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Prognostic value of Pleth Variability Index in patients followed up in the Intensive Care Unit

T. ALBAYRAK[1], B. YUKSEL[2]

[1]Department of Anesthesiology and Reanimation, Medical Faculty, Giresun University, Giresun, Turkey
[2]Internal Medicine Intensive Care Unit, Giresun Training and Research Hospital, Giresun, Turkey

Abstract. – OBJECTIVE: The Pleth Variability Index (PVI) can guide the approach to hypovolemia, which is sometimes the cause and sometimes the result of major diseases; further studies are needed on this index. Therefore, in the present study, we aimed to evaluate the prognostic value of PVI and its relationship with 28-day mortality.

PATIENTS AND METHODS: A total of 158 patients were included. Patients were divided into two groups according to 28-day mortality. Patients who died within 28 days were assigned to Group M (Mortal), while those who survived were included in Group S (Survive). Patients' demographics, definitive diagnosis, arterial blood pressure, fingertip oxygen saturation, PVI, fingertip blood glucose, fever, pulse, shock index, and serum lactate level were recorded.

RESULTS: Regarding demographics, no statistically significant difference was found between the two groups in terms of age, gender, and Body Mass Index (BMI) (p=0.356, p=0.966, and p=0.977, respectively). The rate of intubation, the use of vasopressors, Acute Physiology and Chronic Health Evaluation (APACHE) II score, shock index, and PVI values were statistically significantly higher in Group M compared to Group S (for all, p<0.001). Glasgow Coma Score (GCS), Perfusion Index (PI), and length of stay were statistically significantly lower in Group M than in Group S (p<0.001, p<0.001, and p=0.025, respectively). PVI predicted 28-day mortality with 83.8% sensitivity and 97.9% specificity.

CONCLUSIONS: PVI, serum lactate level, PI, APACHE II, GCS, and need for vasopressors were independent risk factors for 28-day mortality in the Intensive Care Unit (ICU). PVI and serum lactate have a prognostic value in predicting mortality.

Key Words:
Pleth variability index, PVI, Perfusion index, Lactate, ICU, Mortality.

Introduction

Intensive Care Medicine offers interventions that improve morbidity and mortality outcomes; however, these interventions also carry significant risks of adverse events and serious errors. Iatrogenic effects can be reduced through appropriate monitoring[1].

Traditional methods of assessing fluid status, such as static and invasive measurements like central venous pressure and cardiac output, have limitations. Inadequate fluid management can lead to various complications. The concept of goal-targeted fluid therapy, especially in perioperative and shock scenarios, has shown benefits in maintaining hemodynamic stability and reducing complications[2-8].

The Plethysmographic Variability Index (PVI) is introduced as a dynamic and non-invasive method to monitor fluid responsiveness. PVI uses pulse oximetry waveforms to measure respiratory variations in the plethysmographic waveform amplitude[7]. Higher PVI values indicate a higher likelihood of the patient responding positively to fluid infusion with increased cardiac output[9,10]. Recent studies[3,11,12] and meta-analyses have supported PVI's accuracy in predicting fluid responsiveness. The advantages of PVI include its non-invasiveness, quick results, easy bedside application, objectivity, and numerical measurement.

Blood lactate level is crucial in guiding treatment for critically ill patients, and PVI has been suggested[13] to be associated with lactate levels. The combination of PVI, plethysmographic index (PI), and serum lactate levels could aid in the early identification of hemodynamic instability and facilitate prompt intervention. Since PVI can help guide the approach to hypovolemia, further research is needed to explore its potential benefits

Corresponding Author: T. Albayrak, MD; e-mail: tuna.albayrak@giresun.edu.tr

in various diseases. Therefore, the current study aims to assess the predictive value of PVI and its connection to 28-day mortality.

Patients and Methods

A total of 158 patients who were followed up in the Intensive Care Unit (ICU) of Giresun Training and Research Hospital due to various diagnoses between April 2023 and July 2023 were enrolled in the study.

Ethics Considerations

The present study was conducted according to the Declaration of Helsinki and approved by the Clinical Research and Ethics Committee of Giresun University, under the approval number E-90139838-000-151847, dated 13.04.2023.

Patients and/or their relatives were informed about the study objectives and provided written informed consent, adhering to the principles outlined in the 2013 revision of the Declaration of Helsinki.

Study Design

Patients were categorized into two groups based on their 28-day mortality outcome. Group M consisted of patients who died within 28 days, while Group S included patients who survived. Inclusion criteria encompassed patients aged 18 years and above, referred from the emergency department or clinics, with no history of cardiac or respiratory arrest during admission. Exclusions comprised patients under 18 years, those experiencing cardiac or respiratory arrest during ICU admission, and individuals unable to undergo PVI measurement due to factors like dyed skin, nail polish, finger amputation, or refusal of participation by their relatives.

