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Original Research

Bun/creatinine ratio and the inferior vena cava collapsibility index in ventilator associated pneumonia

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Abstract

Aim: The evaluation of the intravascular fluid status of critical patients is of significant importance. Many publications that suggest that measurement of the inferior vena cava diameter is successful in indicating volume status are available. In this study, we aimed to compare the efficacy of the commonly used scoring systems APACHE II, SOFA, and CPIS, the BUN/Cre ratio, and the inferior vena cava collapsibility index (IVC CI) in terms of mortality prediction among patients diagnosed with VAP. Material and Method: Fifty-seven patients who had bacteria isolation in the specimens of the lower respiratory tract were included in the study. The demographic characteristics, comorbid conditions of all patients were recorded. In addition, the biochemical parameters, BUN/Cre ratio, MDRD, APACHE II, SOFA, CPIS, and the final status of each patient were recorded. Results: There was a statistically significant relationship between IVC CI and BCR (p=0.003). A significant correlation was found between MDRD and BCR ($p < 0.001$). There was a positive correlation between procalcitonin and SOFA score ($r=0.618$, $p < 0.001$). An increase in the CPIS value increases mortality to 3.52 times ($p = 0.027$). The mortality risk of those with an IVC CI value of 50 and above is 38.59 times greater than that of those with an IVC CI value below 50 (p=0.003). Discussion: Procalcitonin and CPIS may provide guidance for predicting mortality in patients with VAP. We believe that the calculation of the IVC CI value is a sensitive method for determining and monitoring fluid therapy in patients with VAP and in every patient admitted to the ICU.

Keywords

Ventilator-Associated Pneumonia; Inferior Vena Cava Collapsibility Index; BUN/Creatinin Ratio; Mortality; Intensive Care Unite

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Introduction

Ventilator-associated pneumonia (VAP) is a pneumonia that develops no sooner than 48 hours after intubation in patients receiving invasive mechanical ventilation support who did not have pneumonia at the time of intubation. It is part of the hospital-acquired pneumonia subgroup [1,2].

The incidence of ventilator-associated pneumonia (VAP) is reported to range between 2 and 16 per 1000 ventilator days [3]. Due to the high mortality and morbidity rates of patients admitted to intensive care units, several scoring systems have been developed to predict prognosis and guide the treatments to be applied [4]. Most of these, however, provide more general prognostic predictions like the Acute Physiology and Chronic Health Evaluation II (APACHE II) and the Sequential Organ Failure Assessment (SOFA) scores.

Although admission to intensive care units (ICUs) is less in proportion to the total number of patients hospitalized, invasive interventions that increase the risk of infection affect the incidence of infections and the rate of mortality in relation to this. Ventilator-associated pneumonia (VAP) due to mechanical ventilation stands out in this regard [5]. Because VAP is the most commonly observed infectious disease among critical patients in ICUs, the development of a scoring system for the diagnosis and prognosis of VAP has been an important area of research. The Clinical Pulmonary Infection Score -CPIS, developed for VAP patients with this purpose and different from general scoring models, is taken as a basis in current studies [6]. However, despite the frequent use of the CPIS model, there are studies that question the suitability of this model [5, 7, 8].

The evaluation and management of the intravascular fluid status of critical patients are of significant importance. Currently, methods such as physical examination, vital sign monitoring, biochemical marker monitoring, and ultrasound-based monitoring of the central venous pressure and inferior vena cava diameter are being used for this assessment [9]. Although physical examination is a fast and practical method, it is not fully successful in evaluating intravascular volume [10,11]. The BUN/creatinine ratio is normally 10/1. If the ratio is greater than 10, especially greater than 20, it can be a sign of a reduction in the volume of extracellular fluid. Similarly, with blood pressure monitoring, normal blood pressure values can be found despite a blood loss of up to 30% [12]. Central venous pressure monitoring is found in more successful but invasive methods such as pulmonary artery catheterization, but these invasive methods can bring about complications. Because of this, a non-invasive and highly accurate method is needed. At this point, there are many recent publications suggesting that measurement of the inferior vena cava diameter is successful in indicating volume status [13-19].

