

# The Effect of norepinephrine on Peripheral Perfusion Index and Its Association With the Prognosis of Septic Patients

cui Wang

Peking Union Medical College Hospital

xiaoting wang (✉ [icuting@163.com](mailto:icuting@163.com))

Peking Union Medical College Hospital

hongmin zhang

Peking Union Medical College Hospital

wei huang

Peking Union Medical College Hospital

Dawei Liu

Peking Union Medical College Hospital

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## Research

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# Abstract

**Background:** This study aimed to evaluate whether using norepinephrine during the management of patients with septic shock impacts perfusion index (PI) and patients' outcomes.

**Methods:** We performed a retrospective study among patients with septic shock from January 2014 to December 2018 who had undergone PICCO-plus cardiac output monitoring and using norepinephrine during the management. We collected basic clinical characteristics. Hemodynamic parameters including lactate, PI and dose of norepinephrine at T0 and 24h after PICCO catheterization (T24) were obtained. We analyzed the effect of perfusion index and norepinephrine on prognosis of patients with septic shock and the correlation between perfusion index and the dose of norepinephrine.

**Results:** There were 184 patients with septic shock who received during this period, and of these, 44 patients died during their ICU treatment. The PI of the nonsurvivors group was significantly lower than survivors group at T24 ( $0.5 \pm 0.4$  vs.  $1.5 \pm 1.3$ ,  $P < 0.001$ ), and the Lac of the nonsurvivors group was significantly higher than the survivors group. In the dose of norepinephrine indicators, we found significant statistical differences between the two groups at T0 and T24. Dose of norepinephrine and perfusion index were the most independent risk and protective factors for patient ICU mortality. The areas under the curve for a poor prognosis PI were 0.847 (95% CI: 0.782-0.912). The optimal cutoff value of the PI at T24 to predict ICU mortality was 0.6, with a sensitivity of 77.1% and specificity of 80%. Based upon the optimal cutoff value of the PI at T24, we divided patients into groups of  $PI \geq 0.6$  ( $n = 125$ ) and  $PI < 0.6$  ( $n = 59$ ). The Lac of the  $PI < 0.6$  group was higher than the  $PI \geq 0.6$  group at T24. In the sublingual dose of norepinephrine indicators, the  $PI < 0.6$  group was significantly higher than the  $PI \geq 0.6$  group. The PI was strongly negatively correlated with dose of norepinephrine ( $r = -0.344$ ,  $P < 0.001$ ) and lactate ( $r = -0.291$ ,  $P < 0.001$ ).

**Conclusions:** A higher PI is a protective factor and using of higher dose of norepinephrine is a risk factor for the prognosis of critically ill patients with septic shock. Lower PI was associated with the higher dose of norepinephrine.

## Background

Septic shock is one of the common causes of admission to intensive care unit (ICU) and one of the major causes of death among ICU inpatients. Septic shock is characterized by systemic vasodilatation and vascular leakage arising from systemic inflammation induced by serious infection. The essential step in the management of patients with septic shock is to increase systemic and regional/microcirculatory flow. [1] Increasing arterial blood pressure (ABP) with vasopressors when patients are hypotensive is used to improve the input pressure driving organ perfusion. Norepinephrine is the first choice of vasoactive drugs in patients with septic shock because it can maintain vascular tension and achieve the mean arterial blood pressure (MAP) targets. [2] A double-blind randomized controlled trial revealed norepinephrine administration at the beginning of sepsis with hypotension resuscitation to be associated with a higher

shock control rate by 6 hours compared with the standard treatment.[3] The dose of norepinephrine is based on MAP judged to safeguard organ perfusion. However, excessive dosing of norepinephrine is associated with a risk for extreme vasoconstriction, tissue hypoperfusion, and increased mortality.[4]

As we know, the peripheral vascular bed is the first place where blood flow is sacrificed and the place where it is finally perfused. Peripheral perfusion index (PI) reflects pulsatile flow, which demonstrates the ability of the circulation to provide blood perfusion to tissue.[5] The greater the pulsatile flow, the greater the pulsation intensity, and the greater the PI value. Therefore, tissue perfusion can be reflected by PI, acting as an ongoing monitor of local blood flow fluctuations[6]. Since norepinephrine affects blood flow, does using of norepinephrine during the management of patients with septic shock impact PI and affect patient outcomes? During this study, we used our clinical database to answer this question.

