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THE PROGNOSTIC VALUE OF SERUM MVCD AND MOP1 LEVELS IN EVALUATING THE PROGNOSIS OF PATIENTS WITH SEPSIS

PROGNOSTIČKA VREDNOST SERUMSKIH NIVOA MVCD I MOP1 U PROCENI PROGNOZE KOD PACIJENATA SA SEPSOM

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Summary

Background: To investigate the prognostic significance of serum levels of Member of PAS protein 1 (MOP1) and Mammalian-derived Vascular Endothelial Growth Factor (MVCD) for the prognosis of patients with sepsis in the intensive care unit (ICU).
Methods: We selected 124 patients with sepsis admitted to our hospital's ICU from September 2023 to September 2025 as Group B and another 100 patients admitted to the ICU during the same period without sepsis-related infections as Group A. Additionally, patients with sepsis were split into two groups based on their prognosis after 28 days: a survival group (n = 80) and a mortality group (n=44). The patients' levels of MOP1 and MVCD were measured and compared after admission. In patients with sepsis in the ICU, the predictive significance of serum MVCD and MOP1 was assessed using receiver operating characteristic (ROC) curves. To identify which characteristics affected the prognosis of sepsis patients in the ICU, a multivariate logistic regression analysis was performed.
Results: Serum MOP1 and MVCD levels were significantly higher in Group B than in Group A. In addition, the non-

Kratak sadržaj

Uvod: Cilj je bio da se ispita prognostički značaj serumskih nivoa proteina 1 člana PAS porodice (MOP1) i vaskularnog endotelnog faktora rasta poreklom od sisara (MVCD) na prognozu kod pacijenata sa sepsom u jedinici intenzivne nege (ICU).
Metode: U studiju su uključena 124 pacijenta sa sepsom primljena u jedinicu intenzivne nege naše bolnice u periodu od septembra 2023. do septembra 2025. godine, koji su svrstani u grupu B, kao i dodatnih 100 pacijenata primljenih u ICU u istom periodu bez infekcija povezanih sa sepsom, koji su činili grupu A. Pored toga, pacijenti sa sepsom su, prema ishodu nakon 28 dana, podeljeni na grupu preživelih (n=80) i grupu preminulih (n=44). Nakon prijema određivani su i upoređivani nivoi MOP1 i MVCD. Prediktivni značaj serumskih MVCD i MOP1 kod pacijenata sa sepsom u ICU procenjen je pomoću ROC krivih. Za utvrđivanje faktora koji utiču na prognozu pacijenata sa sepsom u ICU je primenjena multivarijantna logistička regresiona analiza.
Rezultati: Serumski nivoi MOP1 i MVCD u grupi B bili su značajno viši nego u grupi A. U poređenju sa grupom

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survival group had significantly higher serum MVCD and MOP1 levels than the survival group (P<0.05). ROC curve analysis showed that, for predicting the prognosis of ICU patients with sepsis, serum MVCD had an area under the curve (AUC) of 0.877 at a cutoff value of 146.87 ng/L, with a sensitivity of 90.93% and a specificity of 70.00%. Serum MOP1 had an AUC of 0.848 at a cutoff value of 35.53 ng/L, with a sensitivity of 90.93% and a specificity of 62.53%. The combined detection of MVCD and MOP1 yielded an AUC of 0.926, with a sensitivity of 86.39% and a specificity of 62.53%. Multivariate logistic regression analysis showed that serum C-reactive protein level [odds ratio (OR), 95% confidence interval (CI): 2.436, 1.634–3.622], MOP1 level [OR, 95% CI: 3.407, 1.880–6.144], MVCD level [OR, 95% CI: 3.782, 1.859–7.736], Acute Physiology and Chronic Health Evaluation II (APACHE II) score [OR, 95% CI: 3.212, 1.802–5.720], and N-terminal pro-brain natriuretic peptide level [OR, 95% CI: 3.037, 1.739–5.308] were independent risk factors for 28-day mortality in ICU patients with sepsis (P<0.05).

Conclusion: ICU patients with sepsis had elevated peripheral blood levels of MVCD and MOP1, and these increases were closely associated with poor prognosis. These findings suggest that MVCD and MOP1 may serve as useful biomarkers for prognostic evaluation in sepsis.

