The ratio of CRP to albumin levels predict re-admission to intensive care unit in septic patients

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Abstract

Aim: Sepsis is associated with high mortality rates in the intensive care unit. The timely discharge of patients diagnosed with sepsis will reduce mortality and re-admissions thus prevent increased costs. Early discharge of intensive care patients causes the transfer of patients with severe diseases to the wards and may increase re-admission and mortality. Our study aims to evaluate the effectiveness of C-Reactive Protein and Albumin levels in the prediction of the re-admission of patients treated with sepsis in the intensive care unit.

Material and methods: Patients who were treated for sepsis between December 2017 and December 2018 discharged to the ward from the intensive care unit were included within the study. Patient demographic results (age, gender), Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores, biochemical parameters, C-Reactive Protein, Albumin, C-Reactive Protein/Albumin ratios in admission and laboratory results and C-Reactive Protein, Albumin, C-Reactive Protein/Albumin ratios on the day of discharge were recorded both from intensive care unit patient-charts and hospital database.

Results: 300 patients were included in our study. The mean age of the patients was 64±19 years, and the mean APACHE-II was 22±9. The re-admitting group had higher ages and APACHE-II. The C-Reactive Protein, Albumin, C-Reactive Protein/Albumin ratio levels of re-admitted patients were significantly different than discharged patients' levels. In the Receiver Operational Curve analysis, C-Reactive Protein/Albumin ratio 23,5 was the cut-off value for re-admission. Male gender was significantly higher re-admission than females.

Conclusion: C-Reactive Protein/Albumin ratio is a valuable marker for the prediction of the re-admission of patients with sepsis in intensive care unit after discharge.

Key words: readmission, C-reactive protein, albumin, intensive care

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С-РЕАКТИВТІ АҚУЫЗДЫҢ АЛЬБУМИН ДЕҢГЕЙІНЕ ҚАТЫНАСЫ СЕПСИСКЕ ШАЛДЫҚҚАН НАУҚАСТАРДЫҢ ҚАРҚЫНДЫ ТЕРАПИЯ БӨЛІМІНЕ ҚАЙТА ЖАТҚЫЗЫЛАТЫНЫН БОЛЖАЙДЫ

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ТҰЖЫРЫМДАМА

Мақсаты: Сепсис қарқынды терапия бөлімінде өлімнің жоғары көрсеткіштерімен байланысты. Сепсис диагнозы қойылған науқастарды уақтылы шығару өлім-жітімді азайтады, ал ауруханаға қайта қабылдау шығындардың өсуіне жол бермейді. Қарқынды терапия бөлімінен пациенттерді мерзімінен бұрын шығару ауыр науқастарды палаталарға ауыстыруға әкеліп соғады және қайталап госпитализациялау мен өлім-жітімді жоғарылатуы мүмкін. Біздің зерттеуіміз сепсисі бар науқастардың қарқынды терапия бөліміне қайта госпитализациялауды болжауда С-реактивті ақуыз бен альбумин деңгейінің тиімділігін бағалауға бағытталған.

Материал және әдістері: Зерттеуге 2017 жылдың желтоқсанынан 2018 жылдың желтоқсанына дейін сепсиспен емделген, қарқынды терапия бөлімінен палатаға ауыстырылған науқастар кірді. Пациенттің демографиялық көрсеткіштері (жасы, жынысы), жедел және созылмалы функционалды өзгерістерді бағалау шкаласы (APACHE-II), биохимиялық көрсеткіштер, С-реактивті ақуыз, альбумин, қабылдау кезіндегі зертханалық нәтижелердегі С-реактивті ақуыз/альбумин қатынасы және шығарылған күні С-реактивті ақуыз, альбумин, С-реактивті

ақуыз/альбумин қатынасы қарқынды терапия бөлімі пациенттерінің жазбаларынан да, аурухананың деректер базасынан да тіркелді.

