with t-Student or Mann-Whitney for quantitative variables. CT, computed tomography; ns, not significant; NA, not accessible for statistical analysis; ***, p<0.001

Concerning blood parameters, platelet, white blood cell and monocyte count, they did not relate directly to severity or indication of surgery as they did not differ statistically ($p > 0.05$) between 0-II and III-IV Hinchey classes as well as between surgical status. (*see* table 2). However, eosinophil ($p < 0.05$), neutrophil ($p < 0.05$) and lymphocyte ($p < 0.01$) count was related to increasing Hinchey classes and need of surgery. In fact, eosinophil count decreased from 0.1×10^9/L to 0.04×10^9/L in Hinchey III-IV and to 0.02×10^9/L in those operated on; neutrophil increased from 8x10^9/L to 11.1x10^9/l in both Hinchey III-IV and in those who were operated on; and lymphocyte decreased to 1.0x10^9/L in both classes. In addition, the cases submitted to surgery had lower basophil count (0.02x10^9/L *versus* 0.04x10^9/L, $p < 0.01$) and higher CRP (24.2mg/dL *versus* 7.1mg/dL, $p < 0.01$) in comparison to those submitted to conservative therapy. Regarding the blood cell count ratios, the results were similar ($p<0.05$) for all ratios as they increased in patients who were operated on (*see* table 2). In contrast, platelet-to-eosinophil ratio (PER) and neutrophil-to-eosinophil ratio (NER) did not relate with Hinchey aggregated classes (*see* table 2).

TABLE 2 – **Blood parameters according to the modified Hinchey classification and surgery performance.**

	Modified Hinchey classification			**Surgery**		
	0-II	**III-IV**	*Test*	**No**	**Yes**	*Test*
CRP (mg/dL)	7.1 (12.6) (n=132)	13.6 (31.9) (n=5)	259.5^{ns}	7.1 (11.7) (n=126)	24.2 (30.2) (n=13)	**433.5****
Blood cell count (x10^9/L)						
Platelet	126.6 (85.0) (n=131)	233.5 (202.8) (n=6)	345.0^{ns}	233.5 (82.8) (n=126)	243.0 (127.8) (n=14)	721.0^{ns}
WBC	11.5 (5.5) (n=132)	13.0 (9.3) (n=6)	256.0^{ns}	11.5 (5.0) (n=127)	13.1 (4.3) (n=14)	666.5^{ns}
Neutrophil	8.5 (4.9) (n=132)	11.1 (10.5) (n=6)	**206.5***	8.3 (4.3) (n=127)	11.1 (3.9) (n=14)	**509.5****
Lymphocyte	1.9 (1.4) (n=132)	1.0 (0.5) (n=6)	**140.5****	1.9 (1.4) (n=127)	1.0 (0.7) (n=14)	**349.5*****
Eosinophil	0.1 (0.14) (n=132)	0.04 (0.08) (n=6)	**187.5***	0.1 (0.13) (n=127)	0.02 (0.05) (n=14)	**331.0*****
Monocyte	0.8 (0.4) (n=132)	0.6 (1.0) (n=6)	303.5^{ns}	0.8 (0.3) (n=127)	0.6 (0.6) (n=14)	670.0^{ns}
Basophil	0.03 (0.03) (n=132)	0.03 (0.04) (n=6)	297.0^{ns}	0.04 (0.04) (n=127)	0.02 (0.03) (n=14)	**487.0****
Ratios						
PLR	126.6 (109.3) (n=131)	245.9 (290.3) (n=6)		124.2 (108.1) (n=126)	245.9 (355.1) (n=14)	
PER	2107.4 (3502.4) (n=120)	6614.3 (3699.6) (n=4)		2019.7 (3291.9) (n=116)	6864.3 (18197.5) (n=10)	
NER	71.9 (124.9) (n=121)	250.2 (166.6) (n=4)		69.3 (99.4) (n=117)	306.5 (442.6) (n=10)	
NLR	4.7 (4.9) (n=132)	13.8 (15.8) (n=6)		4.3 (4.04) (n=127)	10.1 (15.1) (n=14)	

Results are expressed as median (interquartile range). Comparisons were performed with Mann-Whitney. CRP, C-reactive protein; NER, neutrophil-to-eosinophil ratio; NLR, neutrophil-to-lymphocyte ratio; PER, platelet-to-eosinophil ratio; PLR, platelet-to-lymphocyte ratio; WBC, white blood cell; ns, not significant; *, $p<0.05$; **, $p<0.01$; ***, $p<0.001$