Keywords: septicemia, mammalian-derived vascular endothelial growth factor, member of PAS protein 1, prognostic analysis

umrlih, grupa preživelih imala je značajno niže serumske nivoe MVCD i MOP1. Razlike između grupa bile su statistički značajne (P<0,05). Rezultati ROC analize pokazali su da je, u proceni prognoze pacijenata sa sepsom u JIN, za serumski MVCD površina ispod krive (AUC) iznosila 0,877, uz graničnu vrednost od 146,87 ng/L, dok su senzitivnost i specifičnost iznosile 90,93% i 70,00%. Za serumski MOP1, AUC je iznosila 0,848, uz graničnu vrednost od 35,53 ng/L, a senzitivnost i specifičnost bile su 90,93% i 62,53%. U proceni prognoze sepse u ICU, kombinacija MVCD + MOP1 imala je senzitivnost od 86,39%, specifičnost od 62,53% i AUC od 0,926. Multivarijantna logistička regresiona analiza pokazala je da su serumski nivoi C-reaktivnog proteina [odnos šansi (95% CI) = 2,436 (1,634–3,622)], MOP1 [odnos šansi (95% CI) = 3,407 (1,880–6,144)], MVCD [odnos šansi (95% CI) = 3,782 (1,859–7,736)], skor APACHE [odnos šansi (95% interval poverenja) = 3,212 (1,802–5,720)] i N-terminalni pro-moždani natriuretski peptid [odnos šansi (95% interval poverenja) = 3,037 (1,739–5,308)] faktori rizika koji utiču na smrtnost pacijenata sa sepsom u jedinici intenzivne nege (P<0,05).

Zaključak: Pacijenti sa sepsom u ICU su imali više nivoe ekspresije MVCD i MOP1 u perifernoj krvi, a ovi povišeni nivoi bili su u snažnoj korelaciji sa prognozom pacijenata. Ovi nalazi imaju dobru kliničku vrednost za prognostičku procenu pacijenata sa sepsom u jedinici intenzivne nege.

Ključne reči: sepsa, vaskularni endotelni faktor rasta poreklom od sisara, protein 1 člana PAS porodice, prognostička analiza

Introduction

Sepsis is a prevalent severe illness in the intensive care unit (ICU) and a systemic inflammatory response syndrome brought on by bacterial infection. Its death rate and incidence are both comparatively high. There may be delays in the patient's condition if it is not identified and managed promptly. As the disease progresses further, multiple organ dysfunction syndrome and multiple organ failure occur, ultimately leading to the death of the patients (1, 2). Therefore, early identification of risk factors and intervention is highly important for avoiding further deterioration of the condition and improving patient prognosis. Mammalian-derived Vascular Endothelial Growth Factor (MVCD) is a highly conserved homodimeric glycoprotein that plays important roles in maintaining angiogenesis, regulating the immune system, and promoting endothelial cell health (3). Studies have reported that serum MVCD levels correlate with disease severity in patients with acute pancreatitis (4). Angiogenesis, apoptosis, energy metabolism, and other pathological processes are all influenced by hypoxia-inducible factor-1 alpha (MOP1), which is also a key regulator of cellular oxygen metabolism (5). Research has shown that MOP1 is crucial in newborn hypoxic pulmonary hypertension (6, 7).

However, the purpose of this study was to investigate the significance of serum MVCD and MOP1 levels in assessing the prognosis of ICU patients with sepsis, as their utility in this regard remains unknown.

Materials and Methods

General information

Group B consisted of sixty-two patients with sepsis who were admitted to the ICU of our institution between September 2023 and September 2025.

Inclusion criteria: met the diagnostic criteria for sepsis; provided consent from the patient's guardian. Exclusion criteria: those with functional impairments of important organs such as the liver, kidney, or heart; those with immune system diseases, coagulation disorders, or hematological malignancies; those with a history of bone marrow transplantation, blood transfusion, or infectious diseases before admission; those who had recently received major treatment; those who had received corticosteroids or other immunosuppressants in the past 3 months; those with language or cognitive dysfunction; those with incomplete clinical data; and those who did not cooperate with the study.