## Methods

### Patient Sample

Using the administrative database of Peking Union Medical College Hospital, we performed a retrospective study among patients with septic shock who had undergone PICCO-Plus cardiac output monitoring. All adult patients within 24 h after the onset of severe sepsis or septic shock sequentially admitted to the Department of Critical Care Medicine of Peking Union Medical College Hospital from January 2014 to December 2018, who required to use only a single vasoactive agent (norepinephrine) during the first 24h after PICCO initiation, and mechanical ventilation for resuscitation, were eligible for the study. Patients who were younger than 18 years old or who were admitted to the ICU for fewer than 24 hours were excluded. The Institutional Research and Ethics Committee of Peking Union Medical College Hospital approved this study for human subjects(No.S-K980).

### PI Measurement and Hemodynamic monitoring

PI in a finger was measured continuously with the IntelliVue MP70 monitor (Philips Medical Systems, Boblingen, Germany). The MP70 system calculates PI as the ratio between a pulsatile component and a nonpulsatile component of a light reaching a light-sensitive cell of a pulse oximetry probe. The ambient temperature of the room was consistent at approximately 23–25°C (climate controlled).

The thermodilution cardiac output was measured by injecting 15 ml of 0.9% saline at 0°C for the PICCO-Plus (the PICCO system: Pulsion Medical System, Munich, Germany). Three cardiac outputs, which were within 10% of each other, were obtained and averaged. These global hemodynamic variables such as cardiac output(CO) and Global end-diastolic volume index(GEDVI) were recorded simultaneously.

Simultaneous basic blood gases from the arterial, central venous catheters were obtained (the placement of a central venous catheter in the superior vena cava was confirmed by chest radiography). Blood gas samples were taken anaerobically in 3 ml heparinized syringes (PL67BP; BD Diagnostics, Plymouth, UK) and analyzed on blood gas bedside machines (GEM Premier 3000, model 5700; Lexington, MA, USA) or (ABL90: Radiometer, Copenhagen, Denmark).

## **Data collection**

Basic clinical characteristics were collected, including age, gender, Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, SOFA score, Comorbidities, Primary site of infection, Blood temperature, Serum white blood cell (WBC) count, continuous renal replacement therapy (CRRT) and 28-day prognosis after PICCO initiation. Hemodynamic parameters such as central venous pressure (CVP), heart rate (HR), MAP, CO, GEDVI, superior vena cava oxygen saturation (ScvO<sub>2</sub>), the dose of norepinephrine, lactate and PI at the time of T0 and T24 were observed. T0 represents the time when PICCO starts monitoring and T24 represents the time at 24 h after PICCO initiation.

## **Statistical analysis**

Descriptive analysis was performed. Abnormal outliers were defined as data with a SD value over 3 based upon the Pauta criterion. Such data were treated as missing values. Results for continuous variables with normal distributions were presented as mean  $\pm$  standard deviations (SD). Results for continuous variables that were not normally distributed were presented as median (25–75th percentiles) or percentages as appropriate. For the continuous variables, depending on the data distribution and the number of variables, data were analyzed using the t-test or chi square test. Multiple logistic regression models were used to measure the relative risk (RR) and 95% CI for each factor to discover how they indicate a poor prognosis. Correlation analyses were performed using the Spearman test. Receiver operating characteristics (ROC) curves were constructed to compare the accuracy of PI in the prediction of the prognosis of septic patients. All comparisons were two tailed, and a value of  $P < 0.05$  was required to exclude the null hypothesis. Statistical analyses were performed using the SPSS 17.0 software package (SPSS, Chicago, IL, USA).