As for the ROC curves, NER had the best discriminant value in the need of surgery in patients with acute diverticulitis with an area under the ROC curve of 0.86 (95% confidence interval (CI), 0.79 to 0.92). The cut-off NER>244.25 yielded a sensitivity of 80% (95% CI, 44 – 98%), a specificity of 86% (95% CI, 79 – 92%), a positive likelihood ratio of 5.85 (95% CI, 3.40 – 10.10) and a negative likelihood ratio of 0.23 (95% CI, 0.07 – 0.80). Although not statistically different from the ROC curve above, the NLR, the PER and the eosinophil and lymphocyte count had good values of area under the ROC curve: 0.84 (95% CI, 0.77 – 0.90), 0.82 (95% CI, 0.75 – 0.89), 0.81 (95% CI, 0.74 – 0.87) and 0.80 (95% CI, 0.73 to 0.87), respectively. As for the eosinophils, the cut-off <0.04x10^9/L yielded a sensitivity of 79% (95% CI, 49 – 95%), a specificity of 76% (95% CI, 67 – 83%), a positive likelihood ratio of 3.22 (95% CI, 2.10 – 4.90) and a negative likelihood ratio of 0.28 (95% CI, 0.10 – 0.80). CRP did not showed to be a good discriminant variable with an area under the ROC curve of 0.74 (95% CI, 0.65 – 0.81). The cut-off of 22.1mg/dL had a sensitivity of 61% (95% CI, 32 – 86%), a specificity of 89% (95% CI, 82 – 94), a positive likelihood ratio of 5.54 (95% CI, 2.90 – 10.70) and a negative likelihood ratio of 0.43 (0.20 – 0.90).

Table 3 – **Diagnostic performance of the various blood parameters in the prediction of surgery in patients with acute diverticulitis.**

Variable	**No surgery versus surgery**					
	Cut-off value	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio	Area under the receiver operating characteristic curve
CRP (mg/dL)	22.1	61 (32-86)	89 (82-94)	5.54 (2.90-10.70)	0.43 (0.20-0.90)	0.74 (0.65-0.81)
Blood cell count (x10^9/L)						
Platelet	288	43 (18 to 71)	79 (70 to 85)	2.00 (1.00 to 4.00)	0.73 (0.50 to 1.20)	0.59 (0.51 to 0.67)
WBC	12	71 (42 to 92)	59 (50 to 68)	1.74 (1.20 to 2.60)	0.48 (0.20 to 1.10)	0.63 (0.54 to 0.71)
Neutrophil	9.51	79 (49 to 95)	65 (56 to 73)	2.22 (1.50 to 3.20)	0.33 (0.10 to 0.90)	0.71 (0.63 to 0.79)
Lymphocyte	1.57	86 (57 to 98)	65 (56 to 74)	2.47 (1.80 to 3.40)	0.22 (0.06 to 0.80)	0.80 (0.73 to 0.87)
Eosinophil	0.04	79 (49 to 95)	76 (67 to 83)	3.22 (2.10 to 4.90)	0.28 (0.10 to 0.80)	0.81 (0.74 to 0.87)
Monocyte	0.48	43 (18 to 71)	88 (81 to 93)	3.63 (1.70 to 7.80)	0.65 (0.40 to 1.00)	0.62 (0.54 to 0.70)
Basophil	0.02	64 (35 to 87)	72 (63 to 79)	2.27 (1.40 to 3.70)	0.50 (0.20 to 1.00)	0.73 (0.65 to 0.80)
Ratios						
PLR	133.11	93 (66 to 99.8)	54 (45 to 63)	2.02 (1.60 to 2.60)	0.13 (0.02 to 0.90)	0.80 (0.72 to 0.86)
PER	4450	80 (44 to 98)	76 (68 to 84)	3.44 (2.20 to 5.40)	0.26 (0.08 to 0.90)	0.82 (0.75 to 0.89)
NER	244.25	80 (44 to 98)	86 (79 to 92)	5.85 (3.40 to 10.10)	0.23 (0.07 to 0.80)	0.86 (0.79 to 0.92)
NLR	8.42	71 (42 to 92)	85 (77 to 91)	4.77 (2.80 to 8.10)	0.34 (0.10 to 0.80)	0.84 (0.77 to 0.90)

Data in parentheses are 95% confidence intervals. CRP, C-reactive protein; NER, neutrophil-to-eosinophil ratio; NLR, neutrophil-to-lymphocyte ratio; PER, platelet-to-eosinophil ratio; PLR, platelet-to-lymphocyte ratio; WBC, white blood cell.

When verifying the diagnostic capacity of NER in our sample (*see* table 4), we found that NER>244.25 predicted surgery in all patients with Hinchey III-IV. NER failed to predict surgery in only two cases of our sample. From those patients with Hinchey<III and NER>244.24, 14.8% were operated on. 99% of patients with Hinchey <III had a NER≤244.25 and were treated conservatively.