For this reason, we aimed to compare the efficacy of frequently used scoring systems such as APACHE II, SOFA, and CPIS, the BUN/Cre ratio, and the inferior vena cava collapsibility index (IVC CI) in terms of mortality prediction in patients diagnosed with VAP.

Material and Method

Patients who were hospitalized at the Ordu University Faculty of Medicine secondary intensive care unit general intensive care unit between September 1, 2017 and June 1, 2018 and who underwent invasive mechanical ventilation for longer than 48 hours were included in our study. Fifty-seven patients, whose clinical findings were consistent with VAP and who had bacteria isolation in the specimens of the lower respiratory tract, were included in the study. Our study was planned as prospective and unblinded.

Our inclusion criteria are given below.

1. Staying for over 120 hours in the intensive care unit;
2. Being aged over 18 years;
3. Presence of VAP diagnostic criteria in the patient,

- New or progressive infiltration in the chest X-ray without other reasons
- Positive blood or pleural culture identical to the positive tracheal aspirate culture 48 hours after introduction of mechanical ventilation
-The findings having appeared at least 48 hours after the introduction of MV
- At least two of these being positive: Fever, leukocytosis, purulent tracheal aspirate

Our exclusion criteria were:

1. Patients aged below 18 years;
2. Patients diagnosed with malignant Ca;
3. Patients with an HIV infection and neutropenic patients;
4. Patients who underwent invasive mechanical ventilation for less than 48 hours;
5. Patients with symptoms of pneumonia who were infected with the same bacteria before intubation
6. Tracheostomized patients with a home mechanical ventilator were not included in the study.

The research was carried out with the permission of the Ordu University Faculty of Medicine Clinical Research Ethics Committee dated 24.08.2017 and numbered 2017/92. Written informed consent was obtained from all patients and their relatives.

A 3.5 Mhz abdominal probe was used for IVC diameter measurements. An M-mode abdominal probe was used to measure the minimum and maximum IVC diameters between respiratory cycles. The IVC diameter was measured with an abdominal probe in the supine position. The probe was placed in the subxiphoid region and a sagittal section IVC image was obtained. In order to standardize the measurements, measurements were made from 2 cm on the caudal part of the area of intersection of the IVC and the right atrium via a subxiphoid window. Measurements were made on a sagittal IVC section on the longitudinal plane, in M-mode, between the internal IVC walls. Maximum and minimum IVC diameters were measured separately in M-mode. The inspiratory and expiratory diameters were recorded during measurements. The inferior vena cava collapsibility index (IVC CI) was calculated. This index was obtained by dividing the difference between the vena cava inferior expiratory diameter (exp IVC, maximal diameter) and vena cava inferior inspiratory diameter (insp IVC, minimal diameter) by the vena cava inferior expiratory diameter.

IVC CI=(exp IVC-insp IVC)/exp IVC ×100 . Picture of inferior vena cava collapsibility index measurement is shown in **Figure 1.**

