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Can C-reactive protein-to-albumin ratio be a predictor of short-term mortality in community-acquired pneumonia?

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Abstract

Aim: This study aimed to investigate the predictive ability of the C-reactive protein (CRP)-to-albumin ratio for short-term mortality in patients presenting to the emergency department with community-acquired pneumonia.

Material and Methods: This retrospective study was conducted with patients admitted to our clinic with community-acquired pneumonia diagnosed based on computed tomography findings and clinical findings between March 2018 and February 2020. Baseline characteristics, comorbid diseases, laboratory findings, CRP and albumin concentrations and their ratios, clinical outcomes for the first 24 hours, and 30-day all-cause mortality data were recorded. The relationship between the CRP-to-albumin ratio and short-term mortality was evaluated.

Results: A total of 958 patients with community-acquired pneumonia were included in the study for analyses. The rates of outpatient treatment, need for hospitalization in other hospital services, need for intensive care, death in the emergency department and 30-day mortality were 33.4%, 35.3%, 30.2%, 1.1% and 30.1%, respectively. Significant differences were observed in albumin, CRP, CRP-to-albumin ratio, and neutrophil-to-lymphocyte ratio (NLR) between the non-survivor and survivor groups ($p<0.001$ for all). The cut-off value for the CRP-to-albumin ratio was 2.72 (sensitivity: 62.5%, specificity: 59.55%), area under the curve (AUC) was 0.651 (95% confidence interval 0,613 – 0,688). The AUC of the CRP-to-albumin ratio was similar to that of NLR ($p=0.534$).

Discussion: The CRP-to-albumin ratio can be useful in determining the short-term mortality from community-acquired pneumonia in patients presenting to the emergency department.

Keywords

C-reactive Proteins; Albumins; Prognosis; Community-Acquired Pneumonia; Pneumonia

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Introduction

Acute infections, especially community-acquired pneumonia (CAP), are the most common cause of hospitalization, morbidity, and mortality. In patients hospitalized with CAP, the 30-day mortality rate is 7.3-13.3% [1]. Scoring systems, such as SMART-COP, SCAP, ATS 2001, ATS/IDSA 2007, PSI, CURB, CRB-65, and CURB-65 are used to predict mortality and severe complications in hospital admissions due to CAP [2-4]. Similarly, various biomarkers, such as procalcitonin, cytokines, pro-vasopressin, pro-adrenomedullin, and C-reactive protein (CRP) are used for diagnostic and prognostic purposes in CAP. Among these, CRP and procalcitonin are the most frequently studied biomarkers [5-8].

CRP is an acute-phase protein used as a prognostic and follow-up test in patients with infection. Studies have concluded that CRP is useful for the diagnosis and follow-up of CAP [9-11]. Albumin is an acute-phase protein, and hypoalbuminemia correlates with the inflammatory response in patients with infection [12, 13]. Recent studies have shown that the CRP-to-albumin ratio predicts mortality in critically ill patients or those with malignancies, infection or sepsis that require intensive care [14-19]. In light of this knowledge, we speculated that the CRP-to-albumin ratio could predict mortality in the emergency department (ED) in patients with CAP. This study aimed to investigate the predictive ability of this ratio for short-term mortality in patients presenting to ED with CAP.

Material and Methods

Study design

This study was designed retrospectively and conducted at University of Health Sciences Umraniye Training and Research Hospital, a tertiary academic healthcare center with an annual ED visits of 438,000 patients and a capacity of 672 beds. We retrospectively recorded data of the patients admitted to the ED with CAP between March 2018 and February 2020.

Study population

The study population consisted of patients presenting to our ED with CAP, diagnosed based on radiographic and clinical findings between March 2018 and February 2020. Computed tomography (CT) was used for radiological evaluation. Chest CT images, demonstrating new infiltrates consistent with a diagnosis of pneumonia were assessed by a radiologist. The patients had acute-onset clinical symptoms suggestive of pneumonia. Eligible patients with the diagnosis of CAP who were hospitalized or treated in the outpatient setting were included. If clinic or intensive care beds were unavailable, the patients requiring hospitalization were transferred to another hospital or held in the ED until a bed became available. Patients younger than 18 years, those with no data of CRP or albumin levels within the first 24 hours of ED admission, those discharged from the hospital within 10 days, those using immunosuppressive agents, chronically immunosuppressed patients, and cases with a history of pneumonia within the past 30 days were excluded.

