RESEARCH

ASSOCIATION BETWEEN C-REACTIVE PROTEIN/ALBUMIN AND C-REACTIVE PROTINE/PROTEIN RATIOS AND POOR OUTCOMES IN PALLIATIVE CARE PATIENTS WITH PRESSURE ULCERS

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.309
2022; 25(4): 514-520

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Received : Aug 04, 2022
Accepted : Nov 21, 2022

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Abstract

Introduction: Pressure ulcers are a significant cause of mortality and morbidity in older adult patients. Inflammatory processes accompany pressure ulcers. C-reactive protein and procalcitonin tests are sufficiently sensitive to show inflammation.Determining the ratios of these tests to each other may show a better performance in diagnosing and predicting the prognosis

Materials and Method: In this retrospective observational study, the records of patients with stage 2 and higher stage pressure ulcers who were followed up in the Adult Palliative Care Unit between January 1, 2019, and December 31, 2019 were reviewed. The National Pressure Injury Advisory Panel staging system was used for pressure ulcer staging. The patients were followed up for one year after hospitalization.

Results: The study included 151 patients with pressure ulcer who met the study criteria [80 (52.9%) female; 71 (47.1%) male] with a mean age of 74.7±12.6 years, and a mean length of hospital stay of 50.7±53.25 days. The one-year mortality rate was 70.8% (107/151).C-reaktif protein/albumin ratio and C-reaktif protein/total protein ratios were found to be significantly higher in the group with mortality ($p<0.05$). A ROC analysis revealed a cut-off value of 30.05 for the prediction of mortality in CRP, as the point at which the sum of the sensitivity and specificity values is the highest. The value of 35.2 predicting mortality for C-reaktif protein albumin ratio is the point at which the sum of the sensitivity and specificity values is the highest.

Conclusion: C-reaktif protein albumin ratio and CRP protein ratios demonstrated better prognosis and mortality prediction performance than CRP, albumin and total protein alone.

Keywords: Pressure Ulcer; Palliative Care; C-Reactive Protein.

INTRODUCTION

Pressure ulcers (PU) typically occur on the skin covering bony prominences and areas of the body that are subject to pressure. PUs are a common condition, especially in bedridden patients with limited mobility and older adults, with two-thirds of those who develop PUs being aged over 70 years (1). In addition to being a leading cause of both morbidity and mortality, PUs are responsible for disabling symptoms and so result in significant healthcare costs (1-2). In fact, the mortality rate associated with PUs has been reported to be 66% within a 12-week median follow-up period (3).

An inflammatory process usually accompanies the formation of PUs. C-reactive protein (CRP) and procalcitonin tests have been found to be sufficiently sensitive for the identification of the inflammation (4). The level of CRP, which is an essential acute-phase protein, is most commonly used for the identification of inflammation in daily practice. Procalcitonin is a calcitonin-related gene product expressed by human epithelial cells in response to bacterial infections (5), and it can be used as a blood infection biomarker for guiding antibiotic therapies in the presence of pulmonary infections (6). Moreover, procalcitonin is an important inflammatory marker for the monitoring of infections, especially in sepsis patients. Prior studies have examined the use of various inflammatory markers for prognostic purposes in relation to several diseases (7, 8), with CRP, albumin, procalcitonin, and protein tests being found to be easily accessible and highly applicable in hospital environments.

A high CRP/albumin ratio has recently been shown to associated with a poor prognosis and increased mortality in patients with various diseases, including sepsis, chronic obstructive pulmonary disease (COPD), liver cirrhosis, restless leg syndrome, inflammation, postoperative complications of abdominal surgeries, and certain malignancies (9,10,11). The CRP/albumin ratio is also a useful indicator of both mortality and morbidity in critically ill patients (12). The prediction of mortality based on the ratios of these parameters is known to be more accurate than the use of any one of them alone (13), although to the best of our knowledge no prior study has investigated the association between PUs and patients' CRP/protein, CRP/albumin, and/or CRP/procalcitonin ratios.

In light of prior findings, the present study examines the association between the CRP/protein, CRP/albumin, and CRP/procalcitonin ratios and mortality in patients with PUs.