# **Results**

## **General characteristics**

During the study period (January 1, 2014, to December 30, 2018), a total of 672 critical ill patients who received PICCO monitoring during treatment were admitted to our department. The main diagnosis of 423 patients was septic shock. Among them, 267 patients were used only a single vasoactive agent

(norepinephrine) during the first 24h after PICCO initiation. The patients who were admitted for fewer than 24 hours ( $n = 36$ ) or who were younger than 18 years old ( $n = 24$ ) were excluded from this study. In addition, there were also some unreasonable values ( $n = 23$ ), such as abnormal outliers, that were considered as missing values and abandoned. After these eliminations, 184 patients were included in the study. The clinical characteristics of all patients involved in this study after ICU admission are shown in Table 1. Based upon ICU mortality, we divided patients into groups of survivors ( $n = 144$ ) and nonsurvivors ( $n = 40$ ). Nonsurvivors were more likely to be female ( $p < 0.001$ ), and they had higher SOFA scores ( $14 \pm 3$  vs.  $12 \pm 4$ ,  $P = 0.007$ ) and higher APACHEII scores ( $28 \pm 8$  vs.  $24 \pm 8$ ,  $P = 0.014$ ). But, there were no significant differences in age, comorbidities, primary site of infection or blood temperature between the groups.

### **The hemodynamics and circulation perfusion targets between the different prognosis groups**

There were no statistical differences in the systemic hemodynamic parameters such as CVP, HR, CO, GEDVI and MAP at T0 and T24 in both groups [Table 2]. PI ( $0.9 \pm 0.8$  vs.  $0.9 \pm 0.7$ ,  $t = 0.222$ ,  $P = 0.824$ ) and Lac ( $4.4 \pm 3.9$  vs.  $7.3 \pm 6.6$ ,  $t = -4.800$ ,  $P = 0.089$ ) were no significant difference between the two groups at T0, but ScvO<sub>2</sub> of the nonsurvivors group was higher than the survivors group ( $75.5 \pm 10.0$  vs.  $71.2 \pm 12.1$ ,  $t = -2.080$ ,  $P = 0.039$ ). After treatment, at the time of T24, the PI of the nonsurvivors group was significantly lower than the survivors group ( $0.5 \pm 0.4$  vs.  $1.5 \pm 1.3$ ,  $t = 5.809$ ,  $P < 0.001$ ), which had statistically difference. The Lac of the nonsurvivors group was significantly higher than the survivors group ( $7.5 \pm 7.1$  vs.  $4.0 \pm 3.7$ ,  $t = 5.809$ ,  $P < 0.001$ ) at the time of T24. However in the sublingual dose of norepinephrine indicators, we found significantly statistical differences between the two groups at T0 and T24.

### **Risk Factors for septic Patient ICU Mortality**

A Multivariate logistic regression analysis was used to examine the possible risk factors for an ICU poor prognosis (Table 3). Gender, APACHEII scores, SOFA scores, T0-ScvO<sub>2</sub>, T0-NE, T24-NE, T24-lac and T24-PI were considered in the model. T24-PI and T24-NE were the most significant statistics entered into the regression equation ( $p < 0.05$ ). The odds ratio (OR) of T24-PI and T24-NE were 0.146 (95% confidence interval [CI], 0.048–0.444) and 1.386 (95% CI, 1.119–1.317), respectively.

### **Receiver Operating Characteristic Analysis**

The ROC curve of the T24-PI to predict ICU mortality is shown in Figure 1. The area under the curve of the ROC was 0.847 (95% CI: 0.782–0.912). The optimal cutoff value of the T24-PI to predict ICU mortality was 0.6, with a sensitivity of 77.1% and specificity of 80%. We used this cutoff for all further analyses.