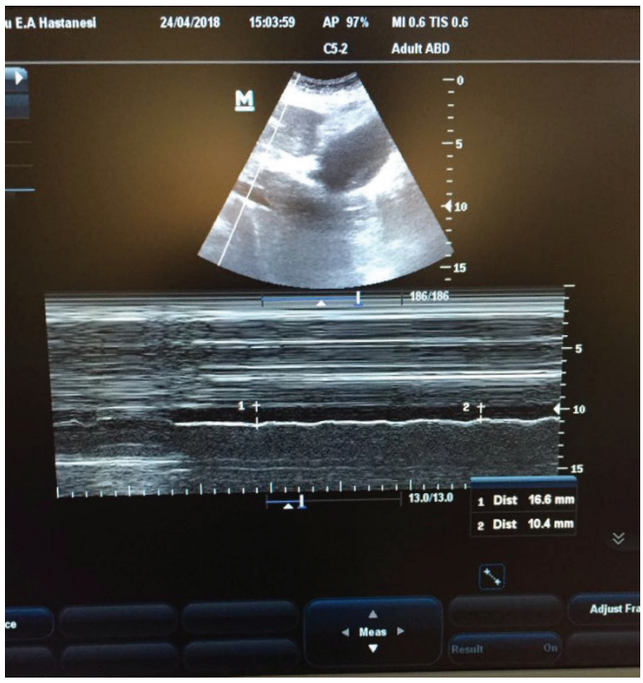

Figure 1. Picture of Inferior Vena Cava Collapsibility Index Measurement

The demographic characteristics such as age, weight, height, and sex, their accompanying comorbid conditions, whether they received renal replacement therapy at the ICU, and whether they received inotropic support were recorded. In addition, the biochemical parameters, BUN/Cre ratio, MDRD (CKD-EPI), proteinuria presence, APACHE II score, SOFA score, CPIS score, and final status (death or discharge) of each patient was separately recorded. The parameters analyzed for our study were the values determined for the day when VAP was diagnosed. The flow diagram of the patients is shown in **Figure 2.**

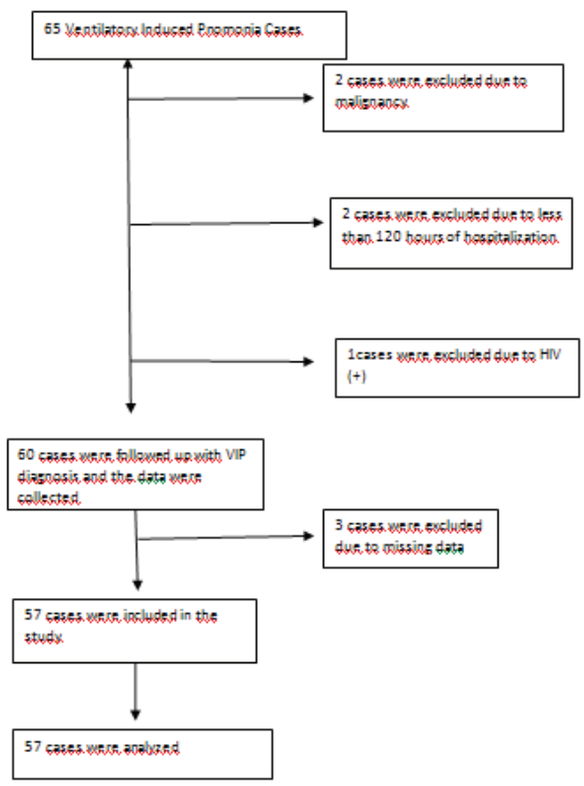

Figure 2. Flow diagram of inclusions and exclusions for patients

Statistical Analysis

The data were analyzed with IBM SPSS v23. The conformity of data to the normal distribution was examined with the Shapiro-Wilk test. The independent samples t-test was used to compare data with normal distribution and the Mann-Whitney U test was used to compare data without normal distribution. The correlation between variables was examined with Spearman's correlation analysis. The binary logistic regression analysis method was used to determine the risk factors affecting mortality. Normally distributed data were expressed as the mean ± standard deviation, and non-normally distributed data were expressed as median (min-max). Qualitative data were expressed as frequencies (percent). The significance level was set at $p<0.05$.

Results

The rate of females included in the study is 47.4% while the rate of males is 52.6%. The rate of those who died is 70.2%, while that of those discharged is 29.8%. When comorbidity is examined, the rate of mix (presence of multiple comorbid conditions) patients is 43.9%, the DM rate is 12.3%, the rate of those with CVD is 12.3%, and the rate of those with HT is 10.5%. The rate of those who received RRT is 26.3%, while the rate of those who received inotropic support is 75.4%. Descriptive statistical values of the patients are given in Table 1.

