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ORIGINAL ARTICLE

Roles of the Ratio of C-Reactive Protein to Serum and Pericardial Fluid Albumin Levels in Predicting in-Hospital Mortality in Patients Undergoing Pericardiocentesis

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Abstract

Background: Pericardial effusions occur due to excessive fluid accumulation in the pericardial space. In effusions not responding to medical treatment, pericardiocentesis is an important method of treatment affecting prognosis. CRP/albumin ratios have been found to be associated with prognosis in conditions such as cardiac failure, sepsis, malignancy, and the routinely available parameters used for the prognosis prediction of the patients who underwent pericardiocentesis are limited. This study aimed to examine the usability of CRP/albumin and CRP/pericardial fluid albumin (CRP/pf-albumin) ratios as predictors for in-hospital mortality of patients who underwent surgery pericardiocentesis.

Methods: This study included 54 patients (25 females and 29 males). All patients underwent pericardiocentesis.

Results: The average age was 67±14 years. When the groups were compared with each other, CRP, CRP/albumin ratio and CRP/pf-Albumin ratio were higher in the in-hospital mortality group compared to the group discharged with recovery [19 (14-25), 6.3 (1-30), p<0.001; 4.27 (3.87-12.02), 1.9 (0.24-10.38), p<0.001; 7 (6.25-13.59), 2.5 (0.28-12.22), p<0.001, respectively]. In the univariate logistic regression analysis, CRP (odds ratio [OR]: 0.821, P: 0.004, 95.0% confidence interval [CI]: 0.918-1.049), CRP/albumin ratio (OR: 0.600, P: 0.011, 95.0% CI: 0.406-0.888) and CRP/pf-Albumin ratio (OR: 0.608, P: 0.004, 95.0% CI: 0.431-0.856) was found to be associated with in-hospital mortality in patients who underwent pericardiocentesis.

Conclusion: For the first time in the literature, we demonstrated that CRP/albumin and CRP/pf-Albumin ratios are associated with in-hospital mortalities in patients who underwent pericardiocentesis, irrespective of the etiology.

Keywords: C-Reactive Protein/Albumin Ratio, Pericardial Fluid Albumin, Mortality, Hospitalized Patients.

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INTRODUCTION

Pericardial fluid is the serous fluid released from the pericardium surrounding the heart to the pericardial space. It helps the heart function more efficiently by holding it in place within the chest cavity and preventing it from rubbing against other tissues. The pericardial sac contains approximately 10-50 mL fluid, and the increased secretion or impaired reabsorption of the fluid results in moderate to severe effusions. While the mild fluid accumulations respond to medical treatment, severe fluid accumulations lead to cardiac dysfunction, and pericardiocentesis is the most beneficial therapeutic procedure unless clinically contraindicated.[1,2]

Pericardial effusions cause clinical signs in patients based on their onset type and size. While they may be asymptomatic, fatal clinical presentations may also be observed. Viral, bacterial, neoplastic, autoimmune, and iatrogenic causes are the most common reasons in the clinical practice; the underlying etiology and the size of the fluid accumulation is associated with the prognosis, and there are no clear biochemical parameters recommended by the guidelines, which can be used for in-hospital mortality.[3]

Being functional in many clinical conditions, albumin and C-reactive protein (CRP) can provide information on inflammatory processes. Several studies have shown that increased CRP levels provide information on prognosis in conditions such as malignancy, stroke, coronary artery disease (CAD), and heart failure (HF).[4-6] Similarly, albumin levels have been documented to provide information on inflammatory conditions.[7] In another study, the CRP-to-albumin ratio was shown to be an independent risk factor for mortality in patients with traumatic brain injury (TBI).[8]

On the contrary, it is not clear whether albumin ratios in the pericardial fluid can be used to predict the patients who underwent pericardiocentesis. Using a combination of parameters rather than individual parameters may provide more information.

Our study aimed to examine the usability of CRP-to-albumin and CRP-to-pericardial fluid albumin ratios in predicting in-hospital mortality in patients who underwent pericardiocentesis.

MATERIALS AND METHOD

Study Population and Data Collection

Our retrospective study enrolled 54 patients who consecutively underwent pericardiocentesis from January 2013 to December 2020 in our university hospital. Patients included in the study were those who did not respond to medical treatment with moderate-large pericardial effusion. The study consisted of patients who underwent pericardiocentesis for the first time. Patients who had to undergo surgical treatment due to pericardiocentesis failure, any contraindication of pericardiocentesis, constrictive pericarditis, and patients under 18 years of age were excluded from the study.