### **The hemodynamics and circulation perfusion targets at T24 between the different PI groups**

Based upon the optimal cutoff value of the T24-PI, we divided patients into groups of  $PI \geq 0.6$  ( $n = 125$ ) and  $PI < 0.6$  ( $n = 59$ ). There were no statistical differences in the systemic hemodynamic parameters such as age, CVP, HR, CO, GEDVI and MAP at T24 between  $PI \geq 0.6$  group and  $PI < 0.6$  group [Table 4]. But APACHEII scores of the  $PI < 0.6$  group was higher than the  $PI \geq 0.6$  group ( $28 \pm 8$  vs.  $24 \pm 7$ ,  $t = -3.145$ ,  $P = 0.002$ ), which

had statistically difference. The Lac of the  $PI \leq 0.6$  group was significantly higher than the  $PI \geq 0.6$  group ( $6.9 \pm 6.6$  vs.  $3.6 \pm 3.5$ ,  $t = -4.396$ ,  $P = 0.001$ ) at the time of T24. In the sublingual dose of norepinephrine indicators, the  $PI \leq 0.6$  group was significantly higher than the  $PI \geq 0.6$  group ( $3.6 \pm 3.3$  vs.  $2.0 \pm 1.8$ ,  $t = -4.423$ ,  $P = 0.001$ ).

### The Correlation Analysis Between PI and Risk Factors

The PI was not correlated with the APACHEII scores ( $r = -0.131$ ,  $P = 0.076$ ). In contrast, the PI was strong negative correlated with NE ( $r = -0.344$ ,  $P < 0.001$ ) and lactate ( $r = -0.291$ ,  $P < 0.001$ ).

## Discussion

The main finding of our study was that a higher PI is a protective factor and using of higher dose of norepinephrine is a risk factor for the prognosis of critically ill patients with septic shock. Using of higher dose of norepinephrine can reduce peripheral blood flow which is reflected in PI. Higher PI was associated with the lower dose of norepinephrine, which may improve the 28-day prognosis in patients with septic shock.

As we know, this is the first study to explore the relationship between PI and norepinephrine in septic patients after resuscitation. The PI, which was defined as the ratio of the pulsatile to non-pulsatile component of the pulse oximetry plethysmograph, is used as a simple and accurate indication of changes in digital blood flow [7, 8]. Changes in finger PI result from blood volume pulsations, the dispensability of the vascular wall, and intravascular pulse pressure. [9] PI has been shown to reflect changes in peripheral circulation perfusion and central hypovolemia, which are both derived from the photoelectric plethysmographic pulse oximetry signal [10]. Some studies showed that PI could be used too as a predictor of early adverse respiratory neonatal outcome after elective cesarean delivery [11]. It has been suggested as a reliable and early indicator of regional block success, and known to increase due to the effect of autonomic blockade during spinal anesthesia. [12] In patients with septic shock, PI are related to 6 h Lactate clearance. [10] Some studies have used an abnormal PI of PI less than 1.4 as a potential trigger to start treatment. In our study, we found that the cutoff of the PI value was  $<0.6$  for predicting ICU mortality with septic shock, resulting in a sensitivity of 77.1% and a specificity of 80%.

Higher dose of norepinephrine is another significant risk factor for critical ill patients with septic shock in our study. Norepinephrine is both an  $\alpha_1$ - and  $\beta_1$ -agonist, and is therefore able to increase vascular tone and contractility. [13] Recent guidelines recommend norepinephrine as the first-line vasopressor in septic shock. [14] Recent studies examined this concern and revealed that norepinephrine did not alter perfusion to the kidney and gut. [15, 16] However, because septic shock is a syndrome that results from a variable combination of decreased venous return, myocardial depression and decreased vascular tone, the place for norepinephrine in initial resuscitation is not straightforward. Although the cause of shock and treatment with norepinephrine were not predictive of death when high doses of the drug were deemed necessary, rescue treatment with high-dose norepinephrine is futile in patients with severe disease and

metabolic acidemia.<sup>[4]</sup>Vasoconstriction induced by norepinephrine may aggravate internal organ ischemia and lead to patient deterioration.<sup>[17]</sup> Adverse cardiac events occurred in 48.2 % of surgical intensive care unit patients with cardiovascular failure and were related to morbidity and mortality. The extent and duration of catecholamine vasopressor therapy were independently associated with and may contribute to the pathogenesis of adverse cardiac events.<sup>[18]</sup>

