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The Relationship between Blood Pressure Response Index and Acute Kidney Injury in Patients with Septic Shock: A Retrospective Study Based on the MIMIC-IV Database

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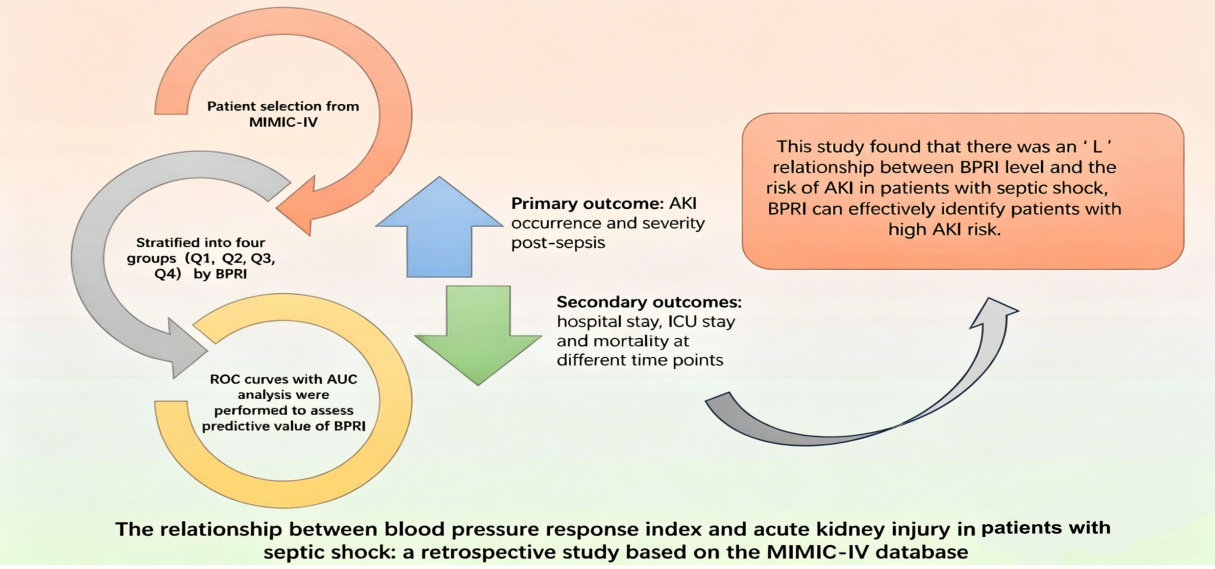
Graphical Abstract



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The Relationship between Blood Pressure Response Index and Acute Kidney Injury in Patients with Septic Shock: A Retrospective Study Based on the MIMIC-IV Database

Jiahui Liu [1,2] , Xinghua Chen [1,2] , Jinglan Wu [1,2] , Li Yao [1,2*]

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Abstract

Background: The blood pressure response index (BPRI) is the ratio of mean arterial pressure (MAP) to the vasoactive-inotropic score (VIS). It accurately reflects the response to vasoactive drugs in patients with septic shock and assesses the patient's vascular status. However, the relationship between BPRI and the occurrence of acute kidney injury (AKI) in patients with septic shock has never been studied.

Methods: This study retrospectively analyzed patients diagnosed with sepsis and using vasoactive drugs in the MIMIC-IV database. The patients were divided into four groups according to the BPRI level. The primary outcome is whether AKI occurs after the diagnosis of sepsis. The association between BPRI and outcome was assessed by constructing logistic regression models and plotting restricted cubic spline (RCS) curves. The predictive value of the BPRI for outcome was evaluated by plotting receiver operating characteristic (ROC) curves and comparing areas under the curves (AUC).

Results: 5524 patients with septic shock were finally included. The median age of the patients was 68.8 years, and 84.3% developed AKI after the diagnosis of sepsis. In a fully adjusted model, BPRI and the development of AKI were significantly correlated (OR [95%CI], 0.988 [0.979, 0.996], *P*=0.006). The results of the RCS curves suggested an "L"-shaped association and the inflection point was located at the level of 3.98. On the left side of the inflection point, there was a decreasing trend in the risk of AKI in patients as BPRI levels increased (OR [95%CI], 0.82 [0.747, 0.9], *P*<0.001). On the right side of the inflection point, there was no statistically significant association (OR [95%CI], 0.995 [0.985, 1.01], *P*=0.212). In addition, the BPRI showed favorable predictive value for outcome (AUC [95% CI], 0.624 [0.601, 0.639]).

Conclusion: We identified a distinct non-linear association between BPRI and AKI risk in septic shock, characterized by a critical inflection point at 3.98. Below this threshold, the likelihood of AKI rises sharply as BPRI decreases. Integrating perfusion pressure and vasopressor load, the BPRI serves as a readily available metric to stratify renal risk and recognize vascular hyporesponsiveness.

Keywords: septic shock; acute kidney injury; blood pressure response index; intensive care unit; MIMIC-IV database

Introduction

Sepsis is a life-threatening organ dysfunction caused by dysregulation of the body's response to infection and is one of the leading causes of death in intensive care unit (ICU) patients [1]. The incidence of acute kidney injury (AKI) in patients with sepsis is up to 70% or more, with prolonged hospitalization cycles and approximately one-fold higher morbidity and mortality rates in patients with concurrent AKI compared to sepsis patients without concurrent AKI [2-3]. In patients with septic shock, persistent renal insufficiency of perfusion is a major cause of AKI [4]. The Surviving Sepsis Campaign guidelines recommend controlling patients' mean arterial pressure (MAP) above 65 mmHg [5].

