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ORIGINAL RESEARCH

The Predictive Value of PKC and ET-1 Levels in Cerebrospinal Fluid for Vasospasm and Prognosis in Patients with Aneurysmal Subarachnoid Hemorrhage

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Objective: To analyze the predictive value of protein kinase C (PKC) and endothelin-1 (ET-1) in cerebrospinal fluid for vasospasm and prognosis in patients with aneurysmal subarachnoid hemorrhage (ASH).

Methods: One hundred and forty-eight ASH patients hospitalized in our hospital during February 2019 to February 2022 were optioned as observation subjects. These subjects were graded into good prognosis group (mRS score 0–2, n = 102) and poor prognosis group (mRS score 3–6, n = 46) according to the Rankin Revised Scale Score (mRS) after 6 months of follow-up. Cerebrospinal fluid was collected from patients to detect the content of ET-1 and PKC. The prognostic factors were analyzed using multifactorial logistic regression. The predictive value was assessed using receiver operating characteristic (ROC) curve.

Results: The patients with poor prognosis had a higher age level and a higher proportion of ≥2 aneurysms, aneurysm diameter ≥6 mm, cerebral vasospasm, and Hunt-Hess grade ≥III than those with good prognosis ($P < 0.05$). The patients with poor prognosis had higher content of PKC and ET-1 than those with good prognosis ($P < 0.05$). Age, aneurysm diameter ≥6 mm, cerebral vasospasm, Hunt-Hess classification ≥grade III, PKC and ET-1 were all risk factors related to the prognosis of ASH ($P < 0.05$). The area under the curve (AUC) of PKC and ET-1 for diagnosing poor prognosis of ASH was 0.803 and 0.720, respectively. The AUC of the combined detection was 0.873 ($P < 0.05$). Patients with cerebrovascular spasm had higher content of PKC and ET-1 than those without ($P < 0.05$). The AUC of PKC and ET-1 for diagnosing cerebral vasospasm in ASH was 0.891 and 0.816, respectively, which was 0.932 for combined detection ($P < 0.05$).

Conclusion: The combination of PKC and ET-1 in cerebrospinal fluid had certain value in predicting the poor prognosis of patients with ASH.

Keywords: aneurysmal subarachnoid hemorrhage, prognosis, cerebrospinal fluid, PKC, ET-1, diagnosis

Introduction

Subarachnoid hemorrhage (SH) is a common clinical neurosurgery disease, which is mainly caused by the blood flowing into the subarachnoid space after the rupture of intracranial cerebral bottom or cerebral surface vascular lesions. SH mainly occurs in 40–60 years old people, which can lead to intracranial rebleeding, hydrocephalus, delayed cerebral ischemia, cerebral vasospasm and other complications, seriously threatening people's life safety.[1,2] Aneurysmal subarachnoid hemorrhage (ASH) is a common type of SH, which refers to diffuse SH caused by intracranial aneurysm rupture. ASH is generally caused by hemodynamic stress-induced degeneration, thinning, or loss of the inner elastic layer of blood vessels, followed by rupture and bleeding of the aneurysm during exercise, emotional stimulation, or other conditions that can induce high blood pressure. ASH has the characteristics of difficult treatment, high fatality rate and high disability rate. Therefore, the risk of death in ASH patients could be reduced by analyzing the relevant factors

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that affect the prognosis of ASH patients, timely predicting the prognosis of ASH, and providing effective treatment interventions.[1,3]

Cerebral vasospasm is a persistent and reversible narrowing of blood vessels, most commonly occurring 3–14 days after the rupture of an intracranial aneurysm. Severe ASH patients may experience varying degrees of cerebral vasospasm. In severe cases, ASH may lead to delayed cerebral ischemia due to reduced cerebral blood flow in the blood supply area. Without effective and timely control, cerebral ischemia caused by cerebral vasospasm could ultimately lead to cerebral infarction. Endothelin-1 (ET-1) is a group of 21 amino acids composed of similar structure and function of isoform brains, which have the property of strongly maintaining long-lasting vasoactivity. ET-1 is derived from cardiomyocytes, cardiac fibroblasts and vascular endothelium, and is a vasoactive substance that can induce smooth muscle cell relaxation and participate in cerebral vasodilation activity.[4] The study[5] has shown that ET-1 can aggravate ischemic brain injury by reducing blood flow to the brain, and ET-1 can be highly expressed in astrocytes and interact with these cells to further affect the pathological process after intracerebral hemorrhage. As one of the central molecules of G protein signaling pathway, protein kinase C (PKC) can regulate members of the water channel family to participate in vasoconstriction, relaxation and other activities.[6] It was found that around the hematoma after intracerebral hemorrhage, the level of PKC isoenzymes and the number of apoptotic cells were up-regulated, and inhibition of PKC expression could alleviate apoptosis.[7] In addition, PKC promoted extracellular Ca^{2+} influx by activating voltage-dependent Ca^{2+} channels, thereby aggravating neuronal damage caused by intracellular Ca^{2+} overload after cerebral ischemia. Recent studies have found that changes in PKC levels are closely related to cerebral vasospasm.[8] Thus, our present study speculated that changes in PKC and ET-1 might affect the prognosis of patients with ASH.