In the application of norepinephrine, attention should be paid not only to the effect of norepinephrine to arterial contraction, but also to the effect on microcirculation perfusion. The patients in our study with a higher dose of norepinephrine and lower PI had worse outcomes. It is an interesting fact that the relationship between high dose of norepinephrine and PI was demonstrated. In other words, high dose of norepinephrine can decrease peripheral perfusion by affecting peripheral blood flow. Introduction of norepinephrine in severely hypotensive septic shock patients is associated with an increase in cardiac output <sup>[19]</sup>. In a series of 14 patients with septic shock, correction of severe hypotension with norepinephrine administration resulted in an increase in MAP from  $51 \pm 3$  mmHg to  $79 \pm 7$  mmHg, and norepinephrine has positive effects on renal function in septic patients<sup>[20]</sup>. These results suggest that norepinephrine improves tissue perfusion when used to correct severe hypotension, even though evidence was limited. But, most of these clinical trials evaluated the short-term effects of vasopressors and some of these beneficial effects may vanish over time. In healthy conditions, both norepinephrine and vasopressin decreased microvascular perfusion<sup>[21]</sup>. Accordingly, the net result of increasing perfusion pressure on tissue perfusion may depend on the balance between the potential beneficial effects on organ blood flow and negative impact on microvascular perfusion. Therefore, we need to focus on the causal interaction between norepinephrine and PI, especially when PI is lower than 0.6 during the first day of septic shock. Vasopressive catecholamines may be associated with excessive vasoconstriction which may result in an impairment in tissue perfusion, even when perfusion pressure is restored<sup>[22]</sup>. However, We should titrate high dose of norepinephrine based upon PI level to some extent, which means that we should set the hemodynamic target based upon patient PI. PI could be used as one of the reference indicators for making dose of norepinephrine adjustments to achieve circulatory protection. However, this study is based upon a single center with datas, and so it still requires additional clinical research and clinical practice for confirmation.

## Conclusions

Based upon the analysis of a large set of data from septic patients, it can be observed that a higher PI is a protective factor and using of higher dose of norepinephrine is a risk factor for the prognosis of critically ill patients with septic shock. Using of higher dose of norepinephrine and lower PI provided a worse prognosis for the patients in our study, and in addition, these two variables had a casual interaction. Using of higher dose of norepinephrine can reduce peripheral blood flow which is reflected in PI. Higher PI was associated with the lower dose of norepinephrine, which may improve the prognosis in patients with septic shock.

## Abbreviations

PI,Perfusion Index; HTN,hypertension;DM Diabetes Mellitus;CAD,Coronary Artery Disease;WBC,White Blood Cell; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment score; HR,heart rate;CVP,central venous pressure;; CO,Cadiac Output; GEDVI,global end-diastolic volume index;ScvO<sub>2</sub>,Central-venous oxygen saturation(%);NE, norepinephrine (μg/kg/min);LAC,lactate(mmol/L);MAP, mean arterial pressure; ROC,receiver operating characteristic;TTE,Transthoracic echocardiography; CRRT,Continuous renal replacement therapy.

## Declarations

### Ethics approval and consent to participate

The Institutional Research and Ethics Committee of Peking Union Medical College Hospital approved this study for human subjects(No.S-K980).

### Consent for publication

All authors agree to publish in this journal.

### Availability of data and material

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.

### Funding

None.

### Authors' contributions

Xiaoting Wang and Dawei Liu conceived and designed the study, interpreted data and helped draft the manuscript. Cui Wang participated in the study conception and design, recruited patients, collected data, performed the statistical analysis, interpreted the data and drafted the manuscript. Hongmin Zhang and Wei Huang participated in patient recruitment, data collection, technical support and contributed to the critical review of the manuscript. All of the authors read and approved the final manuscript.