Table 1. Descriptive statistical values of the patients

	mean ± s. deviation	median (min-max)
ex cases age	72.5±10.1	82(61-97)
discharge cases age	69.8±9.7	71(55-74)
age total	77.9 ± 11.1	79 (46 - 97)
mdrd ex cases	50.4 ± 30.7	47 (8 - 133)
mdrd discharge cases	71.7±21.5	49(25-161)
mdrd total	53.1 ± 34.5	45 (7 - 125)
bcr ex cases	78.4±21.2	80(23-40)
bcr discharge cases	51.7±10.9	31 (1.8-141.5)
bcr total	42.6 ± 32.2	33.8 (1.6 - 159.3)
procalsitonin ex cases	15.5±23.1	4.1(21-100)
procalsitonin discharge cases	11.2±7.5	2(0-23)
procalcitonin total	9.4 ± 21.9	1.8 (0 - 100)
apache ii ex cases	34.2 ±5.3	27(11-42)
apache ii discharge cases	20.5±3.1	11(4-31)
apache ii total	25.2 ± 6.7	25 (6 - 38)
sofa ex cases	9.1±2.1	15(12-19)
sofa discharge cases	7.3±2.8	11(13-17)
sofa total cases	8.7 ± 3.3	9 (2 - 16)
cpis ex cases	9.1±3.4	8(7-19.2)
cpis discharge cases	6.7±1.8	7(5-13.4)
cpis total cases	7.5 ± 1.6	7 (6 - 16.6)
ivc ci ex cases	31.7±10.1	32.8(9.4-50)
ivc ci discharge cases	23.4±6.9	20(7.4-39)
ivc ci	26.9 ± 8.2	26.4 (8.4 - 50)

BUN: Blood Urea Nitrogen; Cre: Creatinine; BCR: BUN/Crea ratio; WBC: White Blood Cell; Hgb: Hemoglobin; Plt: Platelet; CRP: C - reactive protein; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment;
CPIS: Clinical Pulmonary Infection Score; insp IVC: inspiratory inferior vena cava diameter (IVC min) exp IVC: expiratory inferior vena cava diameter (IVC max); MDRD: Modification of Diet in Renal Disease

A statistically significant, weak negative correlation was found between BCR and the SOFA score (r = -0.308, p = 0.020). As BCR increases, the SOFA score value decreases. The correlation between BCR and the APACHE II and CPIS scores was not statistically significant. Table 2 shows the relationship between BCR and the scoring systems used.

Table 2. The correlation between BCR, IVC CI and the APACHE II, SOFA, and CPIS scores

		BCR	IVC CI
APACHE II	r	-0.088	-0.101
	p	0.515	0.457
SOFA	r	-0.308	-0.076
	p	0.020	0.574
CPIS	r	-0.207	-0.065
	p	0.122	0.629

r: Spearman's correlation coefficient

There was no statistically significant correlation between IVC CI and the APACHE II and CPIS scores (r-values -0.101, -0.076, and -0.065, respectively). There was a statistically significant relationship and a weak positive correlation between IVC CI and BCR (r = 0.325 p = 0.003).

There was no difference between median BCR values based on receiving or not receiving inotropic support or not (p = 0.926). While the median value was 32.5 for those who did not receive support, it was found as 34.1 for those who did receive support. There was no difference between IVC CI values based on receiving or not receiving inotropic support (p = 0.292). While the mean value was 28.5 for those who did not receive inotropic support, it was found as 26.4 for those who did receive inotropic support.

A moderate positive significant correlation was found between MDRD and BCR (r = 0.457, p < 0.001). As MDRD increases, so does BCR. There was no statistically significant relationship between MDRD and IVC CI. Table 4 shows the relationship between BCR and IVC CI. There was a statistically significant, moderate positive correlation between procalcitonin and SOFA (r = 0.618, p < 0.001). As procalcitonin increases, so does the SOFA value. There was no statistically significant relationship between procalcitonin and BCR, the caval index, APACHE II, and CPIS. Table 3 shows the relationship between procalcitonin and BCR, IVC CI, and intensive care scores.