In this study, 148 ASH patients hospitalized at our hospital between February 2019 and February 2022 were optioned as observation subjects. We aimed to analyze the predictive value of PKC and ET-1 in cerebrospinal fluid for vasospasm and prognosis in patients with ASH.

Materials and Methods

General Materials

Total of 148 ASH patients hospitalized in our hospital between February 2019 and February 2022 were optioned as observation subjects. The selection process of general materials was shown in Figure 1. Inclusion criteria: (1) All patients were all in line with the diagnostic criteria for ASH in the European Stroke Organization's 2013 Guidelines for the Treatment of Intracranial Aneurysms and SH;[9] (2) All patients were diagnosed for the first time and were admitted to the hospital within 3 days of onset; (3) The patient and their families were informed and all signed informed consent forms. They could cooperate with the examination and treatment with good compliance. Exclusion criteria: (1) Patients with other brain diseases or previous history of brain surgery; (2) Patients with malignant tumors; (3) Patients who used anticoagulants within 2 weeks; (4) Patients with severe dysfunction in important organs; (5) Patients with combined autoimmune or blood-related diseases; (6) Patients with cerebral artery stenosis. All experimental operations had been ratified by the hospital Ethics Committee and complied with the Declaration of Helsinki.

Outcome Measures

Clinical data: The clinical data of patients was collected and compared, including the gender, age, body mass index (BMI) value, operation mode, smoking history, drinking history, hypertension history, diabetes history, aneurysm location, number of aneurysms, aneurysm diameter, middle cerebral artery, cerebral vasospasm, Hunt-Hess grading, etc.

Judgment of cerebral vasospasm:[10] Transcranial Doppler was used to detect cerebral blood flow velocity on the second day after admission to diagnose cerebral vasospasm. According to commonly used international standards, the middle cerebral artery flow velocity (VMCA)>120 cm/s was designated as cerebral vasospasm, with mild spasms ranging from 120 to 140 cm/s, moderate spasms ranging from 140 to 200 cm/s, and severe spasms >200 cm/n/s.

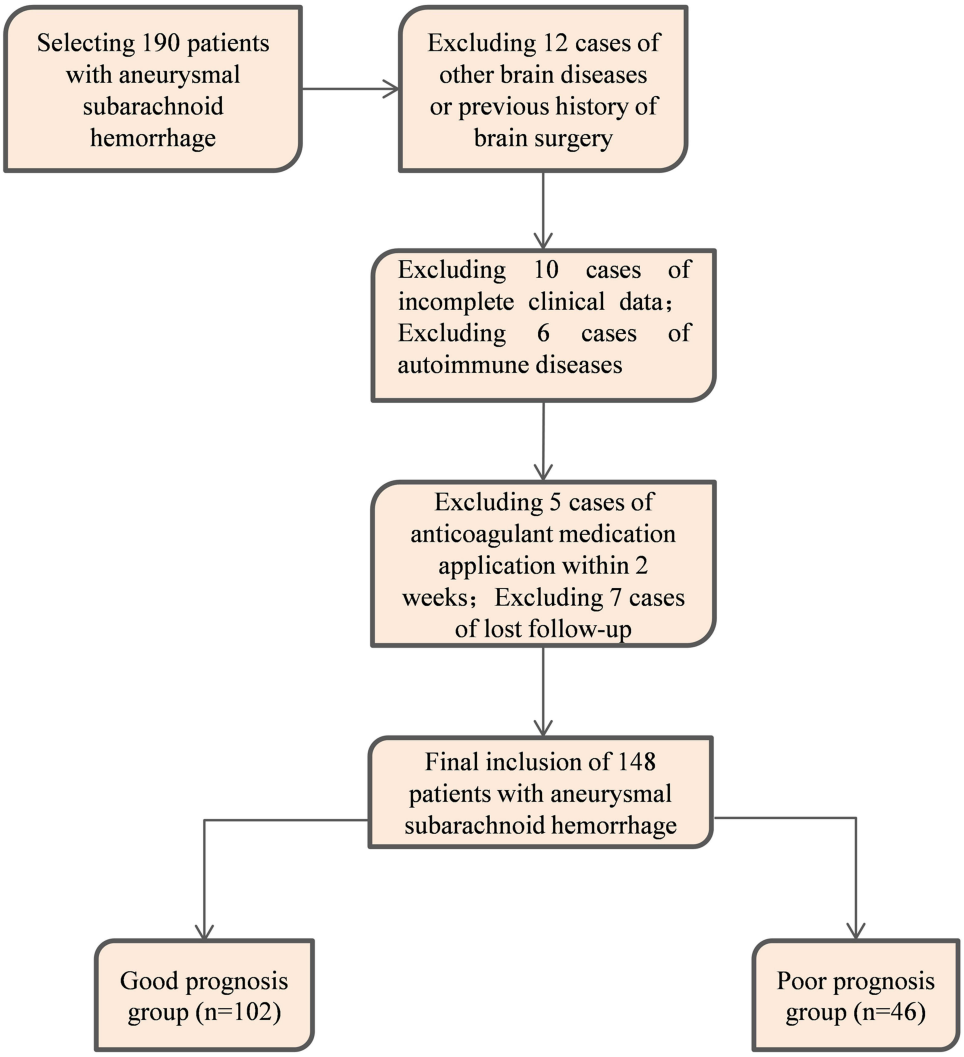

Figure 1 The selection process of general materials.

