Original Article
First day POEM scores predict outcomes for septic shock patients: a retrospective observational study

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Abstract: Objective: The aim of the current study was to evaluate association levels between POEM scores and arterial blood lactate values, APACHE II scores, and SOFA scores in septic shock patients, validating the predictive value of microcirculation POEM scores for septic shock. Methods: Experimental data was gathered on all patients diagnosed with septic shock in the Emergency Department and ICU of Shanghai Changzheng Hospital, between July 2017 and June 2018. Video-microscopy images of microcirculation at the sub-labial mucosa were captured on the first day, as the final diagnosis of septic shock was made. APACHE II scores and SOFA scores were employed to monitor heart rates, mean arterial pressure, and blood lactate, along with other indicators. Correlation levels between POEM scores and arterial blood lactate values, APACHE II scores, and SOFA scores were investigated via statistical analysis. Moreover, ROC curves were established, aiming to compare the prognostic evaluation of POEM scores, arterial blood lactate, APACHE scores, and SOFA scores for patients with septic shock. Results: POEM scores and APACHE II scores of patients with septic shock showed a negative correlation and a linear correlation, with $P = 0.0032$ and $r = -0.346$. POEM scores and SOFA scores showed a negative correlation and a linear correlation, with $P = 0.0121$ and $r = -0.242$. POEM scores and blood lactate values showed a negative correlation and a linear correlation, with $P = 0.0085$ and $r = -0.348$. ROC curves were also established. They were based on POEM scores, APACHE II scores, SOFA scores, and blood lactate values (within 24 hours), evaluating the prognosis of septic shock. The largest areas under ROC curves were for POEM scores and blood lactic acid, showing 0.841 and 0.823 respectively, indicating that these two parameters provide better predictive value for prognosis evaluation. The optimal cut-off value of POEM scores was 3.5. Moreover, specificity was 77.6%, sensitivity was 88.9%, and the Youden value was 0.655. Conclusion: POEM scores can evaluate patient microcirculation and predict prognosis for septic shock, as with APACHE II scores, SOFA scores, and blood lactate value. The optimal cut-off value was 3.5. Thus, POEM scores may become a new clinical index for condition evaluation and prognosis prediction of septic shock patients.

Keywords: POEM scoreprognosisseptic shock

Introduction

Sepsis is one of the most serious diseases in emergency medicine. When pathogenic microorganisms invade the human body, excessive inflammatory reactions may lead to serious complications, as well as progression to MODS [1]. Septic shock patients usually show decreased cardiovascular function with or without a loss of cardiac output. This is due to pathogens and inflammatory reactions. Ischemia and hypoxia of tissues are prominent in patients with septic shock. Thus, microcirculation becomes obstructed. Consequently, metabolites are accumulated. This forms a vicious circle, leading

to dysfunction. Hemodynamic abnormalities can often be corrected by rapid fluid resuscitation and vasoactive drugs. However, correction of microcirculation is quite complicated. Lag effects may exist. It is possible that the macrocirculation will be improved, but the microcirculation may continue to deteriorate. Accordingly, improvements in microcirculation are more significant to the resuscitation of septic shock patients [2, 3].

There are many indicators reflecting the microcirculation, including blood acid, SVO_2, $ScVO_2$, pH of gastric mucosa, and sublingual CO_2. Blood lactic acid has been used as the most

accurate indicator in assessing tissue metabolism. International sepsis guidelines suggest re-ducing blood lactic acid levels to normal as the 6-hour target for treatment of sepsis [4]. Many studies have verified that blood lactic acid (BLA) may be considered a sign of improvement in perfusion, as well as an important indicator in the prognosis in sepsis patients. In a multicenter RCT study, it was shown that reducing BLA to normal could dramatically bring down mortality rates of sepsis patients. However, this method requires blood samples from patients. Some patients may already have a disorder of lactic acid metabolism due to liver dysfunction, limiting clinical application. Furthermore, the pH of gastric mucosa is an indicator of tissue perfusion in septic shock patients. The gastrointestinal tract may be the first organ to suffer from ischemia. It has been proven that pH changes of gastric mucosa could indicate perfusion of the gastrointestinal tract [5], especially in patients with acute pancreatitis and trauma [6-8]. However, interventional manipulation may limit its use to some degree [5]. Moreover, there are many techniques available for observation of organ perfusion directly. These are still under exploration due to technical limitations, including OPS, SDF, sublingual capnometry [9-11], and NIRS [12-14].