Table 3. The relationship between MDRD and BCR and IVC CI

		Procalcitonin
BCR	r	-0.201
	p	0.134
IVC CI	r	-0.119
	p	0.379
APACHE II score	r	0.204
	p	0.127
SOFA score	r	0.618
	p	< 0.001
CPIS score	r	0.131
	p	0.331

r: Spearman's correlation coefficient

Whether variables like age, sex, receiving inotropic support, MDRD, procalcitonin, APACHE II score, SOFA score, CPIS score, BUN, creatinine, Na, K, albumin, WBC, Hgb, Plt, lactate, CRP, insp IVC, exp IVC, BCR, and the inferior vena cava collapsibility index (IVC CI) were independent risk factors for mortality was investigated with a binary logistic regression analysis. The MDRD, Procalcitonin, CPIS, Hgb, and IVC CI variables were found to be independent risk factors for mortality. Increased MDRD, Procalcitonin, and Hgb have a protective effect against mortality. An increase in the CPIS value increases mortality by 3.52 times (p = 0.027). The IVC CI value was incorporated in the model by dividing it into 2 groups as 35 and above and below 35, and the mortality risk of those with an IVC CI value of 35 and above is 21.1 times higher compared to those with an IVC CI value below 35 (p = 0.008). Table 4 shows the logistic regression analysis results.

Table 4. Logistic regression analysis results

	Coefficient B	Standard Error	Wald Test Statistic	p	OR
MDRD	-0.05	0.02	7,10	0.008	0.95
Procalcitonin	-0,07	0.03	8.06	0.005	0.93
CPIS	1.26	0.57	4.90	0.027	3.52
Hgb	-0.86	0.30	7.88	0.005	0.43
IVC CI	3.65	1.25	8.54	0.008	21.1

Classification accuracy rate: 84.2%

Discussion

Dehydration should be distinguished from hypovolemia. Dehydration is the loss of total body water content, while hypovolemia is only the loss of the intravascular compartment [20].

In a study by Orso et al., the relationship between the IVC CI and dehydration presence in elderly patients was investigated. They divided the elderly population included in the study into two groups as those with a BUN/Cre ratio above 20 and those with a BUN/Cre ratio below 20. They identified the group with a BUN/Cre ratio above 20 as the group with high caval indexes and found a high level of statistical significance. The authors state that the BUN/Cre ratio is not the gold standard for diagnosing dehydration and that bedside measurement of the inferior vena cava diameter and the inferior vena cava collapsibility index (IVC CI) are much more sensitive [21]. In our study, we found a weak correlation between our IVC CI values and the BUN/Cre ratio.

In a study conducted by Yoon et al., it was found that an increased BUN/Cre ratio is not associated with mortality in patients with severe burns. At the same time, the authors state that an increased BUN/Cre ratio does not have predictive value with respect to early acute renal damage development and progression to renal replacement therapy [22]. In our study, an increased BUN/Cre ratio was not found to be correlated with mortality according to the binary logistic regression analysis we performed.

In a study that Kim et al. conducted on 182 patients with deep vein thrombosis and lower extremity weakness that had ischemic strokes, it is stated in those with a BUN/Cre ratio above

15, it is an independent risk factor for the development of acute ischemic stroke. It is reported that a high BUN/Cre ratio is a safe marker for the diagnosis of dehydration [23]. Our results are partially consistent with the results of Kim et al. In our study, we found that a BUN/Cre ratio elevation does not have a mortality predictive value, but that it is correlated with the IVC CI, which is another indirect indicator of hypovolemia. The fact that we could not determine a relationship between BCR and volume status could be due to the small number of our cases.