Hunt-Hess grading: The severity of ASH patients was graded using Hunt-Hess grading, including 0–5 levels. The higher the grading was, the more severe the condition was. Among them, level 0 represented an unruptured aneurysm; Level 1 was mild headache and mild neck stiffness; Level 2 was moderate-to-severe headache, with neck stiffness and no other neurological deficits except for cranial nerve paralysis; Level 3 referred to drowsiness, blurred consciousness, or mild focal neurological deficits; Grade 4 was characterized by numbness, moderate or severe hemiparalysis, and might have early denervated rigidity and autonomic nervous system dysfunction; Level 5 was characterized by deep coma, cerebral rigidity, and a dying state.

Laboratory testing: 3 mL of cerebrospinal fluid was collected from enrolled patients 1 day after surgery (between February 2019 and February 2022), and centrifuged at 1000 r/min at −5°C for 15 minutes. The supernatant and sediment were carefully collected and stored at −70°C to avoid repeated freeze-thaw cycles. Enzyme-linked immunosorbent assay was adopted to value the content of ET-1 and PKC in cerebrospinal fluid (the ET-1 kit was purchased from Shanghai Xinfan Biotechnology Co Ltd., batch number: RIA-53, specification: 100T), (the PKC kit was purchased from Shanghai Yuanmu Biotechnology Co., Ltd., product number: YM-EM10042, specification: 48T/98T). The specific steps were listed as follows: The standard hole and sample hole were set separately. Fifty microliter different concentrations of standard and the sample to be tested were added into the standard well and sample hole, respectively. Nothing was added to the blank holes. Except for blank wells, 100 μL detection antibody

labeled with horseradish peroxidase was added to each well of the standard and sample wells. The reaction pore was sealed with a sealing film and incubated in a 37°C water bath or constant temperature oven for 60 minutes. The liquid in the hole was discarded, and the plate was patted dry on absorbent paper. Each hole was filled with washing solution (350 μL) and stood for 1 minute. The washing solution was discarded, and the plate was patted dry on absorbent paper, repeating for 5 times (it could also be washed by a washing machine). Fifty microliter substrates A and B were added to each well, and the plated was incubated in dark at 37°C for 15 minutes. Fifty microliter termination solutions were added to each well. The OD value of each well was measured at a wavelength of 450nm within 15 minutes.

Follow-up and outcome assessment: According to the Rankin Revised Scale Score (mRS) after 6 months of follow-up, the patients were divided into a good prognosis group (mRS score 0–2 points, n = 102) and a poor prognosis group (mRS score 3–6 points, n = 46).

Statistical Analysis

The experimental data were analyzed using SPSS 20.0 software. Measurement data such as age, BMI, and ET-1 were represented by ($\bar{x}\pm$ s) and compared using *t*-test. Enumeration data such as gender, surgical method, and smoking history was shown as (%) and compared using χ^2 test. The clinical data of patients with ASH were analyzed by univariate analysis, and the statistically significant variables were selected for further multivariate logistic regression analysis. The receiver operating characteristic (ROC) curve was used to evaluate the value of PKC and ET-1 in cerebrospinal fluid in predicting the poor prognosis of patients with malignant ASH. The statistically significant results were those with $P < 0.05$.

Results

Comparison of Clinical Data Between Two Groups of Patients

These 148 patients with ASH were followed up for 6 months. There were 46 patients with an mRS score of 3–6, which was graded as the poor prognosis group. There were 102 patients with an mRS score of 0–2. Comparison of clinical data pointed out that the patients with poor prognosis had a higher age level and a higher proportion of ≥2 aneurysms, aneurysm diameter ≥6 mm, cerebral vasospasm, and Hunt-Hess grade ≥III than those in the good prognosis ($P < 0.05$, Table 1).

Comparison of Cerebrospinal Fluid PKC and ET-1 Levels

Patients in the poor prognosis group had much higher content of PKC and ET-1 than those with good prognosis group ($P < 0.05$, Table 2 and Figure 2).

Comparison of PKC and ET-1 Levels in the Cerebrospinal Fluid (CSF) in Patients with Different Clinical Features

There was no significant difference in the levels of PKC and ET-1 in the cerebrospinal fluid (CSF) among patients of different ages and genders ($P > 0.05$), but these in patients with Hunt-Hess grade ≥ III were significantly higher than those in patients with Hunt-Hess grade I–II ($P < 0.05$, Table 3).

Multivariate Analysis of Prognostic Factors of ASH

The interference of related confounding factors such as treatment effect on the research results was excluded, and multivariate logistic regression analysis was performed. The results showed that age, aneurysm diameter ≥6 mm, cerebral vasospasm, Hunt-Hess classification ≥grade III, PKC, and ET-1 were all risk factors affecting the prognosis of ASH ($P < 0.05$, Table 4).