In this study, 100 patients admitted to the ICU during the same period, without sepsis, were selected as Group A.

General data collection

The basic information and biochemical indicators of the subjects in this study were collected and compared using methods such as reviewing outpatient and inpatient medical records and physical examination reports. These comprised the following: age, sex, duration of mechanical ventilation, length of stay in the intensive care unit (ICU), respiratory rate, white blood cell count (WBC), C-reactive protein (CRP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), and acute and chronic health status score (APACHE II).

Testing methods

Collect 5 ml of fasting peripheral venous blood using the BD Company vacuum blood collection tube (item number: 367880). The blood sample is sent to our medical laboratory department within 30 minutes after collection and processed by professional technicians. The blood sample is placed in a centrifuge manufactured by Eppendorf in Germany (model 5810R). It is centrifuged at 3,000 rpm at room temperature for 5 minutes. The supernatant is transferred to a 1.5 mL PE tube and immediately stored in a -80 °C ultra-low temperature refrigerator (Thermo Scientific, United States, model: Forma 900 Series) for future use. Serum MVCD and MOP1 levels are determined by enzyme-linked immunosorbent assay (ELISA). Sigma-Aldrich Company produces the MVCD detection kit in the United States (item number: RAB0506), and R&D Systems Company produces the MOP1 detection kit in the United States (item number: DHY330). The experimental operation is carried out strictly according to the instructions for the kits, and detection is performed using a microplate reader from BioTek (United States; model ELx800).

Each 96-well plate is set with standard sample wells, blank control wells, and sample duplicate wells. The standard curve is calculated using the four-parameter fitting method to determine the sample concentration. Internal quality control samples are used during the experiment to ensure that intra- and inter-batch differences are less than 10%. All tests are completed by the same technician in the same laboratory to minimize operational errors and ensure the reliability and comparability of the data.

Statistical methods

Receiver operating characteristic (ROC) curves were utilized to assess the predictive value of serum MVCD and MOP1 for the prognosis of patients with sepsis in the intensive care unit (ICU), and multivariate logistic regression analysis was utilized to investigate the factors influencing the prognosis of patients with sepsis in the ICU. The measurement data were expressed as the means ± standard deviations ($\bar{x}\pm s$), and comparisons between groups were done using t tests.

Results

Comparison of the general data of the patients in Group A and Group B

There were no statistically significant differences in age, sex, time from onset to admission, mechanical ventilation time, ICU stay time, respiratory rate, heart rate, or WBC count between the two groups ($P > 0.05$). The levels of CRP, NT-proBNP, and APACHE II score in Group B were significantly higher than those in Group A ($P < 0.05$; see *Table I)*.

Comparison of serum MVCD and MOP1 levels between Group A and Group B patients

The serum MVCD and MOP1 levels of patients in Group B were significantly higher than those in Group A ($P<0.05$; see *Table II*).

The expression levels of these two factors in the serum of patients with sepsis were significantly higher than those in non-sepsis patients, suggesting that MVCD and MOP1 may be closely related to the pathophysiological processes of sepsis. MOP1, as an oxygen-inducible factor, may participate in the disease process by regulating the body's response to hypoxia under sepsis conditions; while MVCD, as a vascular endothelial growth factor, may play an important role in the vascular dysfunction and inflammatory response caused by sepsis.

Comparison of serum MVCD and MOP1 levels between the surviving group and the nonsurviving group

Patients with sepsis were split into two groups based on their prognosis 28 days later: a survival group (n=80) and a death group (n=44). The survival group had significantly lower levels of serum MVCD, MOP1, CRP, and NT-proBNP, as well as a lower APACHE II score, than the nonsurviving group ($P<0.05$; see *Table III*).

Evaluation value of serum MVCD and MOP1 for the prognosis of patients with sepsis in the ICU

The area under the curve for serum MVCD in predicting sepsis prognosis in the ICU was 0.877,

Table I Comparison of general data between Group A and Group B ($\bar{x}\pm s$).