However, in distributed shock due to infection, although sufficient cardiac output and large circulation pressure can be maintained, persistent organ hypoperfusion may still occur due to the loss of automatic regulation of vasoconstriction and decreased arterial tension [6-7]. Moreover, due to the widespread use of vasoactive drugs, MAP-based monitoring may not reflect the actual organ perfusion of the patient [8-9]. The blood pressure response index (BPRI) is the ratio between MAP and the vasoactive-inotropic score (VIS) [10-11]. Recently, it has been found that the BPRI accurately responds to vasoactive medications in patients with septic shock, allowing for a convenient assessment of the patient's vascular status [11]. In multicenter cohort studies, BPRI has been shown to be strongly associated with poor patient prognosis [11]. However, the relationship between BPRI and the development of AKI in patients with septic shock is unclear.

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In this study, we hypothesize that BPRI and the occurrence of AKI in septic shock patients are closely related and can be used as an accurate predictor. We will test this hypothesis by retrospectively analyzing a large sample of septic shock patients in the Medical Information Mart for Intensive Care-IV database.

Materials and Methods

Data Sources

All data for this study were obtained from the Beth Israel Deaconess Medical Center (BIDMC) intensive care unit database (MIMIC-IV 2.2) [12]. The database covers the period from 2008 to 2019 and includes detailed medical information on nearly 200,000 hospitalizations as well as over 50,000 patients admitted to the ICU. In addition, MIMIC-IV data are rigorously de-identified to ensure that patient privacy is effectively protected. It is worth mentioning that all patients included in this database were adults (age >18 years). The institutional review board of BIDMC waived the declaration of ethical review and informed consent and approved the sharing of research resources. One of the authors has applied for access to this database (Certificate number: 58951192).

Study Objects

All patients were admitted to the ICU for the first time and stayed for more than 24 hours. These patients were diagnosed with sepsis on the first day of ICU admission and were treated with vasoactive drugs. Sepsis was defined using the Third International Consensus on Sepsis and Septic Shock (Sepsis-3) as an increase of at least 2 points in the sequential organ failure assessment (SOFA) score from baseline on the basis of infection or suspected infection [13].

Formulas and Outcomes

VIS formula: dopamine (μg/kg/min) + dobutamine (μg/kg/min) + epinephrine (μg/kg/min) × 100 + norepinephrine (μg/kg/min) × 100 + vasopressin (U/kg/min) × 10,000 + milrinone (μg/kg/min) × 10 [14]. We chose the MAP with maximal support of vasoactive drugs and calculated the BPRI based on the ratio of MAP to VIS. Patients were categorized into four groups based on quartiles of BPRI: Q1 group (BPRI<1.90), Q2 group (BPRI: 1.90-4.03), Q3 group (BPRI: 4.02-8.84), and Q2 group (BPRI>8.84). The primary outcome of the study was whether AKI occurred after the diagnosis of septic shock and during ICU hospitalization. Secondary outcomes included: AKI staging, renal replacement therapy, in-hospital all-cause mortality, 30-day, 180-day, and 365-day all-cause mortality. The diagnosis and staging of AKI were determined according to the guidelines of Kidney Disease: Improving Global Outcomes (KDIGO-2012) [15]. The study flow chart is shown in Figure 1.

Data Collection

The following information was collected from the database by Navicat Premium 16.0 software. 1) General information: age, gender, weight, race, smoking history, type of ICU admission. 2) Comorbidities: hypertension, diabetes mellitus (DM), coronary heart disease (CHD), heart failure (HF), chronic obstructive pulmonary disease (COPD), chronic liver disease (CLD), chronic kidney disease (CKD). 3) Disease severity scores: acute physiology score-Ⅲ (APS-Ⅲ), SOFA score, charles comorbidity index (CCI), glasgow coma scale (GCS) score. 4) Various inspections on the first day in the ICU: white blood cell (WBC) count, red blood cell (RBC) count, platelet (PLT) count, hemoglobin (Hb), serum creatinine (SCr), blood urea nitrogen (BUN), lactic acid, bicarbonate, pH, prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), sodium, potassium, chlorine, urine volume. 5) Treatments received on the first day of ICU admission: diuretics, Sedative drugs, and invasive mechanical ventilation (IMV).

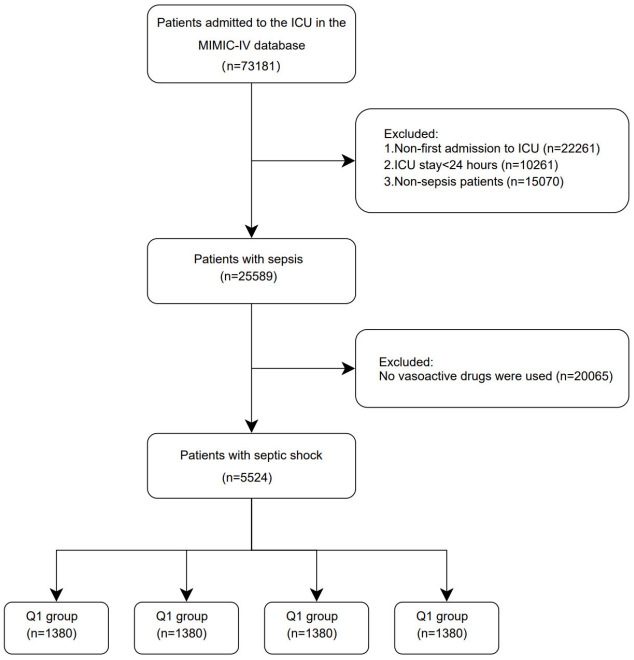

Figure 1. Flow chart.