Data collection

The data extracted from the computer-based system of our hospital included baseline characteristics, comorbid diseases, laboratory findings, CRP and albumin concentrations and their ratio, and clinical outcomes for the first 24 hours. Comorbid diseases were recorded as congestive heart failure, cerebrovascular disease, history of malignancy, chronic kidney disease, and chronic liver disease. Clinical outcomes within the first 24 hours of ED admission were recorded as discharge, need for hospitalization in other hospital services, need for intensive care, and death in the ED. Initial laboratory data analyzed within the first 24 hours of ED visit consisted of hematocrit, hemoglobin, platelet count, neutrophil count, lymphocyte count, white blood cell count, CRP, albumin, sodium, serum creatinine, blood urea nitrogen, lactate and glucose levels. The CRP-to-albumin ratio, platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR) were calculated. A 30-day all-cause mortality of the patients was also noted.

The primary outcome of this study was short-term mortality after ED admission. The secondary outcomes were the need for hospitalization in other hospital services or intensive care units (ICU), vasopressor requirement in ED, and mechanical ventilation use in ED.

Statistical analysis

IBM SPSS Statistics for Mac, Version 27.0. Armonk, NY, IBM Corp was used to perform statistical analyses. The Kolmogorov-Smirnov test was conducted for the evaluation of the conformance of variables to a normal distribution. The data that matched a normal distribution were presented with mean and standard deviation and values, and the remaining data were expressed as interquartile range and median values. Categorical data were presented with the number of cases and percentages. For the comparison of quantitative and qualitative data between two groups, the chi-square and Mann-Whitney U tests were used. We also formed a receiver-operating characteristic curve (ROC) for 30-day mortality and obtained the area under the curve (AUC) for individual variables. The AUC values of the parameters were calculated and tested mutually for significance with the DeLong equality test. A p- value lower than 0.05 was considered statistically significant in all analyses.

Ethics

Ethical approval for the study was obtained from the Ethics Committee of Clinical Research of Umraniye Training and Research Hospital with the approval number B.10.1. TKH.4.34. H.GP.0.01/73. We retrospectively reviewed the data extracted from the computer-based hospital information management system. The extracted data were solely clinical, and did not include any personal, identifiable information. Therefore, the need for informed consent was waived.

Results

Patient characteristics

A total of 845,050 patients presented to ED during the study period, and 1,202 were diagnosed with pneumonia. We excluded 153 patients because they were younger than 18 years or had no data of CRP or albumin levels measured within the first 24 hours of ED admission. Next 91 patients were excluded since they were discharged within 10 days of hospitalization, had a history of pneumonia within the past 30 days, used immunosuppressive agents, or were chronically immunosuppressed. Therefore, for the final analysis, 958 patients were included. The flowchart of the study is presented in Figure 1.

Table 1. Baseline characteristics of the enrolled patients and comparison of demographic and clinical characteristics between the survivor and non-survivor groups

