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Original Article EMERGENCY MEDICINE

The role of C-reactive protein and albumin combined ındexes in predicting the need for ıntubation in acute heart failure: A prospective observational study

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ABSTRACT

OBJECTIVE: Heart failure is a clinical syndrome, caused by functional or structural dysfunction of the heart. Taking early decisions for interventional procedures and predicting the treatment process will be beneficial for patients and will shorten the waiting times for the emergency department. We evaluated the capability of C-reactive protein (CRP) and albumin combined indexes to predict the need for intubation in acute heart failure.

METHODS: This study was designed prospectively. Patients with signs and symptoms such as weakness, shortness of breath, abnormal findings in lung sounds, jugular fullness, peripheral edema, and ankle swelling at the time of admission were evaluated. All patients were diagnosed with acute heart failure in the Emergency Department (ED).

RESULTS: A total of 220 patients were included. The median age was 77. CRP Albumin Ratio (CAR) was higher in the intubated group. Glasgow Prognostic Score (GPS) and modified Glasgow Prognostic Score (mGPS) sensitivity, specificity, accuracy and other values were the same.

CONCLUSION: These scores, which are simple and do not require additional examination, can be used to predict the clinical progress of patients.

Keywords: C-reactive protein; heart failure; serum albumin.

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Functional or structural dysfunction of the heart is expressed as heart failure (HF) [1]. Myocardial disorders, including systolic, diastolic, or both, are the most common cause [2]. Etiological causes include many diseases such as coronary artery disease, heart valve disease, hypertension, atrial and ventricular arrhythmias. It is categorized according to the left ventricular ejection fraction measured by echocardiography. Conditions that begin suddenly or gradually and result in the need for urgent or unplanned inpatient treatment are defined as acute heart failure (AHF). Some of these patients have a known history of heart failure or have recently started. The one-year mortality rate ranges from 22% to 37% [3].

Inflammation markers rise in heart failure [4]. The most notables are C-reactive protein (CRP), tumor necrosis factor alpha, interleukin-1, and interleukin-6 [5]. No correlation between left ventricular

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ejection fraction and inflammation [6]. The elevation of inflammatory markers is effective in predicting the prognosis. It is known that high inflammatory values, which are a cause or result of heart failure, provide information about short-term mortality in this patient group [7]. CRP albumin ratio (CAR), Glasgow Prognostic Score (GPS), and Modified Glasgow Prognostic Score (mGPS) are prognostic scores calculated with inflammatory markers [8]. Lymphocyte to CRP ratio score (LCRs) is identified to predict poor outcome, especially in malignancy patients [9, 10]. In previous studies, these scores were recommended to be used because they were successful in predicting poor outcomes, could be calculated practically, and their parameters were common.

Heart failure patients have high mortality and treatment costs. Therefore, taking early decisions for interventional procedures and predicting the treatment process will be beneficial for patients and will shorten the waiting times for the emergency department (ED). In order to make proactive and correct decisions in treatment and interventional procedures, it will be advantageous to use existing parameters without the need for additional examination or imaging procedures. In this study, we evaluated the capability of CRP and albumin combined indexes to predict the need for intubation in acute heart failure.

Highlight key points

- Intubated patients exhibited significantly higher CAR levels, indicating its predictive potential.
- The Lymphocyte to CRP Ratio Score (LCRS) achieved the highest diagnostic accuracy (AUC: 0.720) and sensitivity (80%).
- Both GPS and mGPS scores were significant predictors of intubation, correlating with adverse outcomes related to inflammation and malnutrition.

MATERIALS AND METHODS

This study was conducted with the approval of the Clinical Research Ethics Committee of the Umraniye Training and Research Hospital, under the reference number B.10.1.TKH.4.34.H.GP.0.01/01 on 26.01.2023. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Study Population and Data Collection

This study was designed prospectively. Patients who were admitted to ED of UmraniyeTraining and Research Hospital between 02-02-2023 and 02-06-2023 were evaluated. Patients with signs and symptoms such as fatigue, shortness of breath, abnormal findings in lung sounds, jugular fullness, peripheral edema, and ankle swelling at the time of admission were evaluated. All patients were diagnosed with AHF in the ED. Patients less than the age of 18 were excluded.

Demographic data of the patients were recorded. C-reactive protein, albumin, platelet count, lymphocyte count, neutrophil count, white blood cell count (WBC), hematocrit, hemoglobin, mean platelet volume, left ventricular ejection fraction, systolic and diastolic blood pressure, pro-Brain Natriüretic Peptid (proBNP) values, troponin at first admission Values of comorbid diseases and endotracheal intubation attempt in the ED were documented.