For biochemical parameters, blood samples taken from the upper extremity peripheral venous route and pericardial fluid samples collected during pericardiocentesis were studied within the same timeframe, and data for the variables were obtained. Hemogram, CRP, complete blood count (CBC), pericardial fluid albumin, and lactate dehydrogenase (LDH) tests were studied for all patients. Demographic information, clinical results, biochemical and echocardiographic data of the patients were obtained from the hospital records, and all data were compared between the groups.

Patients who were discharged with recovery were placed in Group 1, and patients who died during hospitalization were placed in Group 2.

This study was approved by the Çanakkale Onsekiz Mart University ethics committee of the hospital in which it took place in line with the recommendations of the Declaration of Helsinki (Date: 09.12.2020 Decision no: 2020-14).

Pericardiocentesis procedure and definitions

Any pericardial effusion smaller than 10 mm is defined as minimal effusions between 10 and 20 mm are defined as moderate, and effusions greater than 20 mm are defined as large effusion. In all patients, it was performed by Seldinger technique using 6F sheath at an angle of 30^0 towards the left shoulder under fluoroscopy in a coronary angiography laboratory setting.[9] 500 ml fluid was discharged from all patients in the laboratory. After successful pericardiocentesis, the pigtail catheter was left in the pericardial cavity for drainage. The catheter was removed when the control echocardiography showed effusion smaller than 10 mm.

Echocardiographic assessment

Pre- and post-procedural echocardiographic assessments were performed using a 2.5-Mhz probe in the Vivid 7 Pro device (GE, Norway). LVEF values were calculated using modified Simpson's rule. TTE examinations were performed in line with the imaging guidelines recommended by the US and EU associations.[10]

Statistical analysis

SPSS 20.0 (SPSS Inc, Chicago, IL, USA) software was used for the statistical analysis. The distribution normality of the parameters was analyzed using the Kolmogorov-Smirnov test with continuous variables being expressed as mean ± standard deviation and categorical variables being expressed as percentage and number. Independent samples t-test and Mann-Whitney U test were used for the comparison of normally and non-normally distributed parameters, respectively. A chi-squared test was used for the comparison of odds ratios for categorical variables.

Univariate logistic regression analysis was used to assess the association of biochemical and demographic parameters with in-hospital mortality in patients who underwent pericardiocentesis.

Standardized beta coefficients were calculated with 95% confidence intervals. Receiver operating characteristic (ROC) analysis was performed to determine the ability of CRP/albumin and CRP/pf-Albumin ratios to predict in-hospital mortality. P values under 0.05 were considered to be statistically significant.

RESULTS

Our study consisted of 54 patients and two groups. No life-threatening complication was observed during the pericardiocentesis procedure. The mean age of the patients was 67.87±14.91. Table 1 shows the intergroup comparisons. No statistical difference was detected between the groups in terms of LDH, pericardial fluid lactate dehydrogenase (pf-LDH), albumin, and pf-Albumin values (p>0.05 for all) (Table 1 and 2).

Table 1. Demographic, clinical and laboratory features of the patients

Variables	All patients (n=54)	Discharged patients (n=49)	In hospital death (n=5)	P
Age (years)	67.87±14.91	67.51±14.12	71.40±23.19	0.583
Female n (%)	25(46)	24(49)	1(20)	0.223
HT n (%)	15(28)	14(29)	1(20)	0.690
DM n (%)	13(20)	12(25)	1(20)	0.827
LVEF (%)	51.17±8.17	51.47±7.96	48.20±10.54	0.399
Systolic blood pressure (mmHg)	131.11±9.37	131.47±9.20	127.60±11.43	0.384
Diastolic blood pressure (mmHg)	75.43±9.68	75.51±10.03	74.60±5.68	0.844
Heart rate (beats/min)	90.8±85.4	90.86±89.56	80.4±15.3	0.788
Laboratory values				
Glucose (mg/dl)	118.46±35.78	117.72±36.16	125.68±34.68	0.640
Creatinine (mg/dL)	1.22±0.73	1.19±0.67	1.44±1.27	0.487
Sodium (mEq/L)	140.81±6.97	141.06±7.14	138.40±4.82	0.421
Potassium (mEq/L)	4.25±0.70	4.22±0.66	4.57±1.09	0.301
TSH (mU/L)	2.31±1.59	2.30±1.62	2.32±1.46	0.980
Alanine aminotransferase (U/L)	38.48±55.51	39.68±58.11	26.76±10.70	0.625
Aspartate aminotransferase (U/L)	33.24±31.15	34.08±32.44	25.00±11.57	0.540
Calcium (mg/dl)	9.07±0.52	9.10±0.51	8.74±0.57	0.140
LDH (U/L)	321.63±189.70	317.69±187.04	360.20±234.44	0.638
LDH of Fluid (U/L)	575.48±880.576	599.57±929.832	339.40±210.165	0.534
WBC count, ($x10^3$ μL)	9.93±5.28	10.12±5.47	8.04±2.55	0.407
Hemoglobin g/dL	13.66±13.88	13.58±14.32	14.41±9.58	0.901
Trombosit count ($x10^3$ μL)	276.55±140.03	282.357±142.79	219.700±103.26	0.345
Neutrophil count, ($\times 10^3$ /L)	7.76±4.78	7.79±4.89	7.50±3.94	0.898
Lymphocyte count ($\times 10^3$ /L)	1.38±0.93	1.39±0.93	1.21±1.05	0.683