Table 4 – **Number of patients submitted to surgery according to the modified Hinchey classification and the neutrophil-to-eosinophil ratio cut-off of 244.25.**

NER ≤ 244.25	Modified Hinchey classification	
Surgery	0-II	III-IV
No	98 (99)	0
Yes	1 (1.0) (n=99)	1 (100) (n=1)
NER>244.25	**Modified Hinchey classification**	
Surgery	0-II	III-IV
No	52 (85.2)	0
Yes	9 (14.8) (n=61)	6 (100) (n=6)

Results expressed as number (valid percentage) of individuals. NER, neutrophil-to-eosinophil ratio.

Correlations

Neutrophil (r = 0.222), lymphocyte (r = -0.314), eosinophil (r = -0.326) and basophil (r = -0.236) count and CRP (r = 0.35) related to the need of surgery (p<0.01). Likewise, all ratios PER, NER, platelet-to--lymphocyte (PLR), and neutrophil-to-lymphocyte (NLR) weekly correlated (r = 0.3, p<0.01) with surgery. No correlation was found between platelets, white blood cell count and need of surgery. Similar results were obtained when correlating the preceding variables with the Hinchey classes, with the exception of platelet count which was not significantly correlated.

DISCUSSION

The present study is the first to suggest NER as an important marker in differentiating non-surgical and surgical treatment in patients with acute diverticulitis. Our findings show NER with the best values of sensitivity and specificity in comparison to other blood parameters. NER ≤244.25 showed to be a good predictor of conservative therapy as 98 of 99 patients with Hinchey between 0 and II were treated conservatively. NER>244.24 predicted surgery in the more severe stages of diverticulitis and in 14.8% of patients with modified Hinchey classification <III. Still, more studies are needed to confirm these findings as this study was performed on a small sample and on a small number of patients operated on.

Neutrophil, eosinophil and lymphocyte were the only blood cells to significantly (p<0.05) change between Hinchey aggregated classes and when surgery was performed. The same occurred with the ratios PLR and NLR. With NER we did not find a significant difference between Hinchey aggregated classes, probably due to the low number of patients with Hinchey III-IV (n=4).

Some possible explanations for the blood cell count changes found in this study are here described.

In inflammation, neutrophil count level first increases as it is responsible for initiating and modulating the systemic inflammatory reaction which is characterised by increased levels of circulating cytokines and chemokines[9,14]. Neutrophils are an essential effector of the innate immune response and are abundant in the blood but absent in normal tissues. In the early phase of the systemic inflammatory reaction, a considerable reserve pool of mature neutrophils within the bone marrow can be rapidly mobilized, resulting in a dramatic rise in circulating neutrophil numbers, and thereby the number of neutrophils available for recruitment into sites of tissue injury increases. The failure of neutrophil migration may lead to an increased number of bacteria in peritoneal exudates and blood, followed by tissue injury and systemic inflammation, and neutrophil sequestration in the lung and other organs. Therefore, an impaired recruitment and migration of neutrophils contribute to the pathogenesis of sepsis and are correlated with a poor outcome in severe sepsis[14]. In our study, we did not found neutropenia to be associated to more severe presentation of diverticulitis.

The decline of eosinophils could be due to various processes: (a) peripheral sequestration of eosinophils in sites such as the inflammatory region, presumably by chemotactic substances released during acute inflammation (in the draining lymph nodes or spleen), by diffuse intravascular margination, or by destruction of eosinophils; (b) suppression of egress of mature eosinophils from the bone marrow; and (c) suppression of eosinophil production[8].

The decline of lymphocytes can be linked to severe infection and sepsis due to impaired T cell mitogens, circulating suppressor lymphocytes, serum factors suppressive of lymphocyte activation and apoptosis[14, 15]. Of note, that neutrophils can also induce lymphocyte apoptosis, and hence lymphopenia[14].

Platelet count elevation is also frequent in inflammation and infection. Platelets contribute to host defence as they recognize bacteria, recruit traditional immune cells to the site of infection and secrete bactericidal mediators[13]. Platelet count also rises from Hinchey 0 to Hinchey grade III ($p < 0.01$, data not shown). At Hinchey IV there was a reduction in platelet count which is in accordance with the more dramatic presentation: faecal peritonitis. In fact, thrombocytopenia accompanies severe sepsis[16]. When aggregating Hinchey classes into 0-II and III-IV, there was no significant difference in platelet count. The same occurred for the need of surgery (ROC curve in agreement). Therefore, platelet count itself does not seem to be associated to the need of surgical intervention in patients with acute diverticulitis.

Furthermore, CRP is known as an index of inflammatory response and we found as Tursi A.[11] a similar cut-off for CRP in patients with acute diverticulitis who need a surgical procedure (22.1mg/dl versus 20mg/dl according to Tursi A.[11]). However, CRP was not found to be a good marker for identifying patients who need or not a surgical procedure.