Patient demographics, such as age, gender, definitive diagnosis, arterial blood pressure, fingertip oxygen saturation, Pleth variability index (PVI), fingertip blood glucose, fever status, pulse rate, shock index, and serum lactate level, were recorded. PVI was measured from the right index finger using a PVI probe (Radical-7®; Masimo Corp., Irvine, CA, USA), with light protection. If technical issues arose with the index finger, measurements were taken from the nearest fingers. Two measurements were averaged, taken 30 seconds apart. Medical staff, including evaluating physicians and treating nurses, were blinded to the study during patient evaluation and treatment. Patients were followed up until ICU discharge or mortality.

Statistical Analysis

Data were analyzed using SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Variable distribution normality was assessed using the Kolmogorov-Smirnov method. Continuous variables were expressed as mean and standard deviation or median (25-75 percentile) based on distribution. Categorical variables were presented as numbers and percentages. Parametric or non-parametric tests were applied for continuous variable analysis based on distribution. Categorical variable analysis used the Chi-square test. Logistic regression identified independent risk factors associated with patient mortality. Receiver Operating Characteristic (ROC) analysis determined cut-off values for numerical variables in mortality prediction. Microsoft Excel 2010 software aided in determining the cut-off value with the highest sensitivity and specificity. Statistically significant values were defined as $p<0.05$.

Results

47 patients who died were included in Group M, while 111 patients who survived were assigned to Group S.

Regarding demographics, no statistically significant difference was found between the two groups in terms of age, gender, and BMI ($p=0.356$, $p=0.966$, and $p=0.977$, respectively). Similarly, there was no statistically significant difference between the groups in terms of all parameters including disease history (for all, $p>0.05$). There was no statistically significant difference between the groups in terms of the indications for admission to the ICU.

When patient parameters during stay in the ICU were evaluated; the rate of intubation, the use of vasopressors, APACHE II score, shock index and PVI values were statistically significantly higher in Group M compared to Group S (for all, $p<0.001$). On the other hand, GCS score, PI and length of stay were statistically significantly lower in Group M than in Group S ($p<0.001$, $p<0.001$ and $p=0.025$; respectively) (Table I).

Among blood parameters, serum lactate level was statistically significantly lower in Group S (1.40; 1.10-2.00) compared to Group M (3.60;

Table I. ICU parameters of the groups.

Characteristics		Group S (n = 111)	Group M (n = 47)	*p*-value
Vasopressor	No	69 (62.2%)	14 (29.8%)	**< 0.001**
	Yes	42 (37.8%)	33 (70.2%)	
Intubation	No	46 (41.4%)	1 (2.1%)	**< 0.001**
	Yes	65 (58.6%)	46 (97.9%)	
MAP (mmHg)		78 ± 18	72 ± 19	**0.042**
SpO_2 (%)		94 (91-97)	93 (91-97)	0.801
Fever		36.8 (36.4-37.0)	37.0 (36.4-37.5)	0.069
Pulse		95 (82-112)	110 (89-122)	0.086
APACHE II		18 (12-23)	29 (27-31)	**< 0.001**
GCS		12 (8-15)	9 (4-12)	**< 0.001**
Shock index		0.800 (0.660-0.990)	1.200 (0.940-1.600)	**< 0.001**
PVI		23 (16-28)	39 (36-47)	**< 0.001**
PI		2.10 (0.82-3.90)	0.77 (0.36-2.10)	**< 0.001**
Length of stay		19 (8-35)	10 (7-23)	**0.025**

While continuous variables were expressed as mean±SD or median (25-75 percentiles), categorical variables were presented as n (%). While the Chi-square test was applied for categorical variables, the *t*-test or Mann-Whitney U test was applied for continuous variables. ICU: Intensive Care Unit, PVI: Pleth Variability Index, MAP: Mean Arterial Pressure, PI: Plethysmographic Index, GCS: Glasgow Coma Score, APACHE: Acute Physiology and Chronic Health Evaluation.

250-4.30). Multivariate logistic regression analysis was performed using statistically significant and significant variables in patients who developed 28-day mortality. Of these variables, lactate (OR=9.430, CI=2.489-35.735), PVI (OR=1.133, GA=1.006-1.275), APACHE II (OR=1.191, CI=1.002-1.414), and GCS (OR=0.657, CI=0.484-0.892) values were found to be independent parameters associated with mortality (Table II).

ROC analysis was used to determine the cutoff point for lactate, PVI, APACHE II, and GCS parameters to estimate mortality. The best cut-off points for predicting mortality were ≥2.05, ≥31, ≥25.5, and ≤6.5, respectively. The sensitivity, specificity, and areas under the ROC curve for these cut-off values are shown in Table III.

Table II. Independent parameters associated with 28-day mortality in ICU.

Risk factor	OR (95% CI)	*p*-value
Lactate	9.430 (2.489-35.735)	**0.001**
PVI	1.133 (1.006-1.275)	**0.039**
PI	1.033 (0.542-1.971)	0.921
APACHE II	1.191 (1.002-1.414)	**0.047**
GCS	0.657 (0.484-0.892)	**0.007**
Need for vasopressors	0.900 (0.118-6.842)	0.919

OR: Odds ratio, CI: confidence interval, PVI: Pleth Variability Index, PI: Plethysmographic Index, GCS: Glasgow Coma Score, APACHE: Acute Physiology and Chronic Health Evaluation.