Statistical Analysis

Statistical analyses were done through R software (version 4.3.3). Categorical variables were expressed as frequencies (proportions) and continuous variables as medians (interquartile range). Categorical variables were compared by chi-square test. Continuous variables were skewed and compared by the Mann-Whitney U test.

Missing data were observed in less than 15% of the variables. To address this, we employed multiple imputation by chained equations (MICE) to generate five imputed datasets, assuming that data were missing at random (MAR).

The correlation between BPRI and the occurrence of AKI was assessed by univariate and multivariate logistic regression models. We adjusted for potential confounders through three models based on factors from previous studies that may have influenced study variables or outcomes. Model 1 adjusted for general information (age, gender, weight, race, smoking history). Model 2 added comorbidities and various scores (hypertension, DM, CHD, HF, CKD, APS-III, SOFA score, and GCS score) to Model 1. Model 3 adds various tests and treatments (WBC count, PLT count, Hb, lactic acid, pH, PT, INR, potassium, diuretics, sedative drugs, IMV) to Model 2. Restricted cubic spline (RCS) curves were plotted within the framework of the unadjusted model and Model 3 to further assess associations between study variables and outcomes.

Analyze the predictive value of the BPRI for endpoints by plotting the receiver operating characteristic (ROC) curve and comparing the area under the curve (AUC). Incorporate study metrics into existing disease severity scores and compare whether the BRI improves the accuracy of the scores in predicting study outcomes. Predictive performance was compared using the Delong test. In addition, to further assess differences in the impact of BPRI in different populations, we also performed subgroup analyses in adjusted model 3. Two-sided *P* values below 0.05 were considered statistically significant. To verify the robustness of our findings, we performed sensitivity analyses. Specifically, considering the potential use of phenylephrine in septic shock, we recalculated the VIS by incorporating phenylephrine (weighted ×10) and repeated the regression analysis to assess whether the association between BPRI and AKI remained consistent.

Result

Baseline Data Analysis

A final total of 5524 patients with septic shock were included. In the study cohort, the median age of the patients was 68.8 years, 57.6% were female, and 64.1% were white. Patients were divided into 4 groups based on BPRI levels, and the baseline information for each group is shown in Table 1. The patients were also grouped according to the occurrence of AKI, and the baseline information of the two groups is shown in Supplementary Table 1. The profile of study variables and outcomes for each group of patients is shown in Table 2. In the study cohort, norepinephrine was used most frequently (85.5%), followed by vasopressin (27.9%), and dobutamine (5.1%) least frequently. The incidence of AKI in the total population was 84.3%. The odds of developing AKI were significantly higher in all groups of patients as the level of BPRI decreased (*P*<0.001). In addition, patients in the Q1 group had significantly higher final AKI stage, odds of receiving RRT, hospitalization period, and in-hospital all-cause mortality than patients in the other three groups (*P*<0.001). Kaplan-Meyer survival analysis showed a stepwise distribution of 30-, 180-, and 365-day survival rates in each group of patients as BPRI levels decreased (Figure 2).

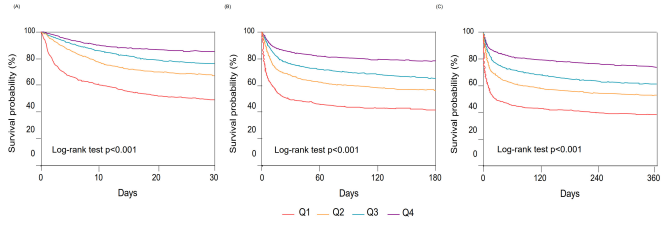

Figure 2. Kaplan-Meyer survival analysis at 30 (A), 180 (B), and 365 days (C) for four groups of patients.

Correlation Analysis

Through constructing a multifactorial logistic regression model, we found that BPRI and the incidence of AKI in septic shock patients during ICU hospitalization were strongly associated. The results were still significant in the unadjusted model (OR [95%CI], 0.982 [0.975, 0.988], *P*<0.001) and the fully adjusted model (OR [95%CI], 0.988 [0.979, 0.996], *P*=0.006). The Q4 group with the lowest incidence of AKI was set as the reference group. The risk of AKI in most groups of patients in each model was significantly higher than that in the Q4 group (Table 3). In both the unadjusted and fully adjusted models, the plotted RCS curves suggested an "L" shaped relationship between the level of BPRI and the risk of occurrence of AKI (Both *P* for no-linear<0.001, Figure 3). Threshold effects analysis suggests that in the adjusted model, the inflection point of the BPRI is located at the 3.98 level. On the left side of the inflection point, there was a decreasing trend in the risk of AKI in patients as BPRI levels increased (OR [95%CI], 0.82 [0.747, 0.9], *P*<0.001). On the right side of the inflection point, there was no statistically significant change in the risk of AKI in patients as BPRI levels increased (OR [95%CI], 0.995 [0.985, 1.01], *P*=0.212) (Supplementary Table 2).