Previous studies have found that we can learn the microcirculation condition of patients with sepsis or septic shock through sub-labial mucosa and sub-lingual mucosa. High-quality images can be obtained more easily and conveniently at the sub-labial mucosa than the sub-lingual mucosa. Parameters, including TVDs, PVDs, MFI, and PPVs, are often used to evaluate the microcirculation. These are mainly obtained by semi-automatic calculations through the AVA3.2 version. This process usually takes 20-30 minutes, sometimes even longer. Currently, the more intelligent data processing version AVA5.0 is available. However, some results from the AVA5.0 version have been far from clinical situations in previous research, limiting its clinical use. A previous study found that the microcirculation can also be assessed by simple blood flow and heterogeneity (POEM scores) [1]. Trained doctors can obtain results in 2-3 minutes through four 4-6 second images. To a certain extent, POEM scores provide greater clinical value than TVDs, PVDs, or PPV obtained from a single image.

The current study aimed to confirm whether POEM scores can predict prognosis for septic shock. First, POEM scores were obtained by monitoring submucosal microcirculation on the day of diagnosis (within 24 hours). Second, this study evaluated the ability of POEM scores to predict 28-day mortality, examining its predictive value for prognosis of septic shock.

Experimental design

With approval of the Ethics Committee and patient consent, the current retrospective analysis was performed with all consecutive patients diagnosed with septic shock, from July 2017 to June 2018, in the Emergency Department and ICU of Shanghai Changzheng Hospital. Video-microscopy images of microcirculation at the sub-labial mucosa were acquired on the first day of diagnosis (within 24 hours). AP-ACHE scores, SOFA scores, heart rates, mean arterial pressure, blood lactic acid levels, and other related indexes were also recorded on the same day. Next, correlation levels between POEM scores, arterial lactate values, APACHE scores, and SOFA scores were analyzed. ROC curves were established, aiming to compare the prognostic value of these indicators for septic shock patients and obtain the optimal cut-off value for prediction of 28-day mortality.

Materials and methods

Materials

A total of 83 cases of septic shock were enrolled in the study. POEM scores were obtained by trained doctors via video microscopy images. Clinical data was collected, including heart rates, blood pressure (average arterial pressure), lactic acid, and D-dimer.

GEM3000 blood gas analyzer, produced by IL company, was used to measure blood lactic acid. MicroVision microcirculation monitor was used for collection and analysis of microcirculation images.

Methods

<u>Case inclusion and exclusion criteria</u>

Inclusion criteria: Patients were at least 18 years old and were diagnosed with septic shock. Diagnosis was defined based on 2016 SSC guidelines. According to these guidelines,

Table 1. Death group and survival group of septic shock patients

	Survival group	Death group	χ^2/T	P value
Total cases	74	9		
Gender (Male/Female)	60/14	5/4		
Age	57.5 ± 15.0	60.0 ± 11.5	0.431	0.668
Arterial lactate acid (mmol/L)	1.735 ± 1.220	4.213 ± 4.420	3.812	< 0.001
APACHE II score	8.320 ± 5.512	14.621 ± 4.723	3.226	0.002
SOFA score	4.320 ± 3.418	6.836 ± 2.824	2.095	0.039
POEM score	3.651 ± 1.032	2.331 ± 0.873	3.944	< 0.001

sepsis is defined as organ dysfunction caused by excessive inflammatory response to infections. Septic shock is a serious type of sepsis, often associated with circulatory failure or organ dysfunction [3]. The current study was approved by the Ethics Committee of Shanghai Changzheng Hospital.

Exclusion criteria: (1) Pregnant women; (2) Patients with oral diseases or obvious oral trauma; (3) Patients with massive hemorrhages that could not be monitored accurately or if the monitoring process affected patient vital signs; (4) Patients with non-invasive ventilation that could not survive without ventilation; and (5) Patients that did not cooperate with image collection.

Acquiring images of sub-labial mucosa

The trained operator gently wiped off secretions from the upper lip with 37°C saline gauze or cotton swabs. The operator then placed the probe between the sub-labial mucosa and the gums. The position and focal length of the probe was adjusted to obtain a clear and stable image, avoiding excessive pressure. A total of 4 images (4-6 seconds) from 2 points on both sides of the lower lip were collected.

Main index

A) Patient information, including gender, age, infection status, APACHE II scores, and SOFA scores on the day of diagnosis of septic shock; B) Arterial blood gas conditions, including lactic acid on the same day; C) Images of microcirculation at the sub-labial mucosa on the day of diagnosis of septic shock.