Table 1 Comparison of Clinical Data Between Two Groups of Patients ($\bar{x}\pm s$)

Indicators		Good prognosis group (n=102)	Poor prognosis group (n=46)	T/χ^2	P
Gender	Male	61 (59.80)	30 (65.22)	0.392	0.531
	Female	41 (40.20)	16 (34.78)		
Age (year)		56.28±8.74	62.19±10.37	3.589	0.001
BMI (kg/m^2)		24.85±2.06	24.96±1.73	0.315	0.753
Operation mode	Clipping technique	70 (68.63)	33 (71.74)	0.145	0.703
	Embolization	32 (31.37)	13 (28.26)		
Hypertension history	Yes	55 (53.92)	30 (65.22)	1.655	0.198
	No	47 (46.08)	16 (34.78)		
Diabetes history	Yes	42 (41.18)	25 (54.35)	2.220	0.136
	No	60 (58.82)	21 (45.65)		
Smoking history	Yes	31 (30.39)	17 (36.96)	0.623	0.430
	No	71 (69.61)	29 (63.04)		
Drinking history	Yes	33 (32.35)	19 (41.30)	1.115	0.291
	No	69 (67.65)	27 (58.70)		
Multiple aneurysms	Yes	22 (21.57)	7 (15.22)	0.812	0.368
	No	80 (78.43)	39 (84.78)		
Aneurysm location	Internal carotid artery system	85 (83.33)	35 (76.09)	1.085	0.298
	Vertebrobasilar artery system	17 (16.67)	11 (23.91)		
Number of aneurysms	1	92 (90.20)	31 (67.39)	11.744	0.001
	≥2	10 (9.80)	15 (32.61)		
Aneurysm diameter	<6 mm	47 (46.08)	7 (15.22)	17.613	< 0.001
	6~15 mm	53 (51.96)	33 (71.74)		
	>15 mm	2 (1.96)	6 (13.04)		
Cerebral vasospasm		21 (20.59)	18 (39.13)	5.616	0.018
Hunt-Hess grading ≥ Grade III		36 (35.29)	33 (71.74)	16.921	< 0.001

Table 2 Comparison of Cerebrospinal Fluid PKC and ET-1 Levels Between Two Groups of Patients ($\bar{x}\pm s$)

Groups	Cases	PKC (ng/L)	ET-1 (ng/mL)
Good prognosis group	102	68.95±7.15	1.43±0.21
Poor prognosis group	46	96.85±10.42	1.93±0.28
t		18.935	12.040
P		< 0.001	< 0.001

Analysis of the Predictive Value of Cerebrospinal Fluid PKC and ET-1 in Diagnosing ASH as Poor Prognosis

ROC curve analysis showed that the AUC of PKC and ET-1 for diagnosing poor prognosis of ASH was 0.803 and 0.720, respectively. The AUC of combined detection was 0.873 ($P < 0.05$, Table 5 and Figure 3).

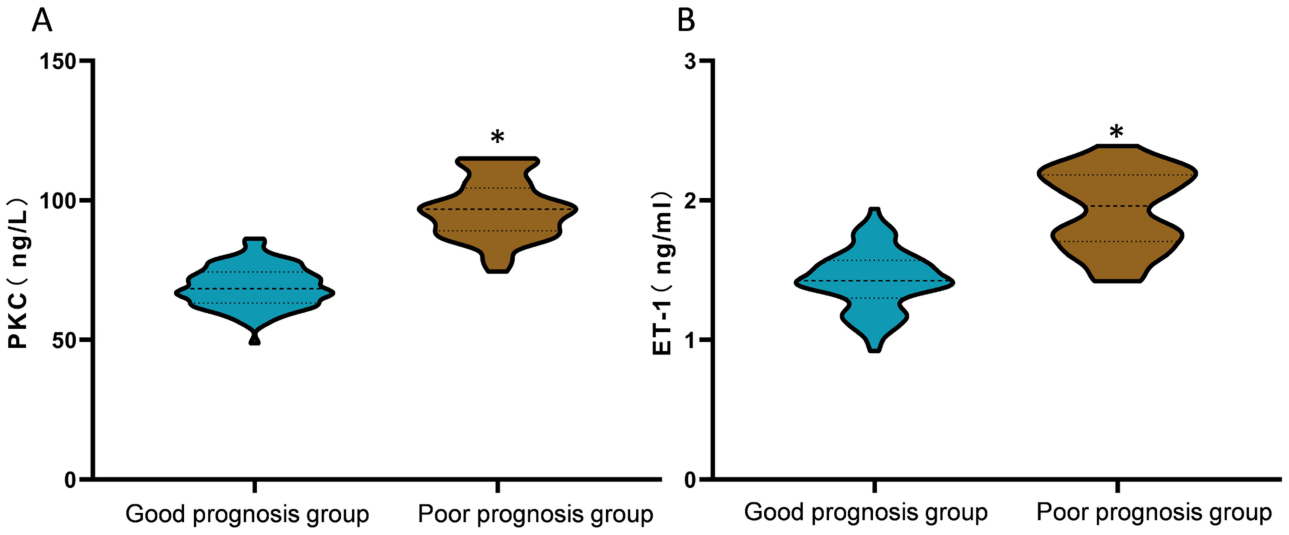

Figure 2 Comparison of cerebrospinal fluid PKC and ET-1 levels. (**A**) Comparison of PKC levels in cerebrospinal fluid; (**B**) Comparison of ET-1 levels in cerebrospinal fluid.
Note: *$P < 0.001$ compared with the group with good prognosis group.