Нәтижелер: біздің зерттеуге 300 науқас енгізілді. Пациенттердің орташа жасы 64±19 жас, ал APACHE-II орташа көрсеткіші 22±9 болды. Қайта госпитализацияланғандар тобындағы пациенттердің жасы үлкен және APACHE-II жоғары болды. Қайта госпитализацияланған пациенттерде С-реактивті ақуыздың, альбуминнің және С-реактивті ақуыздың/альбуминнің қатынасы шығарылған науқастардағы деңгейден айтарлықтай ерекшеленді. ROC-қисық талдауында С-реактивті ақуыз/альбумин қатынасы қайталап госпитализациялау үшін 23,5 шекті болып табылды. Қайта госпитализацияланғандар тобында еркектер әйелдерге қарағанда едәуір көп болды.

Қорытынды: С-реактивті ақуыз/альбумин қатынасы шығарылғаннан кейін сепсиспен ауыратын науқастардың қарқынды терапия бөлімшесіне түсуді болжау үшін құнды маркер болып табылады.

Негізгі сөздер: қайта госпитализация, С-реактивті ақуыз, альбумин, қарқынды терапия

СООТНОШЕНИЕ УРОВНЕЙ С-РЕАКТИВНОГО БЕЛКА И АЛЬБУМИНА ПРОГНОЗИРУЕТ ПОВТОРНУЮ ГОСПИТАЛИЗАЦИЮ ПАЦИЕНТОВ С СЕПСИСОМ В ОТДЕЛЕНИЕ ИНТЕНСИВНОЙ ТЕРАПИИ

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РЕЗЮМЕ

Цель: Сепсис связан с высокими показателями смертности в отделении интенсивной терапии. Своевременная выписка пациентов с диагнозом сепсис снизит смертность, а повторные госпитализации предотвратят увеличение затрат. Ранняя выписка пациентов из отделения интенсивной терапии приводит к переводу пациентов с тяжелыми заболеваниями в палаты и может увеличить уровень повторной госпитализации и смертность. Наше исследование направлено на оценку эффективности уровней С-реактивного белка и альбумина в прогнозировании повторной госпитализации пациентов с сепсисом в отделение интенсивной терапии.

Материал и методы: В исследование были включены пациенты, которых лечили от сепсиса в период с декабря 2017 года по декабрь 2018 года, переведенных в палату из отделения интенсивной терапии. Демографические результаты пациентов (возраст, пол), шкала оценки острых и хронических функциональных изменений (APACHE-II), биохимические показатели, С-реактивный белок, альбумин, соотношение С-реактивный белок/альбумин в результатах лабораторных исследований при приеме и С-реактивный белок, альбумин, соотношение С-реактивный белок/альбумин в день выписки регистрировали как из карт пациентов отделения интенсивной терапии, так и из базы данных больницы.

Результаты: 300 пациентов были включены в наше исследование. Средний возраст пациентов составил 64±19 лет, а средняя оценка APACHE-II - 22±9. Пациенты в группе повторно госпитализированных были старше и с более высокой оценкой APACHE-II. Уровни С-реактивного белка, альбумина, соотношение С-реактивный белок/альбумин у повторно госпитализированных пациентов значительно отличались от уровней выписанных пациентов. В анализе кривой-ROC соотношение С-реактивный белок/альбумин 23,5 было пороговым значением для повторной госпитализации. Мужчин было значительно больше в группе повторно госпитализированных, чем женщин.

Заключение: Соотношение С-реактивный белок/альбумин является ценным маркером для прогнозирования повторной госпитализации пациентов с сепсисом в отделение интенсивной терапии после выписки.

Ключевые слова: повторная госпитализация, С-реактивный белок, альбумин, интенсивная терапия

Introduction

Sepsis is associated with high mortality rates in the intensive care unit (ICU) [1]. It is vital to start early diagnosis and treatment. Early diagnosis is a paramount important step in the treatment of sepsis, a specific test with high sensitivity and specificity in determining its severity has not been reported yet [2]. C-reactive protein (CRP) is a biomarker that can easily be used in the monitoring of inflammation in intensive care units [3]. Albumin (Alb) is a negative acute phase reactant and is an indicator of acute inflammation. Low albumin levels have been associated with the severity of the inflammatory response [4]. In a previous study, it was stated that the CRP/Prealbumin ratio can be used to estimate mortality in ICU [5].