CAR is the CRP/albumin ratio, LCS is the lymphocyte, CRP ratio. GPS and mGPS were calculated by classifying CRP and albumin.

GPS: 2 points if albumin <3.5 g/L and CRP >10 mg/L. 1 point if albumin was normal and CRP >10 mg/L or albumin <3.5 g/L and CRP was normal. If CPR and albumin were normal, it was calculated as 0 points.

Patients with mGPS, CRP ≤10 mg/L and albumin ≥35 g/L scored 0. Patients with albumin ≥35 g/L and CRP >10 mg/L received 1. Patients got 2 points if CRP was >10 mg/L and albumin was <35 g/L. The primary outcome of our study was the need for intubation in the ED.

Statistical Analysis

For statistical calculations, the Jamovi Version 2.3 (Queensland University, Brisbane, Australia) was used. Categorical variables were expressed using frequency (%). Most of the data we obtained in our study did not fit the normal distribution, so continuous variables were expressed as median and interquartile range (IQR) of 25–75. Differences between groups were evaluated with Chi-Square and Mann-Whitney U tests. For the p-value, 05% was accepted as the meaningful upper limit. Area under the curve (AUC) values were calculated using receiver operating characteristic (ROC) curve analysis.

Table 1. Baseline characteristics of the enrolled patients and their comparison between the intubated and non-intubated groups

	Non-intubated %	Intubated %	Total %	p
Age (years) (25th–75th percentile)	76.0 (68.0–84.0)	86.0 (78.0–91.0)	77.0 (69.0–85.0)	0.001
Sex				0.569
Female	52.8	61.9	53.6	
Male	47.2	38.1	46.4	
Comorbidities				
Chronic obstructive pulmonary disease	21.6	23.8	21.8	0.999
Hypertension	46.2	28.6	44.5	0.502
Diabetes mellitus	33.7	23.8	32.7	0.688
Coronary heart disease	20.6	14.3	20.0	0.642
Congestive heart failure	58.8	66.7	59.5	0.344
Chronic kidney disease	21.6	33.3	22.7	0.999
Malignancy	3.5	4.8	3.6	<0.001
Outcome				<0.001
Exitus in emergency department	1 (0.5)	1 (4.8)	2 (0.9)	
Intensive care unit	16 (8.0)	20 (95.2)	36 (16.4)	
Hospitalization	96 (48.2)	0 (0.0)	96 (43.6)	
Discharge	86 (43.2)	0 (0.0)	86 (39.1)	
Mortality	21 (10.6)	12 (57.1)	33 (15.0)	

RESULTS

A total of 220 patients were included. The median age was 77 (IQR 9.85) and the number of women was 118 (54%). Of the patients, 131 (59.5) had a history of congestive heart failure. Hypertension was present in 98 (44.5%) patients. 21 (9.5%) of the patients were intubated, 2 (0.9%) patients died in the ED. 96 (43.6%) of them were hospitalized. The short-term mortality rate was 33 (15.0%). Baseline characteristics of the patients and their differences between the intubated and non-intubated groups are shown in Table 1. WBC (10^3/μL) and CRP (mg/dL) were significantly higher in the intubated group (p=0.017, 0.001, respectively). The median pro-B-type natriuretic peptide value in intubated patients was 2102.2 (pg/ml) (IQR, 1081.5–2881.5) (p=0.003). There was no difference in left ventricular ejection fraction values between the groups (p=0.580). Laboratory and vital parameters of the enrolled patients and their comparison between the intubated and non-intubated groups are presented in Table 2. LCRS was significantly lower in the intubated group 0.2 (IQR, 0.1–0.5) (p=0.001) and CAR was higher in the intubated group 2.1 (IQR, 0.5–3.2) (p=0.002). C-reactive protein-dependent scores are reported in Table 3. The score with the highest sensitivity value in predicting acute heart failure was LCRS (80%). GPS and mGPS sensitivity, specificity, accuracy and other values were the same. The highest AUC value belonged to LCRs (0.720). The odds ratio of the LCRs was 6.7 (95% confidence interval 2.16–20.81). Diagnostic testing accuracy of scores is explained in Table 4.

DISCUSSION

In this analysis, we evaluated that the combined CRP and albumin-related indexes of patients who were admitted to the ED with a clinical diagnosis of AHF could predict the intubation needs of the patients. CAR, GPS, and mGPS were significant in predicting intubation in the ED.