Comparison of PKC and ET-1 Levels in Cerebrospinal Fluid of Patients with Cerebral Vasospasm

Patients with cerebrovascular spasm had much higher content of PKC and ET-1 than those without ($P < 0.05$, Table 6 and Figure 4).

Table 3 Comparison of PKC and ET-1 Levels in the Cerebrospinal Fluid (CSF) in Patients with Different Clinical Features

Clinical features		Cases	PKC (ng/L)	ET-1 (ng/mL)
Age (years)	<50	42	75.42±8.54	1.55±0.87
	≥50	106	76.21±9.62	1.59±0.92
t			0.464	0.242
P			0.643	0.809
Gender	Male	91	77.62±9.32	1.60±0.87
	Female	57	75.33±10.95	1.57±0.73
t			1.359	0.218
P			0.176	0.829
Hunt-Hess grade	I-II	79	80.26±6.25	1.50±0.88
	≥III	69	89.32±7.44	1.92±0.72
t			8.050	3.149
P			<0.001	0.002

Table 4 Multivariate Analysis of Prognostic Factors of ASH

Indicators	*β*	*SE*	*Wald* χ^2 value	*P* value	*OR* value	*95% CI*
Age	1.385	0.469	6.285	0.002	4.096	1.385–12.451
Number of aneurysms ≥ 2	0.631	0.383	2.715	0.087	1.880	0.887~3.982
Aneurysm diameter ≥ 6 mm	0.984	0.317	9.608	0.001	2.675	1.436~4.982
Cerebral vasospasm	1.785	0.631	4.985	0.018	3.561	1.240–10.794
Hunt-Hess grading ≥ III	1.485	0.236	11.954	<0.001	6.231	2.748–14.895
PKC	1.859	0.345	13.748	<0.001	5.120	1.869–12.464
ET-1	1.925	0.531	10.784	<0.001	4.015	1.063–8.856

Table 5 Analysis of the Predictive Value of Cerebrospinal Fluid PKC and ET-1 in Diagnosing ASH as Poor Prognosis

Indicators	*AUC*	*95% CI*	*P* value	Sensitivity	Specificity	Youden's index	Cut-off value
PKC	0.803	0.784–0.869	<0.001	65.20%	85.40%	0.506	84.69
ET-1	0.720	0.621–0.796	<0.001	70.40%	78.60%	0.490	1.66
PKC+ET-1	0.873	0.836–0.938	<0.001	78.70%	90.70%	0.694	/

Analysis of the Predictive Value of Cerebrospinal Fluid PKC and ET-1 in the Diagnosis of Cerebral Vasospasm in ASH

ROC curve analysis indicated that the AUC of PKC and ET-1 for diagnosing cerebral vasospasm in ASH was 0.891 and 0.816, respectively, which was 0.932 for combined detection ($P < 0.05$, Table 7 and Figure 5).

Discussion

ASH is a common acute cereebrovascular disease that seriously endangers the lives of patients. Previous statistics have shown that the mortality rate of ASH is as high as 25% −50%. Even with effective treatment, only 30% of patients can return to a normal state of life. Currently, microsurgical clipping of aneurysms and endovascular intervention therapy are widely chosen in clinical practice. However, subsequent neurological disorders such as emotional disorders and life