DM: Diabetes mellitus, HT: Hypertension, LVEF: Left ventricle ejection fraction, TSH: Thyroid Stimulating Hormone, LDH: Lactate dehydrogenase, CRP: C-Reactive protein

Table 2. C-reactive protein and albumin levels of cardiac tamponade patients

Variables	All patients (n=54)	Discharged patients (n=49)	In hospital death (n=5)	P
Albumin (g/dl)	3.58±0.52	3.60±0.49	3.48±0.87	0.631
Albumin of Fluid (g/dl)	2.80±0.57	2.85±0.57	2.34±0.37	0.062
CRP (mg/L)	7.49(1-30)	6.3(1-30)	19(14-25)	<0.001
CRP/albumin ratio	2.17(0.24-12.02)	1.9(0.24-10.38)	4.27(3.87-12.02)	<0.001
CRP/Albumin of Fluid ratio	2.68(0.28-13.59)	2.5(0.28-12.22)	7(6.25-13.59)	<0.001

CRP: C-Reactive Protein

CRP value was found to be more statistically significant in group 2 patients (p<0.001) (Table 2). Similarly, CRP/albumin ratio and CRP/pf-Albumin ratio were found to be numerically and statistically more significant in group 2 patients (p< 0.001 for both) (Table 2). Five patients had a lung cancer diagnosis, one had breast cancer, one had malignant neoplasm, one had larynx cancer, and five had chronic renal failure (Table 3).

Table 3. Etiology of pericardial effusion

Cause	Discharged patients (n=49)	In hospital death (n=5)	Total (n=54)
Breast CA	1	0	1
Lung CA	4	1	5
Larync CA	1	0	1
Malignant neoplasm	1	0	1
Chronic renal failure	4	1	5
Idiopathic	38	3	41

CA: Cancer

Table 4 shows the association between the in-hospital mortality and CRP (odds ratio [OR]: 0.821, P: 0.004, 95.0% confidence interval [CI]: 0.918-1.049), CRP/albumin ratio (OR: 0.600, P: 0.011, 95.0% CI: 0.406-0.888) and CRP/pf-Albumin ratio (OR: 0.608, P: 0.004, 95.0% CI: 0.431-0.856) in patients who underwent pericardiocentesis.

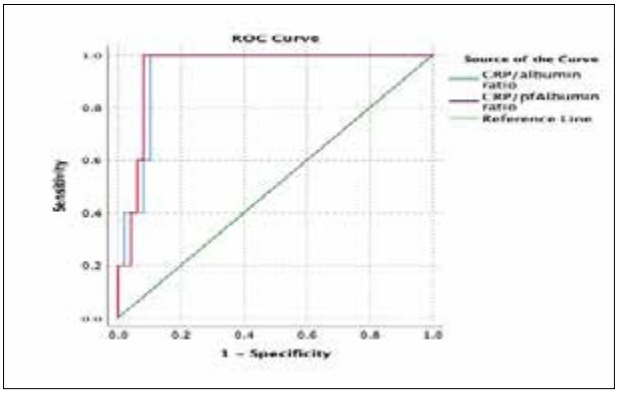
Table 4. Univariate regression analysis to determine in-hospital mortality