MATERIALS AND METHODS

Approval for this retrospective observational study was obtained from the local clinical research ethics committee (No: 2020/10-111).

This study involved a retrospective review of patients with stage 2 or higher PUs who were followed up at the Adult Palliative Care Unit between January 1, 2019 and December 31, 2019. The National Pressure Injury Advisory Panel's staging system was used for the PU staging (14). Of the 195 patients initially reviewed, 44 with stage 1 PUs were excluded from the study due to the possibility of subjectivity in relation to their diagnosis. The remaining patients were followed up for one year after hospitalization. Patients with stage 2 and higher PUs were followed up and survived and non-survived were compared. The required data were retrieved from the electronic hospital information management system and the patients' files. After discharge, the patients were contacted by telephone to establish survival.

The patients' demographic characteristics, comorbidities, length of hospital stay (LOS), and presence of percutaneous enterogastrostomy or other catheters were recorded. The patients' initial laboratory parameters (from within 48 hours of their admission for palliative care) were also recorded from their charts and the electronic hospital information system. Any patients with data missing from their follow-up files were excluded from the study.

The reference values were 0–5 mg/l for CRP, 3.5–5.5 g/dl for albumin, 0–0.5 ng/ml for procalcitonin, and 5.5–8.8 g/l for protein. The CRP/albumin ratio (CAR) was calculated by dividing the CRP level by the albumin level, while the CRP/procalcitonin ratio (CPR) was calculated by dividing the CRP level by the procalcitonin level, and the CRP/protein ratio (CPrR) was calculated by dividing the CRP level by the protein level.

Statistical analyses

All the statistical analyses in this study were conducted using PASW Statistics (version 18.0, SPSS Inc., Chicago, USA) software. The demographic data were presented as the frequency and percentage, while the continuous variables were presented as the mean and standard deviation. A chi-square test was used to compare the categorical variables between the two groups. A Mann-Whitney U test and Student's t-test were used to perform pairwise comparisons of the non-normally and normally distributed continuous data, respectively. A receiver operating characteristic (ROC) analysis was conducted to identify the cut-off values for the ratios. A p-value of <0.05 was considered to be statistically significant.

RESULTS

A total of 195 patients were initially assessed for potential inclusion in this study, although 44 were subsequently excluded due to their decubitus ulcer level and/or missing data. As a consequence, a total of 151 patients with PUs who met the eligibility criteria were included in the study. The final sample comprised 80 (52.9%) females and 71 (47.1%) males. Moreover, the mean age was 74.7±12.6 years, the mean LOS was 50.7±53.2 days, and the one-year mortality rate was 70.8% (107/151). The patients' demographic characteristics and laboratory results are summarized in **Table 1**. The most common comorbidities in both groups (survived and exitus) were found to be similar, including infection (42.4%), cerebrovascular event (35.8%), hypertension (27.8%),

Table 1. Patients' demographic characteristics and laboratory results

Parameters	Exitus mean (SD)	Survived mean (SD)	p*
Age (years)	77.5 (11.0)	71.9 (14.2)	**0.022**
Length of Stay (days)	56.3 (73.7)	45.1 (98.8)	0.537
CRP (mg/dl)	79.4 (61.8)	65.2 (75.1)	0.274
Protein (g/dl)	5.4 (0.8)	5.7 (0.8)	0.082
Albumin (g/dl)	2.6 (0.5)	2.8 (0.5)	0.069
Procalcitonin	0.9 (1.7)	1.6 (4.5)	0.361
Glucose (mg/dl)	134.7 (93.5)	135.6 (65.3)	0.949
BUN (mg/dl)	31.3 (24.4)	24.3 (23.2)	0.103
Creatinine (mg/dl)	0.8 (0.5)	0.8 (0.7)	0.762
ALT (U/l)	27.1 (22.6)	27.6 (25.4)	0.920
AST (U/l)	29.9 (24.1)	30.9 (29.7)	0.856
Sodium (mmol/l)	137.5 (8.2)	136.9 (6.7)	0.607
Potassium (mmol/l)	3.8 (0.6)	3.7 (0.8)	0.402
TSH (uIU/ml)	1.4 (1.3)	1.8 (1.8)	0.257
Vitamin D (ng/ml)	13.7 (9.9)	15.1 (11.5)	0.560
WBC (/1000)	10.1 (5.7)	8.8 (3.7)	0.099
HGB (g/dl)	10.4 (2.2)	10.7 (1.6)	0.368
PLT (/1000)	158.7 (133.7)	193.5 (148.1)	0.180

and neurodegenerative diseases such as dementia or Parkinson's disease (15.3%) (**Table 2**). A comparison of the patients' genders and comorbidities is presented in **Table 3**.