To evaluate the potential influence of phenylephrine, we also recalculated the BPRI by incorporating this agent into the VIS formula. The modified index retained a strong independent association with AKI in multivariable models. The RCS analysis (Supplementary Figure 1) reproduced the "L-shaped" association seen in the primary cohort, identifying a nearly identical inflection point at 4.03. This consistency supports the validity of BPRI as a marker for renal risk, independent of vasopressor choice.

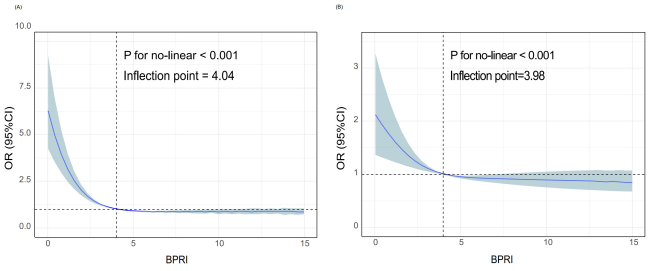

Figure 3. Correlation between BPRI and AKI incidence odds ratio in unadjusted model (A) and adjusted model 3 (B).

Predictive Analysis

ROC analysis indicated that the BPRI demonstrated moderate discriminative ability for predicting AKI (AUC 0.624 [95% CI 0.601–0.639]). Notably, the composite index showed superior predictive performance compared to its individual components, MAP (AUC 0.542 [0.521–0.563]) and VIS (AUC 0.618 [0.599–0.637]), suggesting that integrating vasopressor load with pressure targets offers better risk stratification than either metric alone. Regarding in-hospital mortality, the BPRI exhibited relatively higher prognostic accuracy (AUC 0.697 [0.681–0.712]). Furthermore, the inclusion of BPRI yielded incremental value when combined with established disease severity scores, improving the predictive accuracy of both APS-III and SOFA models (Table 4, Figure 4).

Subgroup analysis

Subgroups of patients were analyzed using age, gender, hypertension, SOFA score, and sedative drugs as stratification factors. The results showed that in different populations, the risk of AKI was higher in groups Q1, Q2, and Q3 compared to group Q4. Interaction tests showed that there was no significant interaction between study variables and stratification factors (Figure 5).

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Table 1. Baseline characteristics of patients in each group.