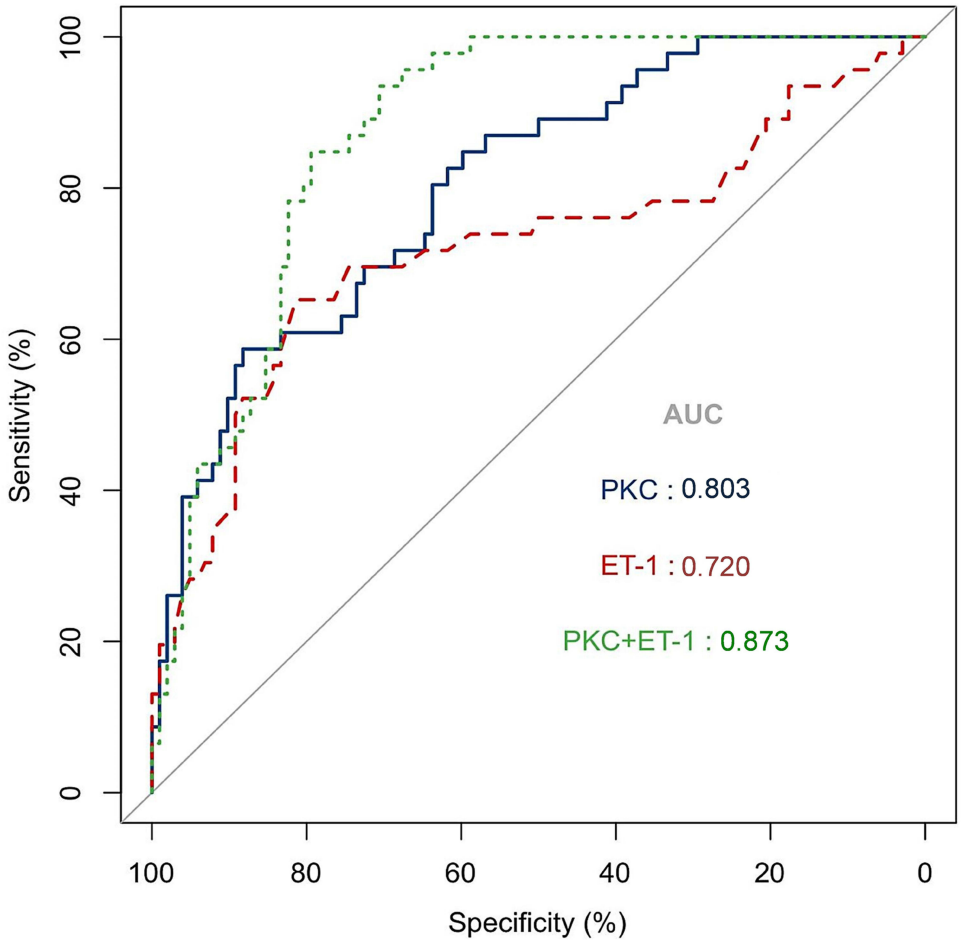

Figure 3 ROC of cerebrospinal fluid PKC and ET-1 in diagnosing poor prognosis of ASH.

Table 6 Comparison of PKC and ET-1 Levels in Cerebrospinal Fluid of Patients with Cerebral Vasospasm ($\bar{x}\pm s$)

Groups	Cases	PKC (ng/L)	ET-1 (ng/mL)
Cerebral vasospasm	39	97.25±11.23	2.01±0.51
Non cerebral vasospasm	109	70.52±6.25	1.52±0.32
t		18.235	6.934
P		< 0.001	< 0.001

execution dysfunction may lead to poor prognosis for patients.[11,12] Therefore, analyzing the prognostic factors and predicting the prognosis of ASH patients can help guide treatment plans and improve treatment effectiveness.

ET is a peptide composed of 21 amino acids, which is also a highly effective Vasoconstriction mainly synthesized in endothelial cells. ET plays a key role in the homeostasis of liquid electrolyte and cardiovascular and neuronal functions.[13,14] Among them, ET-1 is the strongest endogenous Vasoconstriction across multiple Organ system. ET-1 can regulate the MAPK signal pathway by activating vascular smooth muscle, and then regulate Vasodilation and contraction from multiple pathways such as Ion channel and activation of Myosin light-chain kinase. At present, ET-1 has been confirmed to play an important role in pulmonary hypertension and stroke.[15,16] In addition to its vasoconstrictive effects, ET-1 also has the functions of inducing angiogenesis, promoting cell differentiation and mitosis, and these biological activities may play a role in the pathological process after aneurysmal subarachnoid hemorrhage, exacerbating brain tissue damage.[17] ET-1 is not only involved in vasoconstriction, but is also associated with vascular dysfunction associated with a variety of cardiovascular diseases, such as atherosclerosis and hypertension, which may persist during long-term recovery after aneurysmal subarachnoid hemorrhage and affect patient outcomes.[18] PKC is a calcium sensitive protein kinase that can participate in endothelial damage under various pathological conditions. PKC can be activated by OxyHb during brain injury, playing a role in regulating Vasoconstriction and relaxation, breaking the balance of cerebrovascular resistance and cerebral blood flow, leading to cerebral vasospasm, thus aggravating the disease.[19,20] In addition, Kadir RRA[21] and other studies found that PKC participated in the integrity and function of the Blood–brain barrier formed by human brain microvascular endothelial cells. PKC can also participate in ischemia induced Actin Cytoskeleton remodeling, oxidative stress and apoptosis in human brain microvascular endothelial cells. Although the available data do not directly mention the effect of PKC on the prognosis of ASH, its potential role can be