	Total n = 958	Survivor n = 670 (69.9%)	Non-survivor n = 288 (30.1%)	p
Clinical outcome				
Discharge	320 (33.4%)	292 (43.6%)	28 (9.7%)	<0.001
Need for hospitalization in other clinics	338 (35.3%)	254 (37.9%)	84 (29.2%)	
Need for intensive care	289 (30.2%)	124 (18.5%)	165 (57.3%)	
Death in ED	11 (1.1%)	0 (0%)	11 (3.8%)	
Comorbidities (n, %)				
Congestive heart failure	87 (9.1%)	59 (8.8%)	28 (9.7%)	0.651
Chronic kidney disease	65 (6.8%)	46 (6.9%)	19 (6.6%)	0.880
Chronic liver disease	7 (0.7%)	4 (0.6%)	3 (1.0%)	0.435
Cerebrovascular disease	113 (11.8%)	70 (10.4%)	43 (14.9%)	0.049
History of malignancy	126 (13.2%)	61 (9.1%)	65 (22.6%)	<0.001
Clinical findings				
Altered mental status	164 (17.1%)	89 (13.3%)	75 (26.0%)	<0.001
Systolic blood pressure	126.00 (106.00-150.00)	130.00 (112.00-152.00)	118.00 (97.00-144.00)	<0.001
Body temperature	36.80 (36.50-37.60)	37.00 (36.50-37.80)	36.70 (36.50-37.20)	0.011
Respiratory rate	15.00 (14.00-28.00)	15.00 (14.00-25.00)	16.00 (14.00-30.00)	0.434
Heart rate	97.00 (83.25-115.00)	95.00 (84.00-113.00)	100.00 (83.00-120.00)	0.065
Vasopressor requirement in ED	130 (13.6%)	39 (5.8%)	91 (31.6%)	<0.001
Mechanic ventilation use in ED	168 (17.5%)	55 (8.2%)	113 (39.2%)	<0.001
Biochemical test parameters				
Sodium, mEq/L	137.00 (134.00-141.00)	137.00 (134.00-140.00)	138.00 (134.00-143.00)	<0.001
Glucose, mg/dL	132.00 (107.00-184.00)	132.00 (108.00-179.00)	134.00 (102.00-191.00)	0.049
Blood urea nitrogen, mg/dL	55.64 (38.52-89.88)	49.22 (36.38-74.90)	81.32 (51.36-139.10)	<0.001
Creatinine, mg/dL	1.02 (0.77-1.60)	0.96 (0.76-1.45)	1.20 (0.81-2.06)	<0.001
Albumin, g/dL	3.40 (2.90-3.80)	3.59 (3.13-3.90)	2.94 (2.60-3.35)	<0.001
CRP, mg/L	8.00 (2.80-15.10)	6.95 (2.40-13.80)	10.35 (5.00-17.50)	<0.001
CRP-to-albumin ratio	2.48 (0.80-4.96)	2.00 (0.63-4.33)	3.64 (1.61-6.80)	<0.001
Lactate	2.00 (1.40-3.00)	1.90 (1.30-2.60)	2.40 (1.60-3.80)	<0.001
Hematological test parameters				
White blood cell count	11.44 (8.48-15.76)	11.17 (8.26-15.23)	12.48 (8.91-17.12)	0.010
Neutrophil count	9.14 (6.27-13.35)	8.60 (6.07-12.53)	10.36 (6.96-14.62)	0.001
Lymphocyte count	1.23 (0.77-1.88)	1.31 (0.86-1.93)	1.04 (0.69-1.67)	<0.001
Platelet count	239.00 (182.00-319.00)	243.00 (184.50-319.00)	231.00 (178.50-322.50)	0.358
Hemoglobin count	11.70 (9.90-13.20)	12.00 (10.30-13.30)	11.10 (9.15-12.80)	<0.001
Hematocrit	36.60 (31.30-40.80)	37.15 (32.40-41.00)	34.90 (29.25-40.20)	<0.001
Neutrophil-to-lymphocyte ratio	7.50 (4.28-13.66)	6.95 (4.11-12.56)	8.98 (5.18-16.06)	<0.001
Platelet-to-lymphocyte ratio	191.83 (122.48-314.12)	186.27 (122.76-292.21)	211.19 (117.28-368.44)	0.001

Table 2. Accuracy of neutrophil, lymphocyte, platelet, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, and mean platelet volume in the prediction of 30-day all-cause mortality after emergency department admission

	AUC	95% CI	p	Cut-off value	Sensitivity	Specificity	PPV	NPV
CRP	0.611	0.573–.649	<0.001	9.0	56.6%	58.96%	37.21%	75.96%
Albumin	0.751	0.714–.784	<0.001	3.3	70.14%	65.97%	46.98%	83.71%
CRP/albumin ratio	0.651	0.613–.688	<0.001	2.72	62.5%	59.55%	39.91%	78.7%
NLR	0.577	0.537–.617	<0.001	8.0	56.6%	56.12%	35.67%	75.05%

AUC: area under the curve; PPV: positive predictive value; CI: confidence interval; NPV: negative predictive value; CRP: C-reactive protein; NLR: neutrophil-to-lymphocyte ratio