Variables	Total (n=5524)	Q1 group (n=1380)	Q2 group (n=1382)	Q3 group (n=1381)	Q4 group (n=1381)	*P*-value
General information						
Age, year	68.8 (57.8, 79.3)	67.5 (57.0, 78.7)	69.6 (57.3, 80.2)	69.7 (58.2, 79.4)	68.4 (59.0, 78.7)	.021
Gender, female	3181 (57.6%)	782 (56.7%)	775 (56.1%)	790 (57.2%)	834 (60.4%)	.098
Weight, kg	79.1 (66.6, 95.0)	77.2 (65.0, 93.4)	78.2 (65.8, 94.0)	79.0 (66.7, 93.1)	81.2 (68.5, 98.9)	<.001
Race						<.001
White	3542 (64.1%)	798 (57.8%)	881 (63.7%)	901 (65.2%)	962 (69.7%)	
Black	389 (7%)	102 (7.4%)	94 (6.8%)	102 (7.4%)	91 (6.6%)	
Other	1593 (28.8%)	480 (34.8%)	407 (29.5%)	378 (27.4%)	328 (23.8%)	
Smoking history	1567 (28.4%)	353 (25.6%)	400 (28.9%)	428 (31%)	386 (28%)	.016
Type of ICU						<.001
MICU	2668 (48.3%)	730 (52.9%)	717 (51.9%)	708 (51.3%)	513 (37.1%)	
SICU	1041 (18.8%)	332 (24.1%)	292 (21.1%)	258 (18.7%)	159 (11.5%)	
Other	1815 (32.9%)	318 (23%)	373 (27%)	415 (30.1%)	709 (51.3%)	
Complications						
Hypertension	3720 (67.3%)	875 (63.4%)	911 (65.9%)	946 (68.5%)	988 (71.5%)	<.001
DM	1705 (30.9%)	400 (29%)	394 (28.5%)	452 (32.7%)	459 (33.2%)	.008
CHD	1887 (34.2%)	357 (25.9%)	448 (32.4%)	481 (34.8%)	601 (43.5%)	<.001
HF	1512 (27.4%)	340 (24.6%)	381 (27.6%)	394 (28.5%)	397 (28.7%)	.059
COPD	407 (7.4%)	102 (7.4%)	104 (7.5%)	115 (8.3%)	86 (6.2%)	.208
Stroke	404 (7.3%)	100 (7.2%)	123 (8.9%)	80 (5.8%)	101 (7.3%)	.020
CID	611 (11.1%)	202 (14.6%)	162 (11.7%)	155 (11.2%)	92 (6.7%)	<.001
CKD	271 (4.9%)	69 (5%)	82 (5.9%)	62 (4.5%)	58 (4.2%)	.162
Various scores						
APS, III	64.0 (45.0, 90.0)	86.0 (65.0, 110.0)	68.0 (49.0, 92.0)	56.0 (42.0, 77.0)	49.0 (35.0, 71.0)	<.001
SOFA score	10.0 (7.0, 12.0)	12.0 (10.0, 15.0)	10.0 (8.0, 13.0)	9.0 (7.0, 11.0)	7.0 (5.0, 10.0)	<.001
CCI	6.0 (4.0, 8.0)	6.0 (4.0, 8.0)	6.0 (4.0, 8.0)	6.0 (4.0, 8.0)	6.0 (4.0, 7.0)	<.001
GCS score	13.0 (8.0, 15.0)	11.0 (6.0, 14.0)	12.0 (7.0, 14.0)	13.0 (9.0, 15.0)	14.0 (10.0, 15.0)	<.001
VIS	18.1 (8.0, 38.4)	55.8 (48.1, 80.0)	25.4 (20.0, 30.1)	12.0 (10.0, 15.0)	5.0 (3.0, 6.0)	<.001
BPRI	4.0 (1.9, 8.8)	1.3 (0.9, 1.6)	2.8 (2.3, 3.4)	6.1 (4.8, 7.3)	15.3 (11.9, 24.3)	<.001
Various inspections						
WBC count, $\times 10^9$ /L	12.0 (8.7, 16.5)	14.0 (9.7, 20.1)	12.3 (9.0, 17.1)	11.1 (8.0, 15.0)	11.3 (8.4, 14.9)	<.001
RBC count, $\times 10^{12}$ /L	3.2 (2.8, 3.6)	3.2 (2.8, 3.6)	3.2 (2.8, 3.6)	3.2 (2.8, 3.6)	3.3 (2.9, 3.7)	<.001
PLT, ×109/L	144.0 (101.0, 204.0)	127.0 (76.0, 190.0)	147.0 (101.0, 211.0)	153.0 (109.0, 213.0)	145.0 (108.0, 199.0)	<.001
Hb, mg/dl	9.6 (8.5, 10.8)	9.6 (8.4, 10.8)	9.6 (8.4, 10.8)	9.6 (8.5, 10.8)	9.8 (8.7, 10.9)	.005
SCr, mg/dl	1.2 (0.8, 2.1)	1.7 (1.0, 2.8)	1.2 (0.8, 2.1)	1.1 (0.8, 1.9)	1.1 (0.8, 1.5)	<.001
BUN, mg/dl	25.0 (15.0, 41.0)	31.0 (20.0, 47.0)	27.0 (16.0, 41.0)	23.0 (14.0, 39.0)	21.0 (14.0, 32.0)	<.001
Lactic acid, mmol/L	1.6 (1.2, 2.1)	1.9 (1.4, 2.6)	1.5 (1.2, 2.0)	1.4 (1.1, 1.8)	1.5 (1.1, 2.0)	<.001
Bicarbonate, mEp/L	1.5 (1.2, 2.0)	1.7 (1.3, 2.4)	1.5 (1.2, 2.0)	1.4 (1.1, 1.8)	1.5 (1.1, 2.0)	<.001
pH, units	7.4 (7.3, 7.4)	7.4 (7.3, 7.4)	7.4 (7.3, 7.4)	7.4 (7.3, 7.4)	7.4 (7.3, 7.4)	<.001
PT, s	14.8 (13.2, 18.0)	16.6 (13.9, 21.9)	14.9 (13.3, 18.1)	14.4 (12.9, 16.8)	14.1 (12.9, 15.9)	<.001
APTT, s	33.0 (28.8, 42.5)	37.7 (30.7, 50.1)	33.8 (29.2, 42.9)	31.9 (28.2, 39.8)	31.0 (27.8, 37.3)	<.001
INR	1.3 (1.2, 1.6)	1.5 (1.3, 2.0)	1.4 (1.2, 1.6)	1.3 (1.2, 1.5)	1.3 (1.2, 1.5)	<.001
Sodium, mEp/L	138.0 (135.0, 141.0)	137.0 (134.0, 141.0)	138.0 (135.0, 142.0)	139.0 (136.0, 142.0)	138.0 (135.0, 141.0)	<.001
Potassium, mEp/L	4.1 (3.8, 4.5)	4.2 (3.8, 4.8)	4.1 (3.7, 4.5)	4.1 (3.7, 4.4)	4.1 (3.8, 4.4)	<.001
Chlorine, mEp/L	104.0 (100.0, 108.0)	104.0 (98.0, 108.0)	105.0 (101.0, 109.0)	105.0 (101.0, 109.0)	104.0 (100.0, 108.0)	<.001
Urine volume, ml	1335.5 (704.5, 2225.0)	896.0 (365.5, 1765.0)	1245.0 (655.0, 2140.0)	1470.0 (860.0, 2325.0)	1665.0 (1050.0, 2494.0)	<.001
MAP, mmHg	72.7 (68.5, 77.5)	71.6 (66.9, 76.0)	72.5 (68.5, 76.7)	72.7 (68.7, 77.8)	74.3 (70.1, 79.3)	<.001
Received treatment						
Diuretics	1445 (26.2%)	296 (21.4%)	315 (22.8%)	350 (25.3%)	484 (35%)	<.001
Sedative drugs	4221 (76.4%)	1221 (88.5%)	1062 (76.8%)	918 (66.5%)	1020 (73.9%)	<.001
IMV	3938 (71.3%)	1142 (82.8%)	1002 (72.5%)	837 (60.6%)	957 (69.3%)	<.001

Note: Values are the median (interquartile range), or n (%).