Statistical methods

Statistical analysis was conducted using IBM SPSS Statistics 22. Enumeration data are ex-pressed as $\overline{X}$ ± s. Comparisons of the data were analyzed by t-tests. Count data are expressed as frequencies. Analysis was performed using χ^2 tests. Correlation levels between POEM scores, arterial blood lactate values, APACHE II scores, and SOFA scores were compared using Pearson's correlation analysis. P < 0.05 indicates statistical significance. Moreover, r > 0 indicates positive correlation, while r < 0 indicates negative correlation. Greater values of r indicate a stronger correlation. ROC curves were established to compare the predictive value of POEM scores, arterial blood lactate values, APACHE II scores, and SOFA scores to prognosis of patients with septic shock. Larger areas under the curve indicate greater predictive value.

Results

General information of patients with septic shock

A total of 83 cases of septic shock were enrolled in the present study. Primary diseases included 62 cases of severe pneumonia, 3 cases of traumatic abdominal cavity infections, 2 cases of traumatic pancreatitis, 4 cases of diabetes with skin soft tissue infection, 3 cases of acute pancreatitis, 1 case of double lower limbs artery embolism with infection, 2 cases of intestinal obstruction, 1 case of mesenteric artery embolism, 4 cases of abdominal infections, and 1 case of bedsores combined with diabetes. In the end, 9 cases died while 74 survived (**Table 1**).

Correlation analysis of POEM scores, APACHE II scores, and SOFA scores in patients with septic shock

POEM scores and APACHE II scores showed a negative correlation and a linear correlation,
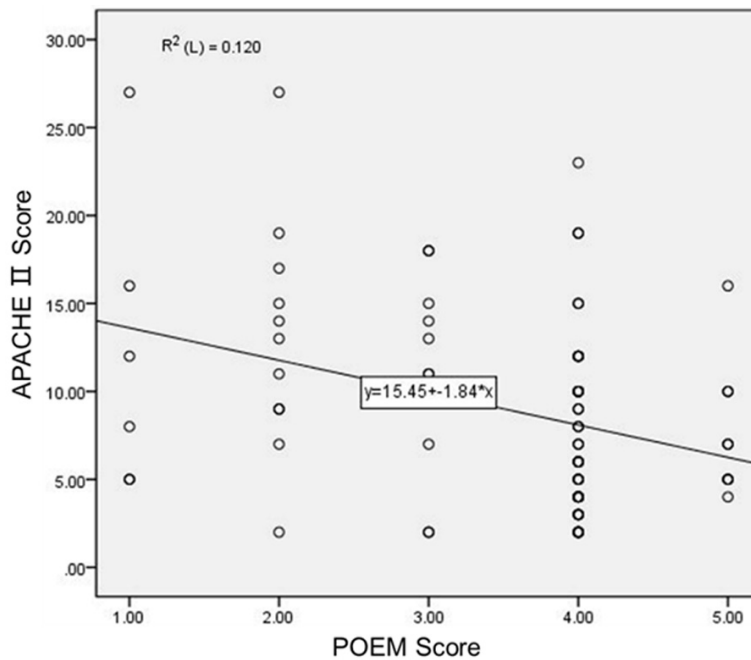
Figure 1. Correlation of POEM scores and APACHE II scores (P = 0.001, r = -0.346).
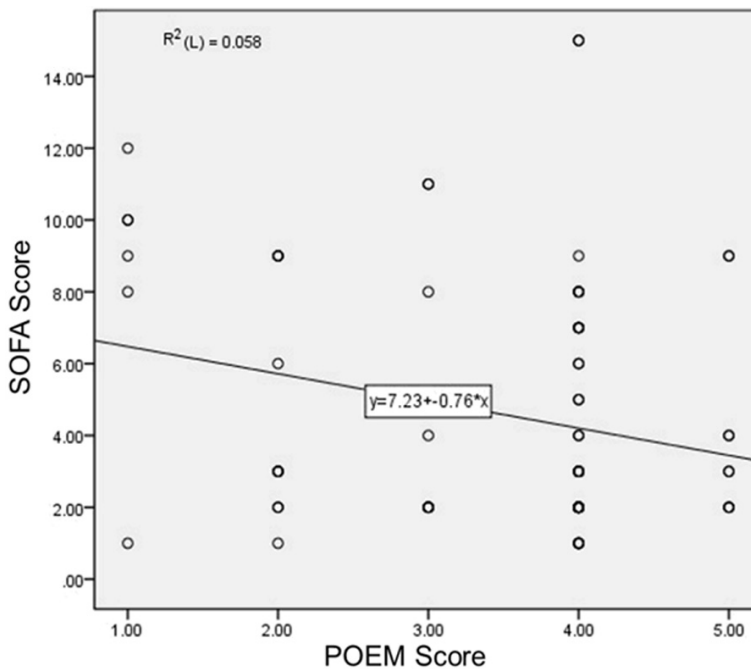
Figure 2. Correlation of POEM scores and SOFA scores (P = 0.028, r = -0.242).

ues showed a negative correlation and a linear correlation, with P < 0.01 and r = -0.348 (**Figures 1**-**3**).