Table 3. Comparison of the demographic and clinical characteristics between the outpatients and inpatients

	Outpatients n = 320 (33.4%)	Inpatients n = 638 (66.6%)	p
Gender (M/F)	171/149	320/318	0.338
Age	75 (63-82)	77 (68-84)	0.0532
CRP	5.6 (1.7-11.9)	9.3 (3.7-15.8)	<0.001
Albumin	3.7 (3.23-3.95)	3.2 (2.8-3.68)	<0.002
White blood cell count	10.18 (7.75-13.91)	12.11 (8.98-16.5)	<0.003
Neutrophil count	7.83 (5.54-11.2)	9.96 (6.95-14.18)	<0.004
Lymphocyte count	1.42 (0.9-2.07)	1.11 (0.72-1.72)	<0.005
Platelet count	239 (187-311)	239 (180-323)	0.928
CRP-to-albumin ratio	1.58 (0.45-3.55)	3.01 (1.08-5.54)	<0.007
NLR	5.76 (3.36-10.02)	8.67 (4.69-15.51)	<0.008
PLR	169.74 (113.64-254.24)	202.70 (125.91-337.93)	<0.009

M / F: male / female; CRP: C-reactive protein; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio

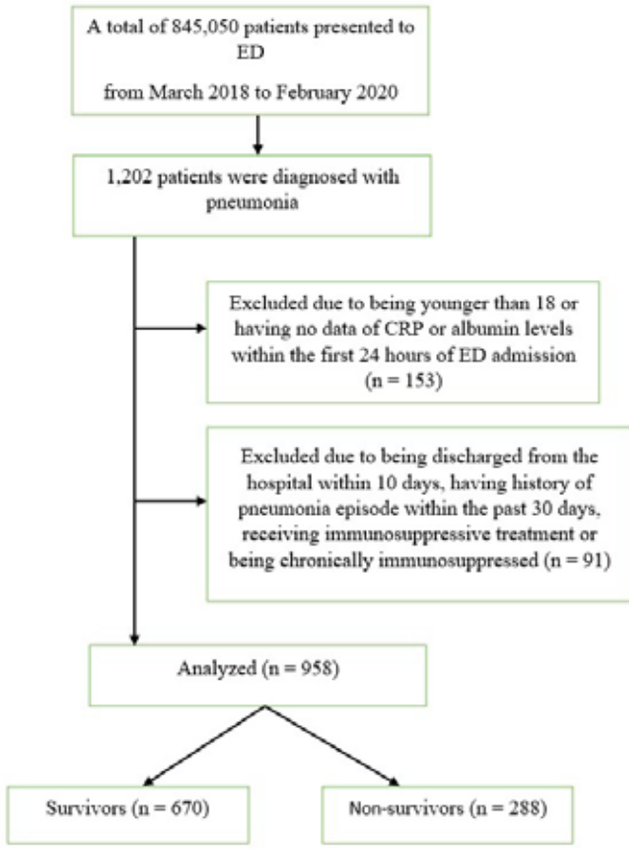

Figure 1. Flowchart of the inclusion and exclusion criteria for the enrolment of patients in the study. ED: emergency department; CRP: C-reactive protein

The median age and interquartile range of the patients was 76 (66 – 83) years, and 491 patients (51.3%) were male. A total of 288 patients died within 30 days of ED admission. The rates of discharge, hospitalization in other hospital services, requirement of intensive care, death in ED, and 30-day mortality were 33.4%, 35.3%, 30.2%, 1.1% and 30.1%, respectively. The patient characteristics according to age and gender, comorbidities, and laboratory findings, including the CRP-to-albumin ratio, NLR, and PLR are shown in Table 1.