Discussion

In this large retrospective cohort study of 5,524 patients with septic shock, we identified a distinct non-linear association between the Blood Pressure-to-Resistivity Index (BPRI) and the risk of developing AKI. A critical inflection point was observed at approximately 3.98. Below this threshold, every 1-unit decrease in BPRI was associated with an 18% increase in the risk of AKI during the ICU stay. Lower BPRI levels were not only independent predictors of severe AKI and the need for renal replacement therapy (RRT) but also correlated significantly with prolonged hospital stays and increased short- and long-term mortality. Notably, our sensitivity analysis incorporating phenylephrine confirmed the robustness of these findings, yielding a nearly identical threshold (4.03). To the best of our knowledge, this is the first study to elucidate the relationship between BPRI—a novel metric integrating perfusion pressure and vasopressor load—and renal outcomes in septic shock.

Renal perfusion insufficiency due to septic shock is the most important cause of AKI in these patients. The kidney is extremely sensitive to hypoxia, and the tubular epithelial cells in the thick segment of the ascending branch of the renal medullary collaterals have a very high oxygen extraction rate, and

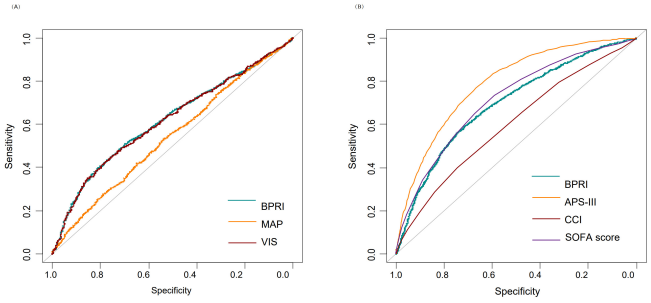

Figure 4. ROC curves for each variable in predicting the occurrence of AKI (A) and in-hospital all-cause mortality (B) in patients with septic shock.

Table 2. Hemodynamic drugs and study outcomes.

	Total (n=5524)	Q1 (n=1380)	Q2 (n=1382)	Q3 (n=1381)	Q4 (n=1381)	P-value
Hemodynamic drugs						
Dopamine	579 (10.5%)	196 (14.2%)	123 (8.9%)	139 (10.1%)	121 (8.8%)	<.001
Dobutamine	282 (5.1%)	132 (9.6%)	62 (4.5%)	32 (2.3%)	56 (4.1%)	<.001
Epinephrine	1021 (18.5%)	331 (24%)	171 (12.4%)	126 (9.1%)	393 (28.5%)	<.001
Norepinephrine	4722 (85.5%)	1373 (99.5%)	1341 (97%)	1251 (90.6%)	757 (54.8%)	<.001
Vasopressin	1542 (27.9%)	887 (64.3%)	419 (30.3%)	133 (9.6%)	103 (7.5%)	<.001
Milrinone	302 (5.5%)	58 (4.2%)	84 (6.1%)	68 (4.9%)	92 (6.7%)	<.001
Outcomes						
AKI	4658 (84.3%)	1287 (93.3%)	1186 (85.8%)	1089 (78.9%)	1096 (79.4%)	<.001
AKI-stages						<.001
0	866 (15.7%)	93 (6.7%)	196 (14.2%)	292 (21.1%)	285 (20.6%)	
1	700 (12.7%)	132 (9.6%)	161 (11.6%)	184 (13.3%)	223 (16.1%)	
2	1845 (33.4%)	378 (27.4%)	456 (33%)	452 (32.7%)	559 (40.5%)	
3	2113 (38.3%)	777 (56.3%)	569 (41.2%)	453 (32.8%)	314 (22.7%)	
RRT	610 (11%)	304 (22%)	162 (11.7%)	83 (6%)	61 (4.4%)	<.001
Hospitalization time, day	9.7 (5.5, 16.8)	10.2 (3.5, 19.5)	10.8 (6.3, 18.1)	9.6 (5.9, 16.2)	8.6 (5.6, 13.7)	<.001
Length of stay in ICU, day	4.1 (2.3, 8.1)	5.0 (2.6, 11.0)	5.0 (2.9, 9.1)	3.8 (2.3, 7.1)	3.1 (1.9, 5.9)	<.001
In-hospital mortality	1536 (27.8%)	676 (49%)	406 (29.4%)	275 (19.9%)	179 (13%)	<.001
30 days mortality	1688 (30.6%)	702 (50.9%)	450 (32.6%)	329 (23.8%)	207 (15%)	<.001
180 days mortality	2191 (39.7%)	802 (58.1%)	605 (43.8%)	479 (34.7%)	305 (22.1%)	<.001
365 days mortality	2391 (43.3%)	851 (61.7%)	653 (47.3%)	535 (38.7%)	352 (25.5%)	<.001

Note: Values are the median (interquartile range), or n (%).

Table 3. Multifactorial logistic regression modeling to evaluate the association between BPRI and the incidence of AKI.