Group	Gender/Cases (Percentage/%)		Age/Year	Time from onset to hospitalization/h	Mechanical ventilation time/d	ICU hospitalization time/d
	Male	Woman				
Group A (n=100)	60 (60.0)	40 (40.0)	46.33±5.77	4.38±0.81	3.18±0.22	6.81±1.11
Group B (n=124)	76 (61.3)	48 (38.7)	49.24±4.69	4.33±0.88	3.24±0.39	6.91±1.28
T/χ^2 value	0.012	-0.683	-0.400	0.958	0.434	
P value	0.882	0.491	0.687	0.345	0.660	
Group	Respiratory rate/time min^{-1}	Heart rate/ time · min^{-1}	WBC/piece · L^{-1}	CRP/mg ·L^{-1}	NT-proBNP/μg^{-1}	APACHE II rating/point
Group A (n=100)	23.05±3.61	113.10±13.22	(13.55±2.43)×10^9	12.39±1.68	0.65±0.18	12.36±3.32
Group B (n=124)	22.35±3.32	112.39±12.33	(13.25±2.35)×10^9	16.45±2.25	1.15±0.29	25.62±6.67
T/χ^2 value	-1.049	-0.337	-0.673	25.716	12.061	12.929
P value	0.291	0.732	0.507	<0.001	<0.001	<0.001

Table II Comparison of serum MVCD and MOP1 levels between group A and group B patients ($\bar{x}\pm s$).

Group	MOP1/ng ·L^{-1}	MVCD/ng^{-1}
A group	27.48±4.40	96.68±24.10
B group	36.69±5.51	152.23±26.68
T value	9.475	11.420
P value	<0.001	<0.001

Table III Comparison of serum MVCD and MOP1 levels between the survival group and the death group ($\bar{x}\pm s$).

Group	CRP/mg ·L^{-1}	NT-proBNP/ μg ·L^{-1}	APACHE II rating/ point	MOP1/ng ·L^{-1}	MVCD/ng ·L^{-1}
Survival group	15.28±2.05	0.82±0.23	20.24±5.10	30.07±5.17	138.99±15.40
Group of Death	17.69±3.28	1.39±0.36	38.39±7.11	48.73±6.28	176.20±18.42
T value	-3.606	-6.996	-11.493	-10.642	-5.075
P value	0.001	<0.001	<0.001	<0.001	<0.001

with a cutoff of 146.87 ng/L, yielding a sensitivity of 90.93% and specificity of 70.03%.

The area under the curve for serum MOP1 was 0.848, with a cutoff of 35.53 ng/L, yielding a sensitivity of 90.93% and specificity of 62.53%. The area under the curve for the combination of MVCD and MOP1 was 0.926, with a sensitivity of 86.39% and specificity of 62.53%, see *Table IV*.

Multivariate logistic regression analysis of the prognosis of patients with severe sepsis in the ICU

The prognosis of patients with severe sepsis in the ICU is designated as the dependent variable (survival group = 0, death group = 1), utilizing serum MVCD and MOP1 and the indicators in Table I as independent variables for multivariate logistic regression analysis, the results revealed that serum MVCD [odds ratio (95% confidence interval) = 3.782

Table IV Evaluation value of serum MVCD and MOP1 in the prognosis of ICU sepsis patients.

Indicator	Area under the curve	95% confidence interval	Truncation value	Sensitivity	Specificity
MOP1	0.848	0.799~0.891	35.53 ng/L	90.93%	62.53%
MVCD	0.877	0.813~0.935	146.87 ng/L	90.93%	70.03%
MVCD+MOP1	0.926	0.893~0.959		86.39%	85.03%

Table V Multivariate logistic regression analysis of prognosis in ICU sepsis patients.

Variable	Regression coefficient	Standard error	Wald x^2 value	P value	Ratio (95% confidence interval)
CRP	0.882	0.207	18.994	<0.001	2.436 (1.634~3.622)
NT-proBNP	1.113	0.288	15.162	<0.001	3.037 (1.739~5.308)
APACHE II score	1.162	0.297	15.813	<0.001	3.212 (1.802~5.720)
MOP1	1.228	0.304	16.566	<0.001	3.407 (1.880~6.144)
VEGF	1.335	0.367	13.394	<0.001	3.782 (1.859~7.736)

(1.859–7.736)], MOP1 [odds ratio (95% confidence interval) = 3.407 (1.880–6.144)], CRP [odds ratio (95% confidence interval) = 2.436 (1.634–3.622)], NT-proBNP [odds ratio (95% confidence interval) = 3.037 (1.739–5.308)], with the APACHE II score [odds ratio (95% confidence interval) = 3.212 (1.802–5.720)] were risk factors that had an impact on patients' ICU sepsis prognosis (P<0.05), see *Table V*.