This study has some limitations worth noting. As between aggregated Hinchey classifications there were no significant differences between gender, age or comorbidities, these were revealing of the biased sample of this study, as we know that female gender and younger age are risk factors for a severe episode of acute diverticulitis in Western populations[17]. Moreover, other variables than those used in this study could also have given important contributions like body temperature, body mass index and smoking status[17]. Unfortunately, we were not able to control for these factors. Finally, we had some missing data that hindered the interpretation of some analysis.

In conclusion, this study is the first one to our knowledge to show NER as the best discriminant blood parameter in deciding the need of surgery in patients with acute diverticulitis. Therefore, as it seems that blood parameters can be helpful clinical tools in patients with acute diverticulitis, other studies are needed to support these findings as well as to establish the best cut-offs.

Acknowledgements: No acknowledgments to report.
Conflicts of interest: None.
Funding: None.

BIBLIOGRAPHY

1. Soumian S, Thomas S, Mohan PP, Khan N, Khan Z, Raju T: **Management of Hinchey II diverticulitis.** *World J Gastroenterol* 2008, **14**:7163-7169.
2. Evans J: **Does a 48-Hour Rule Predict Outcomes in Patients with Acute Sigmoid Diverticulitis?** *J Gastrointest Surg* 2008, **12**:577–582.
3. Ritz JP, Lehmann KS, Loddenkemper C, Frericks B, Buhr HJ, Holmer C: **Preoperative CT staging in sigmoid diverticulitis – does it correlate with intraoperative and histological findings?** *Langenbecks Arch Surg* 2010, **395**:1009–1015.
4. Boostrom SY, Wolff BG, Cima RR, Merchea A, Dozois EJ, Larson DW: **Uncomplicated Diverticulitis, More Complicated than We Thought.** *J Gastrointest Surg* 2012, **16**:1744–1749.
5. Moya P, Arroyo A, Pérez-Legaz J, Serrano P, Candela F, Soriano-Irigaray L *et al*: **Applicability, safety and efficiency of outpatient treatment in uncomplicated diverticulitis.** *Tech Coloproctol* 2012, **16**:301–307.
6. Tursi A: **Diverticular disease: a therapeutic overview.** *World J Gastrointest Pharmacol Ther* 2010, **1**:27-35.
7. Holland M, Alkhalil M, Chandromouli S: **Eosinopenia as a marker of mortality and length of stay in patients admitted with exacerbations of chronic obstructive pulmonary disease.** *Respirology* 2010, **15**:165–167.
8. Abidi K, Khoudri I, Belayachi J, Madani N, Zekraoui A, Zeggwagh AA *et al*: **Research Eosinopenia is a reliable marker of sepsis on admission to medical intensive care units.** *Critical Care* 2008, **12**:R59.
9. Walsh SR, Cook EJ, Goulder F, Justin TA, Keeling NJ: **Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer.** *J Surg Oncol* 2005, **91**:181-4.
10. Kishi Y, Kopetz S, Chun YS, Palavecino M, Abdalla EK, Vauthey JN: **Blood neutrophil-to-lymphocyte ratio predicts survival in patients with colorectal liver metastases treated with systemic chemotherapy.** *Ann Surg Oncol* 2009, **16**:614-22.
11. Tursi A: **Biomarkers in diverticular diseases of the colon.** *Dig Dis* 2012, **30**:12-8
12. World Health Organisation: **The International Classification of Diseases, 9th Revision** [http://icd9cm.chrisendres.com/index.php]
13. McNicol A, Israels SJ: **Beyond Hemostasis: The Role of Platelets in Inflammation, Malignancy and Infection.** *Cardiovasc & Haematol Disord Drug Targets* 2008, **8**:99-117.
14. Luan YY, Dong N, Xie M, Xiao XZ, Yao YM: **The significance and regulatory mechanisms of innate immune cells in the development of sepsis**. *J Interferon Cytokine Res* 2014, 34:2-15.
15. *O'Mahony JB, Palder SB, Wood JJ, McIrvine A, Rodrick ML *et al*: **Depression of cellular immunity after multiple trauma in the absence of sepsis.** J Trauma. 1984, 24:869-75.
16. Lim SY, Jeon EJ, Kim HJ, Jeon K, Um SW, Koh WJ *et al*: **The incidence, causes, and prognostic significance of new-onset thrombocytopenia in intensive care units: a prospective cohort study in a Korean hospital.** *J Korean Med Sci* 2012, **27**:1418-23.
17. Kim SY, Oh TH, Seo JY, Jeon TJ, Seo DD, Shin WC *et al*: **The clinical factors for predicting severe diverticulitis in Korea: a comparison with Western countries.** *Gut Liver* 2012, **6**:78-85.

Correspondência:

GISELA MARCELINO
e-mail: giselamarcelino@sapo.pt

Data de recepção do artigo:
09/12/2014

Data de aceitação do artigo:
01/08/2015