Variables	Unadjusted model	Model 1	Model 2	Model 3
BPRI	0.982 (0.975, 0.988) ***	0.976 (0.969, 0.983) ***	0.996 (0.989, 1.001)	0.988 (0.979, 0.996) **
Q1	3.599 (2.820, 4.630)***	4.493 (3.492, 5.830) ***	2.218 (1.669, 2.968) ***	1.957 (1.453, 2.651) ***
Q2	1.573 (1.290, 1.923) ***	1.780 (1.449, 2.191) ***	1.138 (0.905, 1.432)	1.322 (1.036, 1.690) **
Q3	0.970 (0.807, 1.165)	1.050 (0.868, 1.270)	0.843 (0.686, 1.036)	1.113 (0.893, 1.388)
Q4	Ref.	Ref.	Ref.	Ref.
P for trend	<0.001	<0.001	0.004	<0.001

Note: *P*-value: *P<0.05, **P<0.01, ***P<0.001. Model 1: After adjusting for age, gender, weight, race, and smoking history; Model 2: adjusted for model 1, additionally adjusted for hypertension, DM, CHD, HF, CKD, APS-III, SOFA score, and GCS score; Model 3: adjusted for model 2, additionally adjusted for WBC count, PLT count, Hb, Lactic acid, pH, PT, INR, potassium, diuretics, sedative drugs, and IMV.

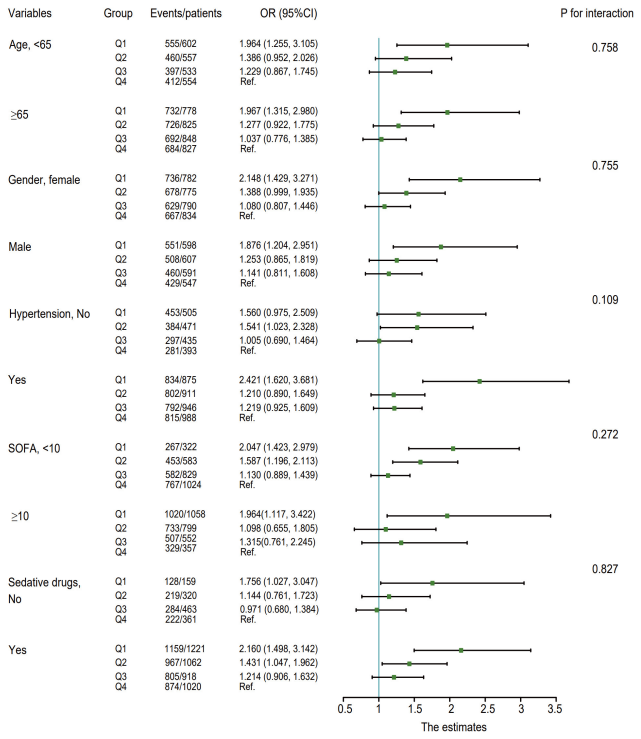

Figure 5. Subgroup analysis with AKI incidence as outcome event.

about 80% of the oxygen delivery is utilized by them [16]. Reduced oxygen supply to them due to decreased renal perfusion pressure makes them more susceptible to renal dysfunction [17]. In our study cohort, all patients with sepsis required treatment with vasoactive drugs and therefore exhibited a higher incidence of AKI relative to other studies [18-19]. A prospective, exploratory cohort study found that in the early stages of diagnosis of infectious shock, patients in the group that developed AKI had significantly lower MAP levels than those in the group that did not develop AKI (MAP: 67±15mmHg VS. 68±17mmHg, *P*=0.043) [20]. Meiping Wang et al. A prospective multicenter cohort study found that among patients with a diagnosis of sepsis and AKI, patients who developed early persistent AKI generally had a lower MAP than patients with late or early transient AKI [21].

As recommended by sepsis management guidelines, norepinephrine is commonly used as a first-line pressor-boosting agent in adult patients with septic shock [13]. In addition combination vasopressin therapy is recommended for patients whose MAP remains difficult to maintain, and positive inotropic agents such as dobutamine are often required for patients with concomitant cardiac insufficiency. The use of vasoactive drugs in patients with infectious shock and the patient's response to the drugs have some individual differences [22-23]. The VIS score can be used to quantitatively assess the strength of hemodynamic support. A retrospective study of 1935 adult patients undergoing cardiovascular surgery found that VIS was strongly associated with the development of postoperative AKI in patients (OR [95% CI], 1.191 [1.11, 1.34], *P*<0.001) [24]. The BPRI combines hemodynamic status and support strength and can be used to accurately respond to a patient's response to vasoactive medications. Crucially, in our subgroup analyses, the protective effect of higher BPRI was more pronounced in patients with hypertension. This likely reflects the rightward shift of the renal autoregulatory curve induced by chronic hypertension. These patients may require higher perfusion pressures to overcome increased varying vascular resistance and maintain glomerular filtration, making them more sensitive to drops in BPRI. In our study, we found that when the BPRI was below the level of 3.98, the risk of AKI in patients increased sharply with the decrease in BPRI. More attention needs to be paid to such patients even in the presence of circulatory stabilization.