In a study conducted by Kaydu et al., they measured the inferior vena cava diameters of patients in the preoperative and early postoperative periods and calculated their IVC CI. While no significant difference was found in the preoperative and postoperative inferior vena cava diameter measurements, preoperative and postoperative IVC CI values were found to be statistically significant. Kaydu et al. state that the IVC CI is a simple, practical, and definitive method for determining fluid requirement in the perioperative period and for detecting fluid deficit in the early postoperative period [24]. Our study results match the study results of Kaydu et al. There were weak positive correlation and statistical significance between BCR values and IVC CI values in patients with VAP in the ICU. We can say that the IVC CI can be reliably used to determine fluid requirement in patients with VAP in ICUs. Our results are consistent with the findings in the literature.

In a study by Torterüe et al., in which they investigated the efficacy of the IVC CI in detecting overhydration in 16 pre-dialysis child patients, it is stated that IVC CI values are not an effective method for determining volume status. It is expressed that the IVC CI will only be helpful for distinguishing volume-dependent hypertension from volume-independent hypertension [25]. Our results do not match the study results of Torterüe et al. As in our study, many studies in the literature emphasize that the caval index is an effective and valuable method for determining volume status. This result may be related to the fact that the sample size of Torterüe et al. is quite small.

In a study Corl et al. conducted on 124 intensive care patients, they compared the IVC CI values obtained after administering 500 ml saline intravenously to patients thought to be hypovolemic with IVC CI values obtained prior to fluid therapy. In the study, which they conducted on a spontaneously breathing patient group not attached to a mechanical ventilator, they report that the IVC CI values measured before and after fluid therapy reflected the response to therapy very effectively. The authors also found the method to be effective in patients who did not respond to fluid therapy [26]. Although our study was conducted on a patient group without spontaneous respiration, attached to mechanical ventilators, we also determined similarly effective measurement values. Our results are consistent with the literature.

The APACHE II score, which is used for predicting intensive care mortality, still remains reliable. Although a newly modified scoring system such as the APACHE IV has entered the literature, Venkataraman et al. obtained more reliable results in mortality prediction with the APACHE II scoring system compared to APACHE IV [27]. In our study, we used APACHE II for predicting mortality. Likewise, in a validation study conducted by Kaymak et al. on 690 adult ICU patients, it is emphasized that the mortality predictive values of the SOFA and APACHE II scores are still valid for the Turkish population [28]. In our study, the SOFA score was also used for predicting mortality in addition to the APACHE II score. In our study, the APACHE II and SOFA scores of mortal cases were high and statistically significant. We think that our results reflect the results of the Turkish population.

In a study conducted by Wongsurakiat and Tulatamakit, it is stated that the clinical correlation of the serum procalcitonin level and the CPIS score is quite strong in VAP patients, and that it is highly reliable for deciding whether to continue or discontinue antibiotics [29]. We also used the procalcitonin level and CPIS score in our study. We found a statistically significant relationship between procalcitonin levels and CPIS scores and the IVC CI and mortality. Our results are consistent with the findings in the literature.

Our study has some limitations. First of all, the number of intensive care beds in our hospital is limited. Therefore, the number of patients intubated is less because our ıntensive care unit is second degree. It was impossible for us to reach the number of patients in our power analysis. The low number of cases in our study is the biggest limiting factor.

In conclusion, CPIS, which is an intensive care scoring system, reflects the severity of pulmonary infection in VAP patients in ICUs. The SOFA and APACHE II scores have mortality predictive value and can be used reliably. Procalcitonin and CPIS may provide guidance for predicting mortality in patients with VAP. Knowing the volume status of VAP patients may bring advantages to the clinician. For this reason, we think that calculating the IVC CI value of VAP patients is a non-invasive, simple, and practical bedside method for the determination and monitoring of fluid therapy. We believe that clinicians to know this measurement (IVC CI) can be useful in the management of fluid and our study will shed light on future studies with a larger population.

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

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