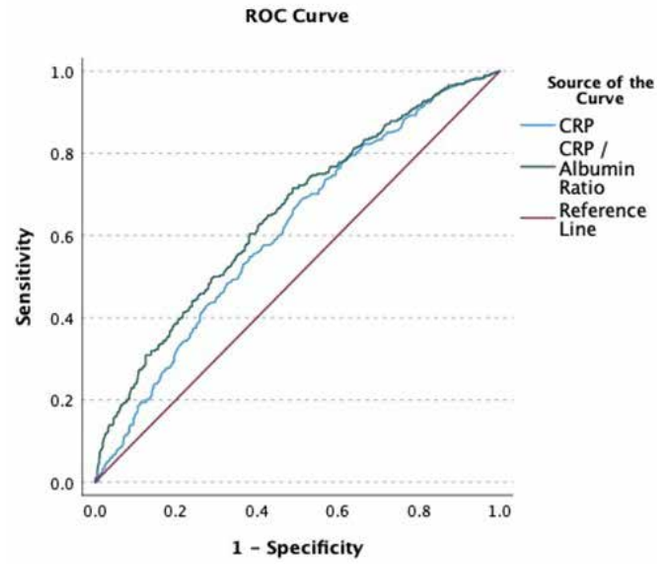

Figure 2. ROC curve for the prediction of 30-day all-cause mortality after ED admission

Laboratory values and Outcomes

The comparisons of the demographic characteristics of the non-survivor and survivor groups are shown in Table 1. Significant differences were observed between the non-survivor and survivor groups in terms of age [75 (64–82) versus 78 (69.5-85) years, p = 0.009], clinical outcome within the first 24 hours, albumin levels [3.59 (3.13–3.90) versus 2.94 (2.60 - 3.35) g/dL], CRP levels [6.95 (2.40–13.80) versus 10.35 (5.00-17.50) mg/L], neutrophil count [8.60 (6.07–12.53) versus 10.36 (6.96–14.62)], lymphocyte count [1.31 (0.86–1.93) versus 1.04 (0.69-1.67)], NLR [6.95 (4.11–12.56) versus 8.98 (5.18–16.06)], PLR [186.27 (122.76–292.21) versus 211.19 (117.28-368.44)] (p < 0.001 for all). The CRP-to-albumin ratio was significantly lower in the survivor patient group than in the non-survivor group [3.64 (1.61-6.80) versus 2.00 (0.63–4.33), p < 0.001] (Table 1).

The results of the ROC curve analysis for the prediction of 30-day all-cause mortality after ED admission are shown in Figure 2. The cut-off and AUC (95% confidence interval) values of CRP, albumin, CRP-to-albumin ratio, and NLR are given in Figure 2 and Table 3. The cut-off value of the CRP-to-albumin ratio was 2.72 (sensitivity: 62.5%, specificity: 59.55%), and the AUC value was 0.651 (95% confidence interval 0.613–0.688). The AUC value of the CRP-to-albumin ratio was significantly higher than that of CRP and NLR (DeLong equality test, p < 0.001 and p = 0.003, respectively).

Data on hospitalization requirements according to age and gender are presented in Table 3. The ROC curve analysis for the prediction of the requirement for hospitalization revealed that the AUC was 0.640 (0.603-0.677) for the CRP-to-albumin ratio, 0.626 (0.589-0.663) for NLR, and 0.569 (0.532-0.607) for PLR. The AUC value of the CRP-to-albumin ratio was similar to that of NLR (p = 0.534), but significantly higher compared to the PLR (p = 0.004).

Significant differences were observed between the hospitalized and outpatient groups in terms of CRP [9.25 (3.70–15.80) versus 5.60 (1.70–11.85) mg/L, p < 0.001], and CRP-to-albumin ratio [3.00 (1.08–3.54) versus 1.60 (0.46–3.55), p < 0.001].

There were significant differences between the mechanically ventilated in ED and not-mechanically ventilated in ED groups in terms of CRP [10.10 (5.60–15.80) versus 7.50 (2.60–14.60) mg/L, p = 0.001], and CRP-to-albumin ratio [3.43 (1.54–6.07) versus 2.23 (0.73–4.80), p < 0.001]. Significant differences were detected between the vasopressor used and not used in ED groups in terms of CRP [11.50 (6.40–18.00) versus 7.50 (2.60–14.40) mg/L, p < 0.001], and CRP-to-albumin ratio [3.93 (2.15–6.37) versus 2.22 (0.70–4.75), p < 0.001].