The CAR and CPrR were found to be significantly higher in the group with mortality ($p<0.05$) (**Table 4**), although there was no statistically significant difference in terms of the CRP between the two groups.

The ROC analysis showed that a value of 30.05 when predicting mortality using the CRP represented the point at which the sum of the sensitivity and selectivity values was the highest (sensitivity 79.1%, specificity 46.2%). Furthermore, a value of 35.2 when predicting mortality using the CAR was the point at which the sum of the sensitivity and selectivity values was the highest (sensitivity 46.5%, specificity 79.2%). In addition, a value of 16.2 when predicting

Table 2. Frequency of patient comorbidities

Parameters	n	%
Infection	64	42.4%
Cerebrovascular Event	54	35.8%
Hypertension	42	27.8%
Neurodegenerative Disease	41	27.2%
Diabetes Mellitus	28	18.5%
Congestive Heart Failure	25	16.6%
Cancer	24	15.9%
Malnutrition	10	6.6%
Urinary Catheter	146	96.7%
Central Venous Catheter	79	52.3%
Percutaneous Endoscopic Gastrostomy	51	33.8%

Table 3. Comparison of patients' gender and comorbidities

Parameters		Exitus, n (%)	Survived, n (%)	p*
Gender	Male	22 (31.0)	49 (69.0)	0.638
	Female	22 (27.5)	58 (72.5)	
Hypertension	No	32 (29.4)	77 (70.6)	0.924
	Yes	12 (28.6)	30 (71.4)	
Diabetes Mellitus	No	38 (30.9)	85 (69.1)	0.320
	Yes	6 (21.4)	22 (78.6)	
Cerebrovascular Event	No	29 (29.9)	68 (70.1)	0.784
	Yes	15 (27.8)	39 (72.2)	
Cancer	No	32 (25.2)	95 (74.8)	**0.014**
	Yes	12 (50.0)	12 (50.0)	

Table 4. Comparison of the CRP, protein, CRP/albumin and CRP/protein results

Parameters	Cut-off value	AUC (95% CI)	p	Sensitivity %	Specificity %
CRP (mg/dl)	30.1	0.621 (0.527-0.716)	0.020	79.1	46.2
CRP/albumin	35.2	0.640 (0.543-0.737)	0.007	46.5	79.2
CRP/protein	6.3	0.633 (0.538-0.728)	0.011	74.4	50.9

mortality using the CPrR was the point at which the sum of the sensitivity and specificity values was the highest (sensitivity 41.9%, specificity 79.2%).

DISCUSSION

The present study sought to identify a laboratory value that can be used alongside the CRP level and inflammation-related parameters to predict mortality in elderly patients with PUs. As there are many factors that influence the CRP level (e.g., infection, rheumatologic disease, cancer, etc.) (15), we explored the ratios of the laboratory values that are less affected by the inflammatory factors assessed when following up PUs. As elderly patients may experience a decrease in their inflammatory response, the CRP level alone may fail to fully indicate the severity of the inflammation in cases of PUs (16).

CRP is recognized as a significant laboratory parameter when it comes to the prediction of survival and mortality (17). The CRP test is sensitive to tissue damage, acute infection, and inflammatory conditions, and the CRP level is known to increase in cases in which tissue damage and inflammation occur together, as is common with PUs (18). Procalcitonin is an acute-phase reactant that increases in patients with infectious diseases such as sepsis, pneumonia, and PUs (19,20). The CAR provides data concerning both inflammation and malnutrition (1), which is why it is commonly used in practice as a prognostic indicator for several diseases, especially during the follow-up of critical patients hospitalized for intensive care or palliative care (2). Indeed, high CRP levels are an important predictor of mortality in critically ill patients (21).