ROC curves were established based on POEM scores, POEM scores, APACHE II scores, SOFA scores, and blood lactate values within 24 hours of septic shock for evaluation of prognosis and the best cutoff value of prognosis

ROC curves showed that POEM scores and blood lactic scores had the largest area under the curve. These were 0.841 and 0.823, respectively, indicating that these two parameters provide better predictive value for prognosis evaluation. The optimal cut-off value of POEM scores was 3.5. Specificity was 77.6%. Sensitivity and Youden values were 88.9% and 0.655, respectively (**Figure 4** and **Table 2**).

Discussion

Microcirculation is composed of small arteries, venules, and capillaries. The diameter of small arteries and venules is about 0-20 um. These vessels are closely related to the function of microcirculation [2]. Changes in microcirculation are caused by multiple factors, including endothelial dysfunction, expression of adhesion molecules, increased leukocyte chemotaxis, degradation of polysaccharide coating, coupling of ligands, vascular leakage, microthrombus formation, and micro-arteriovenous functional shunting of oxygen delivery [15]. Changes in microcirculation in sepsis include heterogeneity of blood perfusion, discontinuity of blood flow and interstitial edema,

with P < 0.01 and r = -0.346. POEM scores and SOFA scores showed a negative correlation and a linear correlation, with P < 0.05 and r = -0.242. POEM scores and blood lactate val-
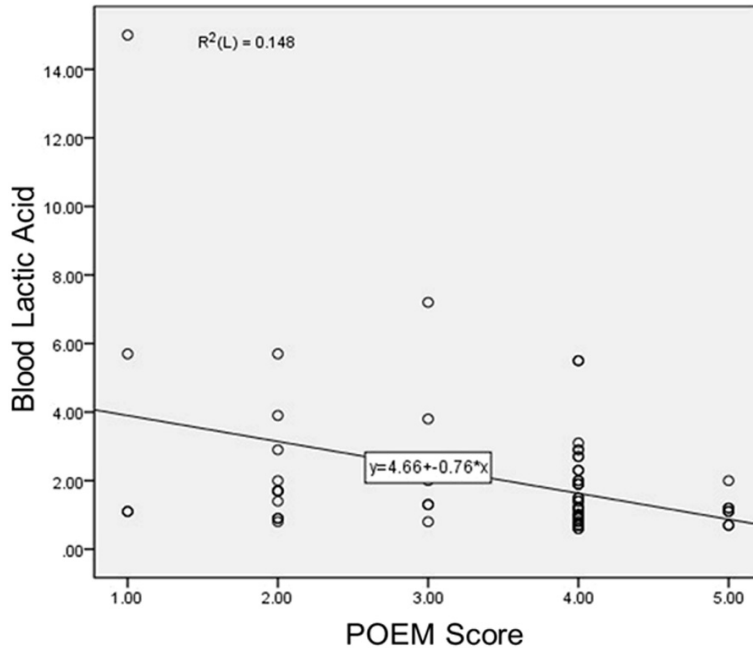
Figure 3. Correlation of POEM scores and blood lactic acid levels (P = 0.001, r = 0.348).
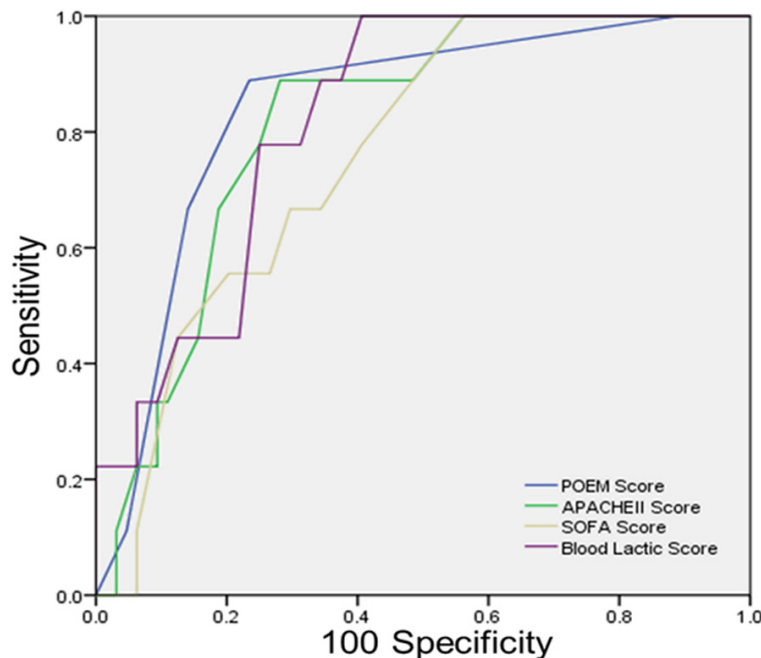
Figure 4. ROC curves based on POEM scores, APACHE II scores, SOFA scores, and blood lactic acid levels.