Discussion

The results of this retrospective study with 958 patients showed that the CRP-to-albumin ratio was associated with short-term mortality, which was especially remarkable in patients with a CRP-to-albumin ratio greater than 2.72. Moreover, the CRP-to-albumin ratio had a higher AUC value than CRP in predicting short-term mortality in patients with CAP. The rates of requirement for hospitalization, hospitalization in other hospital services or ICU, vasopressor requirement in ED, and mechanical ventilation use in ED were also affected by the CRP-to-albumin ratio.

Several studies have investigated the prognostic importance of the CRP-to-albumin ratio in septic or critically ill patients, and most were based on the data of hospitalized patients [15,17-19]. In light of the current literature, our study is the first to demonstrate the relationship between short-term mortality and the CRP-to-albumin ratio in patients with CAP. Another difference of our study from previous studies is that it revealed the differences between the inpatients and outpatients with CAP in terms of the CRP-to-albumin ratio.

CRP expression increases during inflammatory conditions, some cardiovascular diseases, and infection [13-15]. Chalmers et al. and Lee et al. showed that the CRP could predict the severity of CAP at the time of hospital admission in their prospective studies with 570 and 424 patients, respectively [20,21]. In contrast, in a study conducted with a total of 391 patients with a median age of 80 years, Thiem et al. reported that CRP could not predict mortality in patients with CAP [22]. In our study, similar to Chalmers et al. and Lee et al., we determined that the CPR levels were associated with mortality, requirement of hospitalization, mechanical ventilation use, and vasopressor requirement in patients with CAP.

The CRP-to-albumin ratio has been studied as a biological prognostic marker in critically ill patients, as well as those with septic shock, severe sepsis, and other diseases [14-19]. Park et al. showed that the CRP-to-albumin ratio could be a predictor of prognosis in critically ill patients [14]. In that study, the cut-off value for the CRP-to-albumin ratio in predicting 28 day-mortality after ICU admission was reported to be 34.3 in critically ill patients, and the AUC for this ratio was significantly higher than that of CRP (0.594 versus 0.567, p < 0.001) [14]. In a study evaluating patients with septic shock or severe sepsis treated with early gold-directed therapy, the cut-off value for the CRP-to-albumin ratio for the prediction of 180-day all-cause mortality after ICU admission was 5.09, and the AUC of this ratio was significantly higher than that of CRP (0.621 versus 0.562, p < 0.001) [23]. In another study, Ranzani et al. suggested that the CRP-to-albumin ratio could be used as a long-term prognostic indicator instead of standard CRP values alone [17]. Oh et al. showed that the CRP-to-albumin ratio could predict 30-day and 1-year mortality in patients admitted to ICU postoperatively [23]. In the same study, the cut-off value for the CRP-to-albumin ratio was 1,75 and 1,58 for the prediction of 30-day and 1-year mortality, respectively. In the current study, the CRP-to-albumin ratio had greater precision than CRP alone in the prediction of 30-day mortality among the patients that presented to our ED with CAP. Our results are consistent with those of previous studies.

Kaya et al. reported that the NLR of patients with CAP was significantly higher among those receiving inpatient care than those requiring intensive care [24]. In a study conducted with pediatric patients, Kartal et al. showed that the mean NLR and PLR levels of the patients with CAP were significantly higher than in the control group, but there was no statistically significant difference between the inpatient and outpatient groups [25]. In our study, the NLR and CRP-to-albumin ratio levels of the patients with CAP were significantly lower in the outpatient group than in the inpatient group, and the CRP-to-albumin ratio had greater accuracy than NLR in predicting the requirement of hospitalization.

Limitations

The main limitation of our study was its retrospective nature. Secondly, we could not include patients with CAP who were not tested for CRP and albumin. Lastly, our study had a single-center observational design, and therefore the results cannot be generalized to other healthcare institutions.

Conclusion

In this study, we concluded that the CRP-to-albumin ratio was associated with short-term mortality, requirement of hospitalization, vasopressor requirement in ED, and mechanical ventilation use in ED in patients with CAP. In these patients, the predictive power of the CRP-to-albumin ratio for short-term mortality after ED admission was higher than that of CRP alone.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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