Discussion

Septicaemia is a common infectious disease in patients, and multiple organ failure is the main factor leading to the death of patients. Statistics indicate that around 3 million neonates and 1.2 million patients globally are diagnosed with septicaemia annually, with a mortality rate for such patients ranging from 20% to 50% post-onset (8, 9). Therefore, identifying and accurately assessing septicemia at an early stage and implementing treatment as soon as possible has become a hot topic in critical care medicine research in China. In recent years, with in-depth exploration, indicators such as WBC and CRP have been found to play a role in the prognostic assessment of septicemia (10, 11), but many shortcomings remain. This study explored the value of serum MVCD and MOP1 levels in predicting the prognosis of patients with septicemia in the ICU, providing more effective indicators for early diagnosis and prognosis.

MOP1 is a key factor regulating oxygen homeostasis and currently plays an important role in tumor angiogenesis, cell survival, glucose metabolism, infiltration, and metastasis (12). Studies have reported that the serum MOP1 level is abnormally elevated during brain injury and that this change in the level of MOP1 is closely related to the condition and prognosis of patients (13–15). An imbalance in the inflammatory immune response triggered by infection can affect the pathophysiology of sepsis (16). MOP1 is an important transcriptional regulator under hypoxic conditions and an important indicator of cellular hypoxia. However, previous studies have reported that MOP1 regulates the production of various inflammatory mediators. When the body produces inflammatory cytokines, it can activate MOP1 transcription, leading to its production (17). The platelet-derived growth factor family of growth factors includes MVCD. By directly affecting vascular endothelial cells, it can increase vascular permeability and encourage the development of new blood vessels. It also has a role in several physiological and pathological disease processes (18). Studies have reported that serum MVCD is highly expressed in patients with acute pancreatitis and is associated with disease severity (19). The study's findings showed that the surviving group's blood MVCD level was significantly lower than that of the nonsurviving group (P<0.05) and that the serum MVCD level in group B patients was significantly higher than that in group A patients. These results suggest a possible substantial relationship between the occurrence, progression, and prognosis of sepsis and the serum MVCD concentration. With a sensitivity of 86.36% and a specificity of 70.00%, the area under the curve (AUC) for blood MVCD in assessing the prognosis of sepsis patients in the ICU was 0.874, suggesting that serum MVCD level is a significant prognostic factor.

Subsequent investigation showed that the serum MVCD concentration is a risk factor influencing the prognosis of sepsis patients in the intensive care unit (ICU) ($P<0.05$), confirming that the serum MVCD concentration is an effective indicator for assessing patient prognosis and is closely associated with the prognosis of sepsis patients in the ICU. Mammalian-derived Vascular Endothelial Growth Factor and its receptor Flt-1 have been shown to play a role in the body's immunological and anti-inflammatory processes (20–22). When serum vascular endothelial growth factor is abnormally secreted, it can damage vascular endothelial cells and increase microvascular permeability, thereby promoting local inflammatory reactions, releasing various inflammatory factors and procoagulant substances, worsening systemic inflammatory response syndrome in sepsis patients, and ultimately leading to a poor prognosis. The area under the ROC curve for MVCD combined with MOP1 was greater than that for the other factors, indicating that the combined value of serum MVCD and MOP1 was better at predicting the prognosis of ICU sepsis patients.

Conclusion

The levels of MVCD and MOP1 in the peripheral blood of ICU patients with sepsis were both elevated, and the increase in these levels was closely associated with patient prognosis. These findings have good clinical value for the prognostic assessment of patients with sepsis in the ICU.

Authors' contribution

Xiaobo Zhan and Xue Yang made equal contributions to this work.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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