Premature discharge from intensive care promotes the deterioration risk of the patients and may increase re-admission and mortality [6]. Delayed discharges lead to increased infections, increased waiting time, lower patient satisfaction, and staff burnout [7]. The timely discharge of septic patients will reduce hospital mortality and re-admissions. An ideal test to predict the re-admission of patients with sepsis and prevent early discharge has not yet been reported.

Our study aims to evaluate the effectiveness of CRP and albumin levels in predicting the re-admission of patients treated with sepsis in the ICU.

Materials and methods

Our retrospective cohort study was started in parallel with the Helsinki Declaration after obtaining the permission of the Hitit University Ethics Committee (2018-145). Patients who were treated for sepsis between December 2017 and December 2018 discharged to the ward from the ICU were included in the study. Patients younger than 18 years old, those treated other than sepsis, and patients with less than 24 hours of hospitalization were excluded from the study. Patients who died in the intensive care unit as well as the ones discharged to another center or home were not included in the study. Only the first admission of patients was included in the study.

Patient demographic results (age, gender), Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores, biochemical parameters, CRP, Alb, CRP/Alb ratios in admission and laboratory results, CRP, Alb, CRP/Alb ratios on the day of discharge were recorded both from ICU patient-charts and hospital database.

Re-admission was defined as a second admission. Reasons for re-admission to intensive care were classified as neurological deterioration, respiratory failure, and hemodynamic disorder.

The data were analyzed using IBM SPSS 20.0 statistical software. While evaluating the study data, the Pearson Chi-Square Test was used to compare descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max) as well as qualitative data. The suitability of the data to normal distribution was evaluated by Kolmogorov-Smirnow and Shapiro-Wilk tests. The Mann-Whitney U test was used for comparing non-normally distributed data between groups, and the Wilcoxon test was used for intra-group comparison. The ROC curve (Receiver Operating Characteristic) method was used to determine the discrimination of the variables. Values with a probability of (P) □= 0.05 are important and there is a difference between the groups, the larger values are insignificant and there is no difference between the groups.

Results

300 patients were included in our study. The flow diagram is presented in Figure 1. The mean age of the patients was 64±19 years, and the mean APACHE-II was 22±9. 30 patients
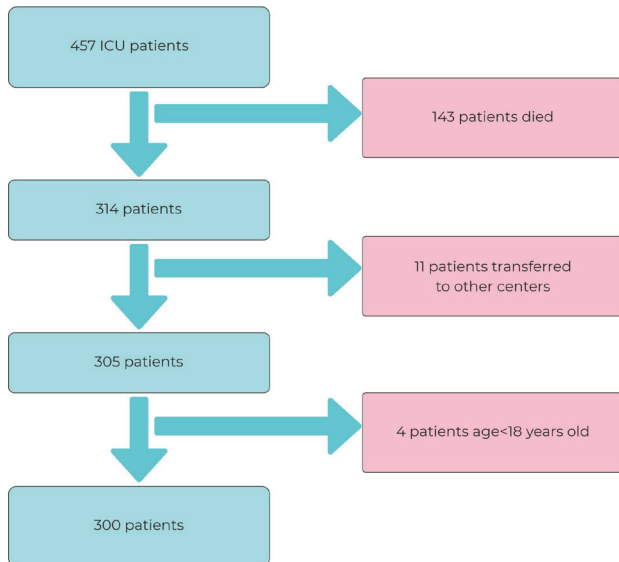
Table 1	Comparison of re-admission and discharge groups						
	Discharge(n=270) (%90)		Re-admission(n=30) (%10)		Total(n=300)		p
	Mean±SD	Min-Max	Mean±SD	Min-Max	Mean±SD	Min-Max	
Age (years)	63±20	20-92	69±13	42-85	64±19	20-92	0,222
APACHEII	22±9	3-42	25±8	6-39	22±9	3-42	0,052
LOSa	6±6	2-43	11±12	2-40	7±7	2-43	0,0321
CRPb	30±20	2-124	122±54	44-262	39±38	2-262	0,0001
Albc	2,9±0,5	1,7-4,7	2,2±0,6	1,4-3,5	2,9±0,5	1,4-4,7	0,0001
CRP/Alb	10,70±7,51	0,91-9,05	55,56±22,46	15,17-124,76	15,19±16,77	0,32-124,76	0,0001