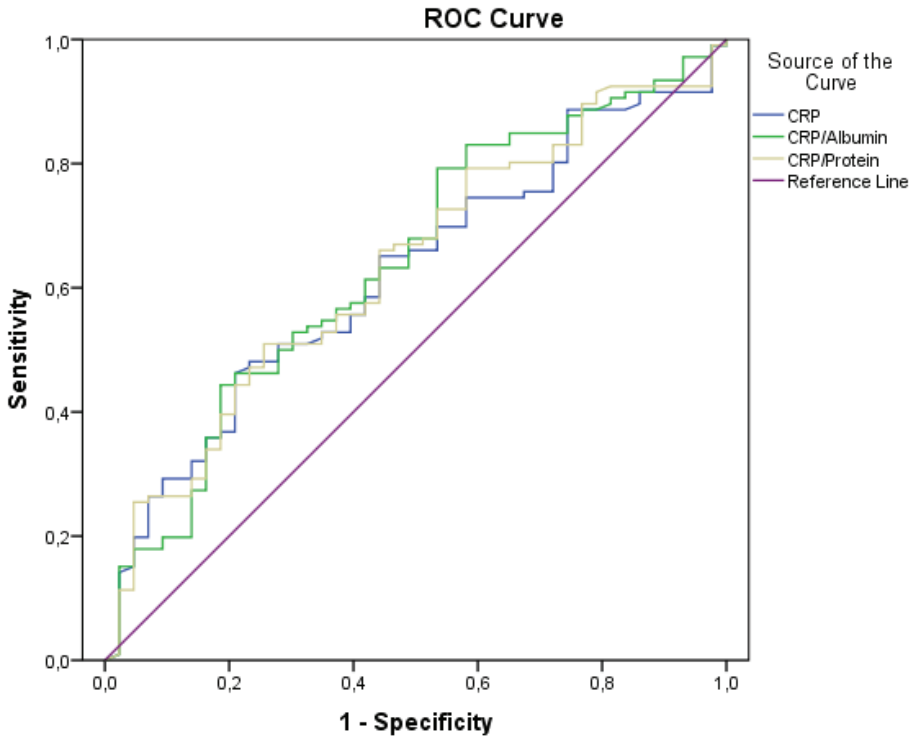
In a previous study, Amano et al. identified a significant relationship between the CRP levels, symptoms, and daily life activities of advanced cancer patients receiving palliative care (22). Ranzani et al. conducted a study involving 334 patients hospitalized in the intensive care unit for a minimum of 72 hours with a diagnosis of sepsis and septic shock, and they found both the CRP level and the CAR to be independent risk factors for mortality (9). Oh et al. reported that a one unit increase in the CAR leads to an 11% increase in the 30-day mortality risk among critically ill intensive care patients, while they identified the albumin level alone as a more reliable parameter than the CAR when it comes to predicting 30-day mortality (12).

CONCLUSION

In the present study, the CAR and CPrR were identified as useful predictors of mortality in patients with PUs, although the contribution of the CPR was found to be more limited. Based on the findings of this study, it can be concluded that the CAR and CPrR can be used as predictive parameters concerning the prognosis and mortality of patients with PUs. While this study found that the CPR could contribute to the determination of patients' prognosis and mortality, its effect was statistically insignificant. This finding may be attributable to the relatively small number of patients involved in the study and/or the impact of PUs and nutritional status on patients' albumin levels.

Limitations

It must be acknowledged that the findings of this study were based on limited data due to its retrospective and single-center design, which limits the generalizability of the results. In addition, the participating PU patients were largely older adults with multiple comorbidities, which may have influenced the results.



Area Under the Curve					
Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
CRP	0.621	0.048	0.020	0.527	0.716
CRP/Albumin	0.640	0.050	0.007	0.543	0.737
CRP/Protein	0.633	0.049	0.011	0.538	0.728
a. Under the nonparametric assumption					
b. Null hypothesis: true area = 0.5					

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