Discussion

In this study, we demonstrated for the first time in the literature that PVI predicted 28-day mortality with an 83.8% sensitivity and 97.9% specificity. Additionally, serum lactate level, PI, APACHE II, GCS, and the need for vasopressors emerged as independent risk factors for mortality.

The mean age of patients admitted to the ICU is increasing due to improved medical care and extended life expectancy[14]. Critically ill patients

Table III. Test values for independent risk factors in predicting mortality.

	Cut-off value	Sensitivity (%)	Specificity (%)	AUC (95% CI)	*p*-value
Lactate	2.05	78.4	89.4	0.900 (0.843-0.957)	**< 0.001**
PVI	31	83.8	97.9	0.925 (0.885-0.966)	**< 0.001**
APACHE II	25.5	84.7	85.1	0.893 (0.843-0.943)	**< 0.001**
GCS	6.5	40.4	86.5	0.698 (0.611-0.785)	**< 0.001**

AUC: Area under ROC curve, CI: confidence interval, PVI: Pleth Variability Index, GCS: Glasgow Coma Score, APACHE: Acute Physiology and Chronic Health Evaluation.

often experience peak mortality within the first 30 days after ICU admission[15]. In our study, the mean age was 74±13 years in the 28-day mortality group and 71±16 years in the survival group, though the difference was not statistically significant.

The prediction of death in patients hospitalized to critical care has been the subject of numerous research[16-20]. PVI, a noninvasive dynamic indicator of fluid responsiveness, proves valuable in managing patients undergoing goal-directed fluid therapy during general anesthesia. PVI relies on variations in arterial pulse pressure: a higher PVI value indicates a greater likelihood of a positive response to fluid infusion, leading to increased cardiac output[21,22]. Yuksek[23] demonstrated PVI's usefulness in predicting mean arterial pressure (MAP) reduction in geriatric patients. Çevikkalp et al[4] highlighted PVI's superiority over central venous pressure monitoring due to its non-invasiveness, better cardiac stabilization with reduced fluid management, and improved accuracy. Dagar and Uzunosmanoğlu[24] suggested that bedside PVI monitoring furnishes clinicians with valuable information regarding volume status in spontaneously breathing critically ill patients. However, a meta-analysis and systematic review by Liu et al[25] reported limited reliability of PVI, while emphasizing its important role in bedside monitoring for mechanically ventilated patients not undergoing surgery.

With mortality impacted by both inadequate and excessive volume restoration, accurate determination and monitoring of volume status are crucial for managing critically ill patients. Although PVI has been recognized as a good predictor of volume status and treatment response in critically ill patients, we found no studies investigating its prognostic value during literature screening. Our study is the first to demonstrate that a PVI value ≥31 predicts 28-day mortality in ICU patients with an 83.8% sensitivity and 97.9% specificity. Multivariate logistic regression analysis further identified PVI, lactate, APACHE II, and GCS as independent factors associated with 28-day mortality in the ICU. Unfortunately, due to the absence of similar studies on this issue in the current literature, a direct-result comparison is unfeasible.

Blood lactate levels offer an indirect yet sensitive gauge of organ perfusion and volume status[25]. Lactate measurements are routinely conducted in most critically ill patients in the ICU and emergency department (ED). Determining serum lactate levels in critically ill patients furnishes valuable and practical insights[25]. He et al[26] established a non-linear positive correlation between serum lactate level and 28-day mortality. Likewise, in our study, a lactate level ≥2.05 predicted 28-day mortality in ICU patients with a sensitivity of 78.4% and specificity of 89.4%.

Study Limitations

This study has several limitations. The major limitations include a relatively small number of patients and being conducted in a single center. In addition, a correlation analysis could not be performed between PVI, serum lactate, and 28-day mortality. Nevertheless, being the first prospective study on this issue in the literature is a strength of the study. We think that our results will be guiding for further comprehensive studies with a larger series of patients.

Conclusions

The outcomes of this study indicate that PVI predicted 28-day mortality with an 83.8% sensitivity and 97.9% specificity. In addition, serum lactate level, PI, APACHE II, GCS, and the need for vasopressors were independent risk factors for mortality. A lactate level ≥2.05 predicted 28-day mortality in ICU patients with a 78.4% sensitivity and 89.4% specificity. However, further studies are warranted to enlighten this issue better.

Conflict of Interest

The authors declare that they have no conflict of interests.

Ethics Approval

Ethics approval was received from the Ethics Committee of Giresun University (date: 13/04/2023, number decision: E-90139838-000-151847).

Informed Consent

Patients were informed in detail about the objectives of the study and gave written consent.

Authors' Contribution

TA: Conception and design, acquisition of data, analysis, interpretation, supervision, and final approval. BY: Acquisition of data, analysis, interpretation, final approval.

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Data Availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID ID
T. Albayrak: 0000-0002-0222-9277
B. Yuksel: 0000-0003-3112-9467

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