1: Mann Whitney-U test

a: Length of Stay, b:C-Reactive Protein (mg/L) c:Albumin (g/dL)

Figure 1

Table 2	Comorbidities of patients	
	n	%
Daibetes mellitus	85	28,3
Hypertension	66	22,0
Congestive heart failure	20	6,7
Pulmonary edema	8	2,7
Demantia	21	7,0
Chronic obstructive pulmonary disease	42	14,0
Type I pulmonary disease	60	20,0
Liver failure	6	2,0
Gastrointestinal hemorrage	10	3,4
Cerebro vascular disease	22	7,3
Traumatic brain injury	8	2,7
Post cardiac arrest	18	6,0
Traffic accident	24	8,0
End stage cancer	22	7,3
Hypotansive shock	42	14,0
Intracranial hemorrage	18	6,0
Renal failure	26	8,7

(10%) were readmitted to intensive care within 48 hours after discharge. The demographic characteristics, APACHE-II, CRP, Alb, and CRP/Alb ratios of patients who are readmitted and not readmitted are presented in Table 1. Comorbidities of the patients are presented in Table 2. When the re-admission group and the discharge group were compared in terms of gender, there was a significant difference between the groups as shown in Table 3.

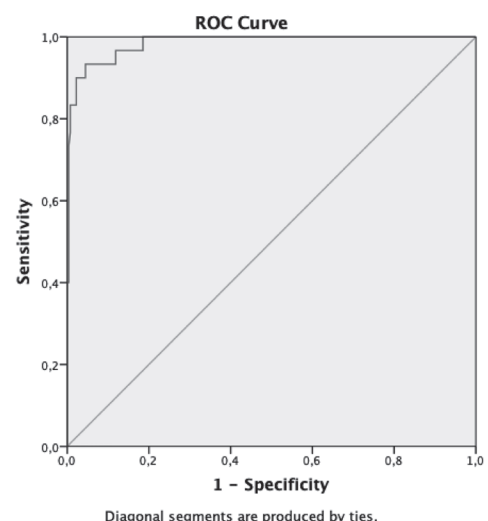| Table 3	Evaluation of the study groups in terms of gender						
	Discharge (n=270) (%90)		Re-admission(n=30) (%10)		Total(n=300)		p
	n	%	n	%	n	%	
Men	118	43,7	22	73,3	140	46,7	0,002*
Women	152	56,3	8	26,7	160	53,3	

* Chi-square

Figure 2 - ROC analysis for CRP
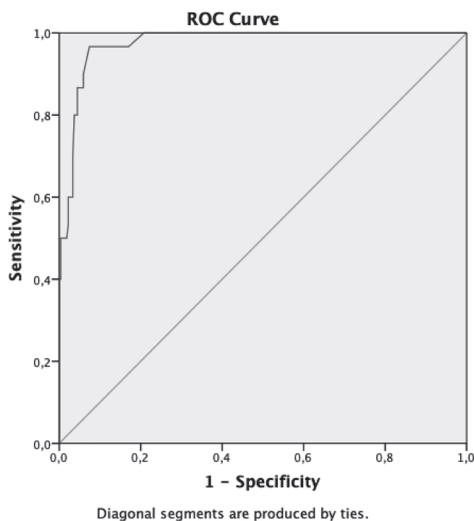
Figure 3 - ROC analysis for CRP / Alb ratio

In the Receiver Operational Curve analysis for re-hospitalization, the area under the curve value 65 mg/L Curve (AUC=0.975; p=0.0001, 95% confidence interval CI: 0.958-992), ROC is shown in Figure 2. The cutoff value for CRP/Alb was found to be 23.5. The area under the curve (AUC=0.985; p=0.0001, 95% confidence interval CI: 0.98-1) and ROC are shown in Figure 3.