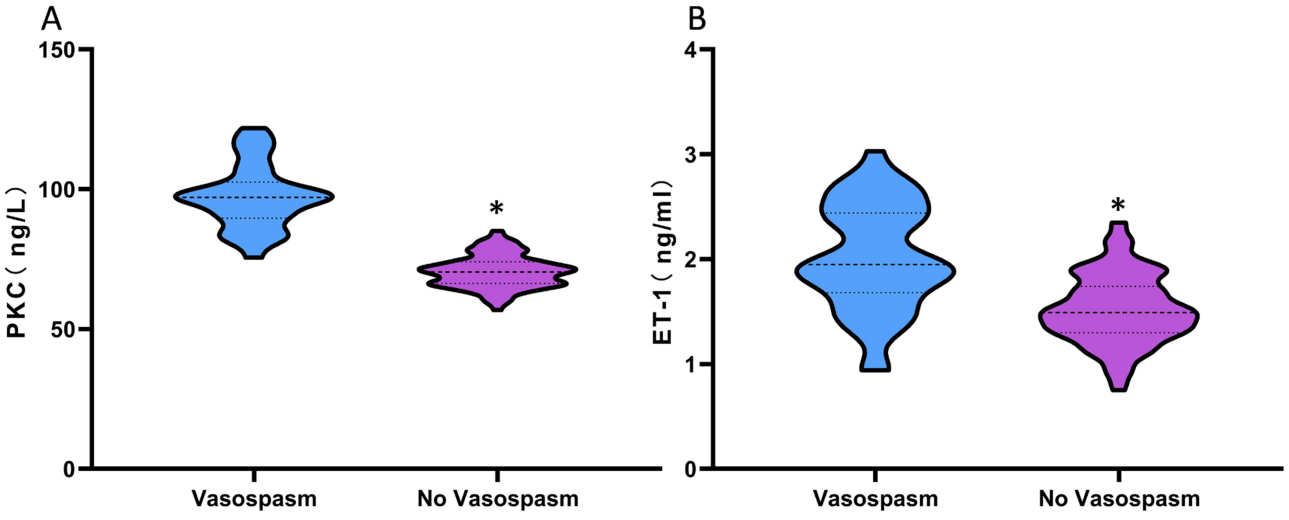

Figure 4 Comparison of PKC and ET-1 levels in cerebrospinal fluid of patients with cerebral vasospasm. (**A**) Comparison of PKC levels in cerebrospinal fluid; (**B**) Comparison of ET-1 levels in cerebrospinal fluid.
Note: *P < 0.001 compared with the cerebral vasospasm group.

Table 7 Analysis of the Predictive Value of Cerebrospinal Fluid PKC and ET-1 in the Diagnosis of Cerebral Vasospasm in ASH

Indicators	*AUC*	*95% CI*	*P* value	Sensitivity	Specificity	Youden's index	Cut-off value
PKC	0.891	0.725~0.924	< 0.001	90.50%	81.00%	0.715	80.25
ET-1	0.816	0.788~0.911	< 0.001	85.40%	72.40%	0.578	1.62
PKC+ET-1	0.932	0.818~0.975	< 0.001	92.40%	82.60%	0.750	/

speculated. For instance, PKC is involved in the regulation of autophagy, which plays an important role in maintaining cellular homeostasis and coping with injury, so the regulation of PKC may affect the repair ability of brain tissue, thereby indirectly affecting the prognosis of patients.[22] In addition, PKC is also associated with a variety of pathological processes, such as the occurrence of cerebral edema. Cerebral edema is one of the common complications in patients with ASH, which seriously affects the quality of life and prognosis of patients. Thus, PKC may affect the formation and development of cerebral edema through its signaling pathway, which in turn affects the prognosis of patients.[23] In this experiment, the levels of cerebrospinal fluid PKC and ET-1 in patients with poor prognosis were much higher than those with good prognosis. This result speculated that the levels of PKC and ET-1 in cerebrospinal fluid might reflect the changes in cerebrovascular function in ASH patients, and there might be a certain correlation with the prognosis of ASH patients. The multivariate logistic regression analysis conducted in this experiment also confirmed that PKC and ET-1 were risk factors that had different degrees of influence on the prognosis of ASH, and further confirmed that the changes