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## Tables

**Table 1** The General Characteristics of the Patients Included in This Study

Variables	Survivors (N=144)	Nonsurvivors (N=40)	$\chi^2 / t$	P value
Age	56±15	58±13	0.932	0.353
Gender (n, %)			12.891*	0.000a
Male	78(54.17)	16(40.00)		
Female	66(45.83)	24(60.00)		
Comorbidities (n, %)				
HTN	49(34.00)	13(32.50)	0.033*	0.856
DM	25(17.36)	7(22.73)	0.000*	0.984
CAD	17(11.81)	4(10.00)	0.592*	0.442
Primary site of infection (n, %)				
Lung	36(25.00)	13(32.5)	0.901*	0.342
Abdomen	25(17.36)	9(20.45)	0.549*	0.459
Blood tract	20(13.89)	7(17.5)	0.326*	0.568
Blood temp	37.4±0.7	37.6±1.0	0.991	0.585
WBC count	17.22±10.6	14.77±12.95	1.247	0.214
APACHE II score	24±8	28±8	-2.485	0.014a
SOFA score	12±4	14±3	-2.704	0.007a
CRRT (n, %)	42(29.17)	10(22.7)	0.268*	0.605

aP < 0.05 for control group vs. septic group. \*  $\chi^2$ . HTN, hypertension; DM Diabetes Mellitus; CAD, Coronary Artery Disease; Age (years); Blood temp (°C); WBC, White Blood Cell ( $\times 10^9/L$ ); APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment score; HR, heart rate; CVP, central venous pressure; CO, Cardiac Output (L/min); ScvO<sub>2</sub>, Central-venous oxygen saturation; MAP, mean arterial pressure (mmHg); CRRT, Continuous renal replacement therapy.

Table 2 Tissue perfusion indicator and hemodynamic index of septic shock at ICU admission

Variables	Survivors (N=144)	Nonsurvivors (N=40)	t	P value
<b>T0</b>				
MAP	64±17	63±18	-0.275	0.784
CVP	10.5±3.4	11.3±3.1	-1.422	0.157
HR	114±24	113±26	0.184	0.854
CO	5.0±1.6	5.5±2.5	-1.750	0.082
GEDVI	709.8±193	723.8±173	-0.414	0.680
ScvO <sub>2</sub>	71.2±12.1	75.5±10.0	-2.080	0.039
NE	0.86±0.78	1.6±0.9	-0.373	0.001
LAC	4.4±3.9	7.3±6.6	-4.800	0.089
PI	0.9±0.8	0.9±0.7	0.222	0.824
<b>T24</b>				
MAP	85±12	81±13	1.116	0.266
CVP	10.0±2.7	10.7±2.6	-1.380	0.169
HR	106.4±19	104.7±19	0.488	0.626
CO	5.3±1.6	5.3±2.5	-0.062	0.951
GEDVI	730.2±180	739.2±198	-0.274	0.784
ScvO <sub>2</sub>	72.95±11.1	72.99±10.27	-0.021	0.984
NE	1.85±1.82	4.7±3.6	-6.905	0.001
LAC	4.0±3.7	7.5±7.1	-3.503	0.001
PI	1.5±1.3	0.5±0.4	5.089	0.001

HR,heart rate; MAP,mean arterial pressure (mmHg); CVP,central venous pressure(mmHg); CO,Cadiac Output (L/min); GEDVI,global end-diastolic volume index(ml/m<sup>2</sup>);ScvO<sub>2</sub>,Central-venous oxygen saturation(%);NE, norepinephrine (µg/kg/min);LAC,lactate(mmol/L);PI, perfusion index.