	Univariate		
Variables	P	OR	95% CI
Age (years)	0.577	0.981	0.918-1.049
Cancer	0.733	1.500	0.146-15.461
LDH (U/L)	0.633	0.999	0.995-1.003
LDH of Fluid (U/L)	0.552	1.001	0.998-1.003
Albumin (g/dl)	0.625	1.540	0.273-8.679
Albumin of Fluid (g/dl)	0.078	4.531	0.843-24.353
CRP (mg/L)	0.004	0.821	0.716-0.940
CRP/albumin ratio	0.011	0.600	0.406-0.888
CRP/Albumin of Fluid ratio	0.004	0.608	0.431-0.856

CI: Confidence interval, OR: Odds ratio, Abbreviations in Table 1

Receiver operating characteristic (ROC) curve analysis indicates that a CRP/albumin ratio higher than 3.8 may predict in-hospital mortality. [(p<0.001) (100% sensitivity and 90% specificity, 0.939 area under the curve 95% CI: 0.872-1.005)]. Similarly, it was observed that CRP/pf-Albumin ratio might predict in-hospital mortality when it is higher than the optimal cutoff value 6. [(p<0.001) (100% sensitivity and 92% specificity, 0.947 area under the curve 95% CI: 0.887-1.007)] (Figure 1).

Figure 1. Receiver operator characteristic curve of C-reactive protein/albumin and C-reactive protein/ pericardial fluid Albumin ratio to predict mortality in patients undergoing pericardiocentesis



DISCUSSION

Pericardiocentesis is a valuable treatment procedure for diagnosing and treating effusions causing tamponade or serious effusions regardless of the etiology. Since the first time, it was described increasing experiences and using fluoroscopic and echocardiographic devices more frequently have increased the safety and success of the procedure.[11]

As there is no randomized trial on pericardiocentesis, data on prognosis is limited. As far as is known, the prognosis is excellent in the absence of neoplastic disease and in cases where viral pathogens are implicated in the etiology.[12] In our study, eight patients had malignancy with no association being observed with mortality in the short term. As can be seen, since the clinical parameters are not always sufficient, additional parameters are needed. Determining and using laboratory parameters in addition to clinical parameters for the prognosis of pericardiocentesis patients will be effective in predicting prognosis.

Several studies investigated and proved the usability of increased CRP levels. Being an acute phase reactant, it reaches plasma peak levels within 48 hours after being released from the liver.[13,14] While high CRP levels were shown to be associated with metabolic disorder, and

another study has associated the high CRP levels with poor negative outcomes in coronary artery disease.[15] Additionally, they were found to be associated with mortality in patients with heart failure.[16] Similar to the literature, increased CRP levels were observed to be associated with short-term in-hospital mortality in patients who underwent pericardiocentesis in our study.

Similar to CRP, another useful parameter is albumin, and recent studies have associated low CRP/albumin ratios with poor prognosis in patients with heart failure and cancer.[17,18] In a long-term follow-up study such as 5 years, in which 212 pancreatic cancer patients were examined, it was shown that CRP values could be used for survival. In another meta-analysis, pre-treatment CRP/albumin ratio is a prognostic marker of poor overall survival (OS) and CSS in patients with gastric cancer (GC). In addition, high levels of CRP/albumin ratio are associated with clinicopathological features reflecting tumor progression.[19,20] Regardless of the underlying specific etiology, CRP/albumin ratio was a decisive parameter in predicting the in-hospital mortality in patients who underwent pericardiocentesis in our study. Additionally, in the comparison of ROC curves, CRP/pf-albumin ratio was a more specific parameter than CRP/albumin ratio in predicting in-hospital mortality.

Moreover, studies have shown that serum LDH levels are a strong indicator of mortality in cancer patients.[21] In our study, contrary to the literature, serum, and pericardial fluid LDH and albumin levels were not useful in predicting in-hospital mortality in patients who underwent pericardiocentesis. That differece might have been caused by the small number of patients and mixed study groups in our study.

Our study had some limitations. Firstly, it was a single-center study with a small number of patients. Secondly, as it was a retrospective study, we do not have information on the long-term usability of the results obtained in patients discharged with recovery. Prospective and multicenter studies are needed to use the study results globally.

For the first time in the literature, we demonstrated that CRP/albumin and CRP/pf-Albumin ratios are associated with in-hospital mortalities after pericardiocentesis, a life-saving procedure in severe pericardial effusions. We believe that this laboratory test which is easy to calculate, may be useful in the risk classification of the patients who underwent pericardiocentesis.

Declarations

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

This study was approved by the Çanakkale Onsekiz Mart University ethics committee of the hospital in which it took place in line with the recommendations of the Declaration of Helsinki (Date: 09.12.2020 Decision no: 2020-14).

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