Heart failure is a complex syndrome that can result in mortality and morbidity by affecting the neuroendocrine, metabolic, and immune systems caused by con-

Table 2. Laboratory and vital parameters of the enrolled patients and their comparison between the intubated and non-intubated groups

	Non-Intubated, (%, 25th–75th percentile) n=199 (90%)	Intubated, (%, 25th–75th percentile) n=21 (9.5%)	Total, % n=220	p
White blood cell count (10^3/μL)	8.8 (6.8–11.8)	12.1 (8.1–14.5)	9.0 (6.9–12.2)	0.017
Neutrophil count (10^3/μL)	6.5 (4.9–9.1)	9.1 (6.8–12.0)	6.6 (5.0–9.3)	0.006
Lymphocyte count (10^3/μL)	1.4 (0.9–1.9)	0.9 (0.7–1.6)	1.3 (0.9–1.9)	0.101
Hemoglobin (g/dL)	10.9 (9.8–12.3)	11.1 (10.0–12.0)	10.9 (9.8–12.3)	0.879
Hematocrit (%)	34.5 (30.8–39.1)	36.1 (32.4–39.6)	34.5 (30.9–39.2)	0.481
Mean corpuscular volume (fL)	87.2 (81.9–91.6)	88.5 (83.1–92.0)	87.3 (81.9–91.8)	0.588
Red cell distribution width (%)	27.6 (25.8–29.2)	27.1 (25.1–28.8)	27.6 (25.7–29.1)	0.572
Neutrophil-to-lymphocyte ratio	4.6 (3.0–7.5)	10.7 (4.4–17.1)	4.9 (3.0–8.3)	0.011
C-reactive protein. (mg/dL)	1.6 (0.4–4.6)	7.5 (1.5–10.3)	1.8 (0.5–5.5)	0.001
Albumin (g/dL)	3.4 (3.2–3.8)	3.4 (2.9–3.8)	3.4 (3.2–3.8)	0.237
Blood urea nitrogen (mg/dL)	70.6 (50.3–115.6)	79.2 (59.9–139.1)	71.7 (51.4–118.2)	0.147
Creatinine (mg/dL)	1.4 (1.0–2.2)	1.6 (1.2–2.8)	1.5 (1.1–2.4)	0.269
pro-B-type natriuretic peptide (pg/ml)	1153.1 (764.2–1936.8)	2102.2 (1081.5–2881.5)	1189.4 (793.5–2110.1)	0.003
Troponin (cTnI) (ng/mL)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	0.0 (0.0–0.1)	0.413
Sodium (mEq/L)	138.0 (135.0–140.0)	140.0 (136.0–141.0)	138.0 (135.0–140.0)	0.196
Potassium (mmol/L)	4.9 (4.5–5.3)	5.3 (4.5–5.8)	5.0 (4.5–5.4)	0.210
Vital parameters				
Systolic blood pressure (mm/hg)	140.0 (123.0–168.2)	142.5 (116.0–157.2)	140.0 (122.0–165.8)	0.578
Diastolic blood pressure (mm/hg)	80.0 (70.0–96.5)	70.0 (60.0–78.5)	80.0 (70.0–96.0)	0.047
Oxygen saturation (%)	91.0 (87.0–95.0)	88.0 (80.0–93.0)	91.0 (86.0–95.0)	0.084
Length of hospital stay (days)	9.0 (4.0–15.0)	10.0 (5.0–23.0)	9.0 (4.0–15.0)	0.324
Left ventricular ejection fraction	45.0 (30.0–55.0)	40.0 (37.5–55.0)	45.0 (30.0–55.0)	0.580

tractility disorder in the myocardia [11]. In heart failure, many blood parameters such as AST, ALT, and inflammatory markers increase [12, 13]. It is not known exactly why inflammatory markers are elevated. Inflammation causes the liver to synthesize many acute-phase reactants. Neutrophil, lymphocyte, CRP and albumin are affected by this condition. In fact, 36% of inpatients with acute decompensated heart failure have been shown to have increased CRP levels between hospitalization and discharge [14]. An increase in CRP level is an independent marker of negative outcome events in heart failure [11]. Albumin is negatively affected by inflammation. Decreased albumin is significantly associated with poor outcomes in heart failure patients [15]. The decrease in albumin level in AHF is thought to be due to impaired liver synthesis, kidney losses, increased fluid retention, and increased vascular permeability. For this reason, it is suggested that albumin can be used to predict prognosis in these patients, as well as biomarkers that predict poor outcomes such as Pro-BNP and troponin.