**Table 3. Multivariable Logistic Regression Analysis for possible risk factors for ICU mortality.**

Variable	B	SE	Wald	P	OR	95% CI for OR	
						Lower	Upper
Gender	-0.928	0.488	3.619	0.057	0.395	0.152	1.028
APACHE II score	0.014	0.031	0.189	0.664	1.014	0.954	1.078\7
SOFA score	0.071	0.065	1.222	0.269	1.074	0.946	1.219
T0-ScvO <sub>2</sub>	0.031	0.022	2.035	0.154	1.032	0.988	1.077
T0-NE	-0.138	0.211	0.428	0.513	0.871	0.576	1.317
T24-NE	0.326	0.109	8.925	0.003	1.386	1.119	1.317
T24-Lac	0.037	0.040	0.849	0.357	1.037	0.960	1.121
T24-PI	-1.923	0.567	11.501	0.001	0.146	0.048	0.444

APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment score;ScvO<sub>2</sub>,Central-venous oxygen saturation(%);NE, norepinephrine (µg/kg/min);LAC,lactate(mmol/L);PI, perfusion index.

Table 4. Hemodynamic index and tissue perfusion indicator of septic shock at T24

Characteristics	PI $\geq$ 0.6(n=125)	PI $<$ 0.6(n=59)	$\chi^2/t$	P value
Age	56 $\pm$ 15	57 $\pm$ 14	-0.049	0.961
APACHE II score	24 $\pm$ 7	28 $\pm$ 8	-3.145	0.002
SOFA score	12 $\pm$ 3	13 $\pm$ 4	-1.752	0.082
HR-24h	105 $\pm$ 19	106 $\pm$ 18	-0.326	0.745
MAP-24h	85 $\pm$ 12	84 $\pm$ 11	2.250	0.126
CO-24h	5.2 $\pm$ 1.8	5.4 $\pm$ 2.0	-0.593	0.554
CVP-24h	9.9 $\pm$ 2.6	10.7 $\pm$ 2.8	-1.813	0.071
GEDVI-24h	728.1 $\pm$ 185	730.3 $\pm$ 182	-0.407	0.685
ScvO <sub>2</sub> -24h	73.4 $\pm$ 11.2	71.9 $\pm$ 10.0	0.847	0.398
NE-24h	2.0 $\pm$ 1.8	3.6 $\pm$ 3.3	-4.423	0.000
LAC-24h	3.6 $\pm$ 3.5	6.9 $\pm$ 6.6	-4.396	0.000
ICU mortality[n,%]	12(9.60)	28(47.46)	34.121*	0.000

\*  $\chi^2$ .PI,perfusion index;Age (years);APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment score; HR,heart rate; MAP,mean arterial pressure (mmHg); CO,Cadiac Output (L/min);CVP,central venous pressure; GEDVI,global end-diastolic volume index(ml/m<sup>2</sup>);ScvO<sub>2</sub>,Central-venous oxygen saturation(%);NE, norepinephrine ( $\mu$ g/kg/min);LAC,lactate(mmol/L);

## Figures

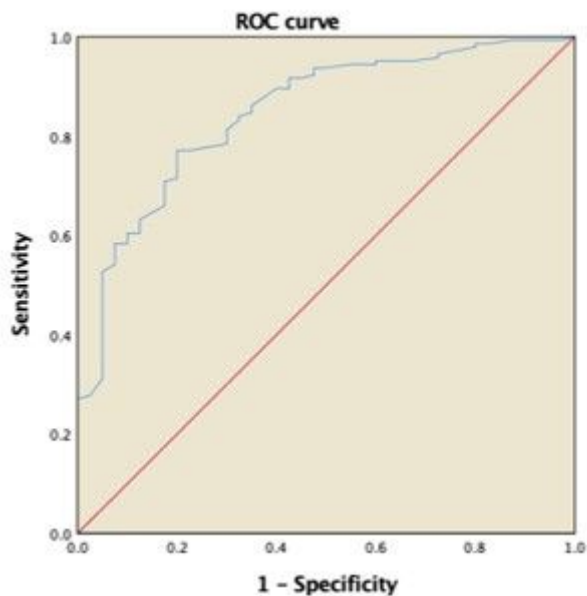


Figure 2

Receiver operating characteristic (ROC) curve using PI for predicting ICU mortality