Discussion

In our study, the rate of re-admission after discharge from the intensive care unit was 10%. There was a significant difference in CRP, Alb, and CRP/Alb ratios of sepsis patients who needed re-admission. In a study involving 2852 patients, Kaben et al. found the rate of re-admission to be 13.4% and highlighted the importance of serious sepsis [8]. In the study conducted by Araujo et al. the rate of re-admission was reported as 9.3% in trauma patients and 13.7% in surgical and medical intensive care units [9]. In the short case series of Kwok et al. re-admission was reported as 1.3% [10]. However, the presence of a high-dependence service that can serve patients with a need for support right next to the intensive care unit and postoperative patients were the factors of a low rate for re-admission. In our study, the rate of re-admission of septic patients was found compatible with the literature.

As well as being effective in showing inflammation and sepsis response of intensive care patients, CRP is an important indicator in the determination of the severity of heart failure and cerebral diseases [11–13]. In our previous study, we proved that CRP values over 98 mg/L increased mortality 38 times [5]. Kwok et al. stated that the CRP values above 100 mg/L were important in the prediction of re-admission. Devran et al. reported that CRP values above 100 mg/L in the study conducted in patients with sepsis increased mortality [13]. We also found that the CRP cut-off value was 65 mg/L in assessing re-admissions. We think that the CRP above this value is effective in the prediction of re-admission within 48 hours.

In our study, we found that the length of stay in the intensive care unit was different between the groups. We determined the average length of intensive care stay of patients treated with sepsis as 7 days. The average length of stay of patients with septic shock was 9 days and 18 days according to the studies realized by Devran et al. [13] and Kim et al. [14], respectively. In the study conducted by Verburg et al. all Dutch intensive care units were analyzed and the average length of stay of sepsis patients was reported as 2.3 days [15]. The average intensive care length of stay in our study was compatible with the literature. We think that patients with a short length of stay period are relatively less serious patients. On the other hand, the patients in need of re-admission have a longer length of stay period and these patients were more severely septic than others.

In our study, although the average age of female patients in the re-admission group was higher than that of men, the re-admission rate was higher in men. We thought that the higher rate of re-admission among the younger patient group needs to be further analyzed.

We revealed that patients in the re-admission group had lower albumin values. Albumin is a negative acute phase reactant and the relationship between albumin levels and mortality has been previously demonstrated in several studies [16,17]. In a study evaluating the 90-day mortality of septic patients, the mean albumin values of the died patient group was reported as 2.2 g/dL, and the cut-off value for mortality was 2.5 g/dL [18]. Vincent et al. reported in a metaanalysis that hypoalbuminemia negatively affected the entire clinical spectrum, mortality, morbidity, hospital stay, and intensive care stay of the patients [19]. In our previous study, we found that albumin levels below 2.1 g/dL were associated with mortality. We also reported that the albumin value below 2.4 g/dL caused a 6.9-fold increase in mortality [5]. In our study, in septic patients, the risk of re-admission was found to be increasing when the albumin level was below 2.4 g/dL.

In septic patients, an increase in CRP/Alb level is observed with both increasing CRP levels and decreasing albumin levels, which is a negative acute-phase reactant. According to the study of Ranzani et al. the septic patients were analyzed and it was realized that the CRP/Alb ratio above 20, predicted 90-day mortality [18]. In their study to estimate the mortality of gastric cancer patients, Toiyama et al. reported that CRP/Alb ratio above 58 increased mortality 2.8 times [20]. In our previous study, we revealed that the CRP/Alb ratio above 44 increases the mortality 29 times [5]. In our study, in septic patients, the CRP/Alb ratio above 23.4 was valuable in the prediction of re-admission to intensive care.

The main weakness of our study is its retrospective manner and being a single-center study. The removal of the lost data is the strength.

Conclusion

CRP/Albumin ratio is a valuable marker in the prediction of the re-admission of patients with sepsis in ICU after discharge. We think that CRP/Albumin ratio can be used as a quality parameter in intensive care units in the future.

Disclosures: There is no conflict of interest for all authors.

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