CAR calculated by proportioning CRP and albumin values was known to be a practical predictor of poor outcomes in heart failure patients [16]. It was stated that it can also be a guide in estimating mortality in COVID-19 patients [17, 18]. In this study, we have shown that CAR is successful in predicting the necessity of intubation.

It was testified that the GPS score was significant in predicting the need for hospitalization and in short-term mortality in HF patients [19]. In patients who developed acute heart failure, GPS was associated with intubation, regardless of previous heart failure. Although albumin, which is composed of the components of GPS, is more affected by chronic processes, it has been a guide for the clinical conditions of patients in acute cases.

Table 3. C–reactive protein dependent scores

Scores	Non–Intubated, % n=199 (90%)	Intubated, % n=21 (9.5%)	Total, % n=220	p
GPS % (%)				0.033
0	48.7	38.1	47.7	
1	44.2	38.1	43.6	
2	7.0	23.8	8.6	
mGPS (%)				0.011
0	92.0	71.4	90.0	
1	1.0	4.8	1.4	
2	7.0	23.8	8.6	
CAR (%, 25th–75th percentile)	0.5 (0.1–1.4)	2.1 (0.5–3.2)	0.5 (0.1–1.6)	0.002
LCRS (%, 25th–75th percentile)	0.8 (0.3–3.5)	0.2 (0.1–0.5)	0.7 (0.2–3.2)	0.001

GPS: Glasgow Prognostic Score; mGPS: Modified Glasgow Prognostic Score; CAR: C-reactive protein albumin ratio; LCRS: Lymphocyte C-reactive protein ratio score.

Table 4. Diagnostic testing accuracy of scores

	GPS	mGPS	CAR	LCRS
Sensitivity (%)	24	24	43	80
Specificity (%)	93	93	16	63
Accuracy (%)	86	86	19	64
Prevalence (%)	10	10	10	9
Positive predictive value (%)	26	26	5	18
Negative predictive value (%)	92	92	73	97
Post-test disease probability (%)	26	26	5	18
Post-test health probability (%)	92	92	73	97
Positive likelihood ratio	3.38	3.38	0.51	2.14
Negative likelihood ratio	0.82	0.82	3.55	0.32
Cut-off	2	1	2.03	0.55
Area under the curve	0.590	0.600	0.710	0.720
Odds ratio (95% confidence interval values)	4.13 (1.32–12.93)	0.17 (-0.03–0.43)	0.14 (0.06–0.37)	6.7 (2.16–20.81)

GPS: Glasgow Prognostic Score; MGPS: Modified Glasgow Prognostic Score; CAR: C- reactive protein albumin ratio; LCRS: Lymphocyte C-reactive protein ratio score.

mGPS is calculated by combining CRP and albumin, and this score has been shown to correlate with survival in malignancy and stable heart failure [20]. In correspondence with GPS, it predicts poor outcomes in diseases that cause inflammation and nutritional deficiency. In addition to these, we found that mGPS can predict the need for intubation. The significance of these scores showed that conditions that trigger inflammation or cause malnutrition in heart failure patients negatively affect the clinical course. Infection or malnutrition conditions that affect the disease state need to be treated quickly.

LCRs were also associated with clinical worsening in acute HF patients, as were GPS, mGPS, and CAR. In addition, patients with high LCRs were 6.7 times more

likely to be intubated. In previous studies, LCRs were known to be associated with malignancy and disease severity in COVID-19 patients [21, 22]. Although it is expected that LCRs, which is the lymphocyte CRP ratio, may be more significant with poor outcomes in infectious diseases, we have shown that it is also associated with poor outcomes in acute heart failure [23]. According to this result, it can be thought that lymphocytes and CRP are affected independently of the infection pathways in heart failure patients.

Limitations

There are some limitations in our study. Underlying infection or inflammatory diseases affect CRP and albumin levels. Infections play an important role in the aggravation of heart failure or the development of acute heart failure. In this study, we did not exclude patients with diseases such as infection, inflammation or cancer that cause acute heart failure. Studies with a larger number of patients and excluding patients with acute heart failure due to infection can be conducted. These results are required for validation.

Conclusion

Inflammation and nutritional scores such as GPS, mGPS, CAR predict poor outcomes and the need for intubation in acute heart failure patients. These scores, which are simple and do not require additional examination, can be used to predict the clinical progress of patients.

Ethics Committee Approval: The Umraniye Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 26.01.2023, number: B.10.1.TKH.4.34.H.GP.0.01/01).

Informed Consent: Written informed consents were obtained from patients who participated in this study.

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