The current diagnosis of AKI is based primarily on increased SCr or decreased urine output. However, sepsis also reduces peripheral perfusion, causing a decrease in muscle blood supply, which results in a decrease in creatine production, leading to a lag in the increase in serum creatinine compared to the actual impairment of renal function [25-26]. And decreased urine output may also be diluted by aggressive fluid resuscitation as well as diuretic use, resulting in failure to diagnose AKI in a timely manner [27]. It is difficult to avoid delays in developing a diagnosis and implementing treatment that are based on the fact that renal failure has already occurred. In patients with septic shock, accurate assessment of renal perfusion status is critical for effective prevention of AKI [28]. Currently, ultrasonic Doppler is most commonly used to approximate renal perfusion by measuring the resistivity index of the interlobar arteries [29]. However, ultrasound Doppler results are more dependent on the skill and experience of the operator. Different pathologies (e.g., renal artery stenosis) may result in similar ultrasound presentations, which adds to the complexity of clinical judgment [30]. Furthermore, abdominal ultrasound can be affected by conditions such as obesity or the presence of abdominal and intestinal gas, which can affect the accuracy of the measurements [31]. In contrast, the BPRI is derived from readily available bedside parameters and requires no special-

Table 4. Predictive performance of each model for different outcomes

Models	AUC (95%CI)	Models	AUC (95%CI)	*P* for comparison
Occurrence of AKI				
BPRI	0.624 (0.601, 0.639)			
MAP	0.542 (0.521, 0.563)			
VIS	0.618 (0.599, 0.637)			
In-hospital mortality				
BPRI	0.697 (0.681, 0.712)			
APS- Ⅲ	0.789 (0.777, 0.802)	+BPRI	0.796 (0.783, 0.808)	<0.001
SOFA score	0.713 (0.699, 0.729)	+BPRI	0.731 (0.717, 0.746)	<0.001
CCI	0.601 (0.584, 0.618)	+BPRI	0.697 (0.682, 0.712)	0.063

ized equipment. Our findings suggest that BPRI may serve as a surrogate marker for renal perfusion status, reflecting the systemic vascular tone. Further prospective validation is warranted to confirm its utility in guiding hemodynamic therapy.

This study is subject to several limitations. Given its retrospective, single-center design, inherent biases preclude definitive causal inference, necessitating validation in larger, multi-center cohorts. A key methodological constraint is the calculation of BPRI at a single time point—the maximum vasopressor dosage. While this cross-sectional approach may introduce lead-time bias due to variable intervals from admission to peak support, we prioritized this specific juncture as it captures the nadir of vascular responsiveness. Theoretically, this represents the phase of maximal hemodynamic instability and potential renal hypoxic insult. Although longitudinal tracking would offer a more granular temporal profile, the peak-dose BPRI serves as a pragmatic indicator of the worst-case physiological status. Furthermore, the lack of baseline MAP data for many patients complicates the assessment of relative hypotension. Despite statistical adjustments for hypertension and heart failure, unmeasured variability in pre-morbid blood pressure remains a potential confounder. Regarding predictive performance, while the AUC of 0.624 indicates moderate discrimination, the BPRI consistently outperformed its individual components (MAP and VIS). Future research should explore whether integrating this index into existing prognostic models enhances their clinical utility.

Conclusions

Our findings establish the BPRI as a significant independent predictor of renal outcomes and survival in septic shock. Specifically, a BPRI below 4.0 signals a sharp increase in AKI risk. As a composite metric, it captures the interplay between perfusion pressure and vasopressor load more effectively than either parameter alone. Although its standalone discrimination is moderate, the BPRI adds important prognostic value, helping clinicians stratify patients based on vascular responsiveness early in their ICU course.

Abbreviations

Acute Kidney Injury: AKI; Acute Physiology Score-III: APS-III; Activated Partial Thromboplastin Time: APTT; Area Under the Curve: AUC; Blood Pressure Response Index: BPRI; Blood Urea Nitrogen: BUN; Charlson Comorbidity Index: CCI; Coronary Heart Disease: CHD; Confidence Interval: CI; Chronic Kidney Disease: CKD; Chronic Liver Disease: CLD; Chronic Obstructive Pulmonary Disease: COPD; Diabetes Mellitus: DM; Glasgow Coma Scale: GCS; Hemoglobin: Hb; Heart Failure: HF; Hazard Ratio: HR; Intensive Care Unit: ICU; Length of Intensive Care Unit Stay: ICU stay; Invasive Mechanical Ventilation: IMV; International Normalized Ratio: INR; Mean Arterial Pressure: MAP; Medical Intensive Care Unit: MICU; Medical Information Mart for Intensive Care IV: MIMIC-IV; Odds Ratio: OR; Platelet: PLT; Prothrombin Time: PT; Quartile: Q; Red Blood Cell: RBC; Restricted Cubic Spline: RCS; Reference: Ref.; Receiver Operating Characteristic: ROC; Renal Replacement Therapy: RRT; Serum Creatinine: SCr; Surgical Intensive Care Unit: SICU; Sequential Organ Failure Assessment: SOFA; Vasoactive Inotropic Score: VIS; White Blood Cell: WBC; Length of Hospital Stay: hospital stay.

Author Contributions

J.H.L., X.H.C., and L.Y. conceived and designed the research, and also participated in the review and revision of the manuscript. J.H.L. and X.H.C. drafted the initial manuscript and collected the data. Z.H.H. and J.L.W conducted the data analysis and interpretation. All authors read and approved the final draft.

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Ethics Approval and Consent to Participate

This study for the MIMIC-IV database was approved by the review boards of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center, and the patient information was de-identified so that there were no ethical concerns.

Competing Interests

The authors declare that they have no existing or potential commercial or financial relationships that could create a conflict of interest at the time of conducting this study.

Data Availability

All data needed to evaluate the conclusions in the paper are present in the paper or the Supplementary Materials. Additional data related to this paper may be requested from the authors.

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