Excessive or delayed blood flow will affect the exchange of nutrients. Early studies have found that decreased blood flow perfusion and density in small blood vessels can be observed in patients with severe sepsis, with dysfunction related to final outcomes [16]. Moreover, different changes in the microcirculation have been found, including discontinuity of blood flow and heterogeneity of microvascular perfusion (type 1 microcirculatory changes) [17, 18]. In sepsis patients, even if the macro-circulation remains constant, there may be regional hypoxic areas due to the heterogeneity of microvascular blood flow. A previous study found that early microcirculation deterioration (the first 24 hours) in sepsis patients was correlated with prognosis, significantly, suggesting that this could be used as a prognostic indicator. It was more sensitive and specific than other indexes of macro-circulation, such as blood pressure, heart rates, CI, and CVP [15]. Results showed a significant decrease in PVD, TVD, PPV, and MFI of small blood vessels within the first 6 hours of sepsis shock, while CI was significantly elevated [19]. In fact, there were statistically significant differences between the death group and survival group. Results indicated that the macro-circulation may be compensated in the early stages of septic shock, while the microcirculation may begin to show significant abnormalities, associated with prognosis [19]. Therefore, restoring perfusion of the microcirculation and increasing tissue perfusion are more significant than simply raising blood pressure or central venous pressure.

and insufficient exchange of oxygen and nutrients in microcirculation. More attention should be paid to small vessels which are affected by continuity and heterogeneity of microcirculation, especially in microcirculation disorders.

Table 2. Area under the curve

Variables	Area	Standard error	Asymp	95% confidence interval	
				Lower limit	upper limit
POEM Score	0.841	0.064	0.001	0.716	0.966
APACHE II Score	0.816	0.059	0.002	0.700	0.932
SOFA Score	0.763	0.067	0.011	0.631	0.895
Blood lactic acid	0.823	0.056	0.002	0.713	0.933

Multiple experimental studies concerning microcirculation have mainly focused on PPV, TVD, PVD, MFI, and other parameters of small blood vessels. De Backer found that the survival rate decreased with small vessel's PPV falling. This is the strongest predictor of outcomes, far more accurate than parameters of the macro-circulation [20]. The severity of microcirculation perfusion disorders is related to organ dysfunction and mortality [16, 18]. It has been shown that abnormal MFI and tachycardia are independent factors for mortality [21]. PVD has been associated with organ dysfunction and mortality through a retrospective analysis in patients with septic shock [16]. Additionally, microcirculation flow index (MFI) values, heterogeneity index values, and the proportion of perfused vessels were lower in patients with sepsis, compared with healthy volunteers [19]. Results indicated that the microcirculation is changed in the early phase of sepsis. This change is more prominent in patients with severe sepsis. Previous studies have mainly focused on the correlation between prognosis and indicators, such as PPV and MFI. The microcirculation flow index (MFI) is obtained by dividing the microscopic field (896 × 672 um, 640 × 480 pixels) into four quadrants with two horizontal and two vertical lines [21]. MFI is the average score of 4 quadrants, while PPV is the ratio of small vessel perfusion. MFI and PPV have been used to evaluate continuity and perfusion of blood flow in the microcirculation. However, in clinical operations, it takes too much time (44 minutes) to analyze collected images, using semi-automatic software such as AVA3.0. If automatic software AVA5.0 or higher is used, its value is far from patient clinical situations. This may due to technical limitations. A previous study evaluated the microcirculation by simple blood flow continuity and heterogeneity, along with POEM scores. These mainly combine these two parts to formulate a score. POEM scores have a linear relation with PPV, MFI, and PPV [4].

In conclusion, POEM scores may be a new and convenient indicator for assessment of sepsis and septic shock. However, the current study was limited due to a small sample size. Thus, present conclusions should be verified by larger samples in future RCT studies.

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Disclosure of conflict of interest

None.

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