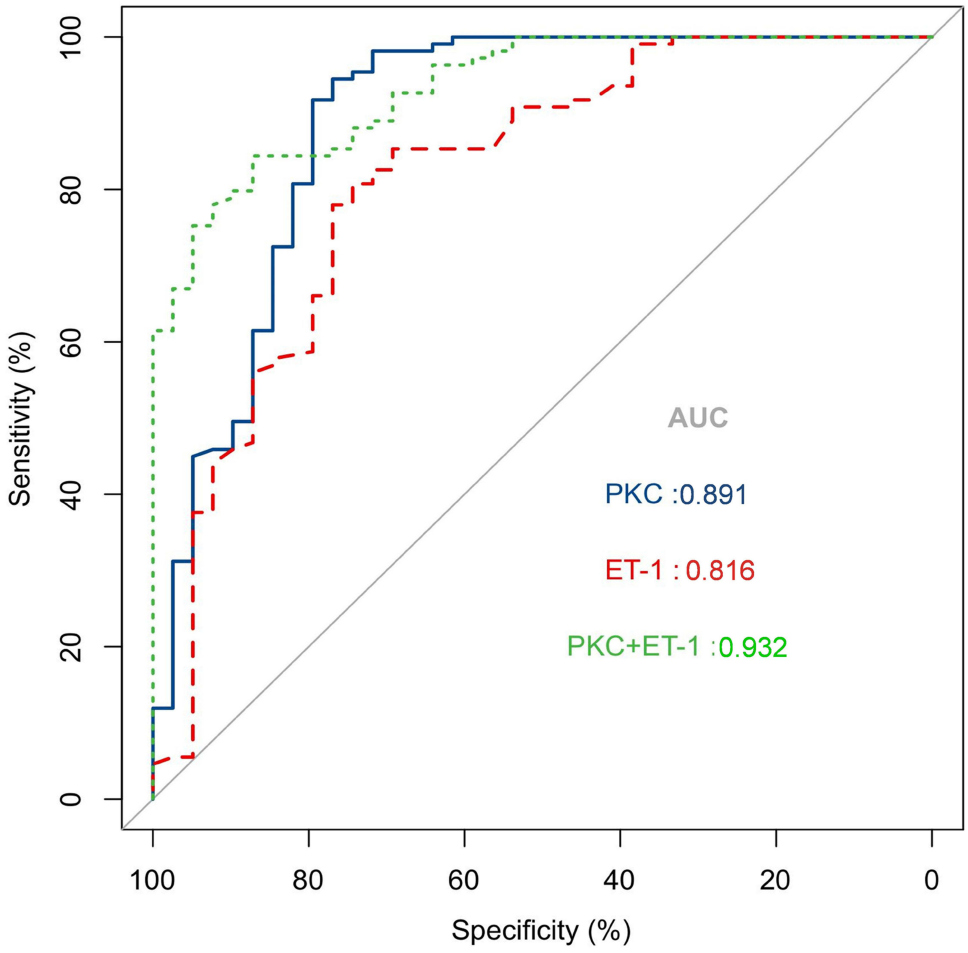

Figure 5 ROC curve of cerebrospinal fluid PKC and ET-1 in diagnosis of cerebral vasospasm in ASH.

in PKC and ET-1 levels might be related to the prognosis of patients with ASH. Regular detection of PKC and ET-1 levels might be helpful to evaluate the prognosis of patients. In addition, this experiment found that age, cerebral vasospasm, and Hunt-Hess grade ≥ III all had varying effects on the prognosis of ASH. The reason for this might be related to the generally poor physical condition of elderly patients, low tolerance to surgery, and high incidence of postoperative complications. Cerebral vasospasm is a continuous contraction of intracranial arteries. As a common complication of ASH, cerebral vasospasm can exacerbate the patient's condition and affect their prognosis. Hunt-Hess grading can reflect the awareness status, changes in condition, and risk of cerebral vasospasm in ASH patients, and is closely related to prognosis.

As a common and dangerous type of subarachnoid hemorrhage, ASH progresses rapidly and has a poor prognosis, and its incidence rate has increased year by year in recent years. Early prediction of the prognosis of ASH patients can help guide treatment plans and improve treatment effectiveness.[24,25] The study[26] has shown that the short-term prognosis of patients with ASH is closely related to early intervention and that patients treated within 24 hours of onset have a significantly better prognosis than those who receive delayed treatment. Therefore, focusing on short-term prognosis can help to detect and treat potential complications early and reduce mortality and disability. At present, research has confirmed that PKC and ET-1 are closely related to cerebral vasodilation and contraction, and there exists a certain relationship with the occurrence and development of ASH.[27] However, there is no research on PKC and ET-1 in predicting the prognosis of ASH. The ROC analysis in this experiment showed that the AUC of cerebrospinal fluid PKC and ET-1 in diagnosing poor prognosis in ASH was 0.803 and 0.720, respectively, the AUC of combined diagnosis in poor prognosis in ASH was 0.873, and the AUC of combined diagnosis in diagnosing cerebral vasospasm in ASH was 0.932. These above results indicated that PKC and ET-1 might have a certain value in predicting poor prognosis and occurrence of cerebral vasospasm in ASH patients, which were expected to be used as an indicator to evaluate the prognosis of patients and guide treatment plans.

In summary, there exist many factors that affect the prognosis of ASH patients, among which age, cerebral vasospasm, Hunt-Hess grade ≥ III, PKC, and ET-1 all have varying degrees of effects on ASH. Moreover, the combination of PKC and ET-1 in cerebrospinal fluid has certain value in predicting the poor prognosis of patients with ASH, and is expected to be used as a prognostic marker. In this study, PKC and ET-1 were not compared in patients with different clinical characteristics, and a multi-center, large-sample clinical trial could be carried out to analyze the relationship between PKC and ET-1 and the clinical characteristics of patients with SH. In addition, this study only observed the short-term prognosis of patients due to time reasons, and the long-term prognosis of patients could be evaluated by extending the follow-up time in the future. The relationship between PKC and ET-1 and the long-term prognosis of patients with SH could be analyzed, in order to provide a reference for the pathogenesis, clinical treatment and prognosis evaluation of SH.

Data Sharing Statement

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

Ethics Approval and Consent to Participate

This study was approved by The Ethics Committee of Panzhihua Central Hospital (pzhszxyyll-2019-27). Informed consent was obtained from participants for the participation in the study, and all methods were carried out in accordance with and complied with the Declaration of Helsinki.

Consent for Publication

Informed consent was obtained from all individual participants included in the study. The patients participating in the study all agree to publish the research results.

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Disclosure

The authors declare that they have no competing interests.

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