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THE PREDICTIVE VALUE OF SERUM SCUBE1, CLEC-2 AND UCP2 IN ACUTE ISCHEMIC STROKE AFTER INTRAVENOUS THROMBOLYSIS

PREDIKTIVNA VREDNOST SERUMSKIH SCUBE1, CLEC-2 I UCP2 PRI AKUTNOM ISHEMIJSKOM MOŽDANOM UDARU NAKON INTRAVENSKE TROMBOLIZE

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Summary

Background: To analyse the predictive value of serum signal peptide-CUB-epidermal growth factor domain-containing protein 1 (SCUBE1), C-type lectin-like receptor-2 (CLEC-2), and uncoupling protein 2 (UCP2) for poor outcome following intravenous thrombolysis (IVT) in patients who have experienced an acute ischemic stroke (AIS).
Methods: A total of 116 AIS patients who received IVT treatment in this hospital from June 2023 to October 2024 were selected as the observation group, and the control group consisted of an additional 116 healthy people who were examined physically in this institution over the same time period. The patients were divided into good- and poor-prognosis groups according to the modified Rankin Scale (mRS) score. After IVT, the factors predicting poor outcomes in AIS patients were examined using multivariate logistic regression. The prognostic significance of serum SCUBE1, CLEC-2, and UCP2 for poor prognosis in AIS patients following IVT was assessed using receiver operating characteristic (ROC) curves.
Results: While the observation group's serum UCP2 level was lower than the control group's, the observation group's levels of SCUBE1 and CLEC-2 were higher. $P<0.05$ indicated that the differences were statistically significant. There

Kratak sadržaj

Uvod: Analiza prediktivne vrednosti serumskog proteina koji sadrži signalni peptid, CUB i domen epidermalnog faktora rasta (SCUBE1), lektinu sličnog receptora 2 C-tipa (CLEC-2) i nevezanog proteina 2 (UCP2) za loš ishod nakon intravenske trombolize (IVT) kod pacijenata koji su doživeli akutni ishemijski moždani udar (AIS).
Metode: U posmatranu grupu je izabrano ukupno 116 pacijenata sa AIS koji su primili IVT tretman u ovoj bolnici od juna 2023. do oktobra 2024. godine, dok je kontrolnu grupu činilo dodatnih 116 zdravih osoba koje su u istom periodu obavile sistematski lekarski pregled u istoj ustanovi. Pacijenti su podeljeni u grupu sa dobrim i grupu sa lošim ishodom na osnovu rezultata modifikovane Rankinove skale (mRS). Nakon IVT tretmana, faktori koji predviđaju loš ishod kod AIS pacijenata su analizirani višestrukom logističkom regresijom. Prognostički značaj serumskih SCUBE1, CLEC-2 i UCP2 za loš ishod kod AIS pacijenata nakon IVT procenjen je pomoću ROC krive.
Rezultati: Nivo serumskog UCP2 u posmatranoj grupi bio je niži u odnosu na kontrolnu grupu, dok su nivoi SCUBE1 i CLEC-2 bili viši ($P<0,05$), što ukazuje na statistički značajne razlike. U grupi sa dobrim ishodom bilo je 75 pacijenata, a u grupi sa lošim ishodom 41 pacijent. Nivoi

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were 75 patients in the good-prognosis group and 41 in the poor-prognosis group. While serum UCP2 levels were lower than those in the good prognosis group ($P<0.05$), the percentage of patients with infarction regions >4 cm^3 and the levels of serum SCUBE1 and CLEC-2 were higher in the bad prognosis group than in the good prognosis group. According to multivariate logistic regression analysis, increased blood levels of SCUBE1 and CLEC-2 were associated with a poor prognosis for AIS patients following IVT ($P<0.05$), and higher blood UCP2 levels were protective factors against a poor outcome in AIS patients following IVT ($P<0.05$). The areas under the curve (AUCs) for serum SCUBE1, CLEC-2, and UCP2 alone in predicting a poor prognosis were 0.752, 0.694, and 0.776, respectively, by ROC analysis after IVT in AIS patients. SCUBE1, CLEC-2, and UCP2 had lower AUCs than the combined three-indicator model, which had an AUC of 0.861. When predicted separately, the AUCs showed the following Z-scores: Z (3-item combination – SCUBE1)=2.358, Z (3-item combination – CLEC-2)=2.714, Z (3-item combination – UCP2)=2.591, with corresponding P-values of 0.018, 0.007, and 0.010, respectively.

Conclusions: The levels of serum SCUBE1 and CLEC-2 in AIS patients with poor prognosis after IVT increase, whereas the level of UCP2 decreases. The combined detection of these three indicators has high predictive value for the poor prognosis of AIS patients after IVT.

Keywords: the signal peptide - CUB-epidermal growth factor domain contains protein 1, C-type lectin-like receptor-2, uncoupling protein 2, acute ischemic stroke, intravenous thrombolysis, predict prognosis

serumskog UCP2 u grupi sa lošom prognozom bili su niži nego u grupi sa dobrom prognozom ($P<0,05$), dok su procenat pacijenata sa infarktnim regionima većim od 4 cm^3, kao i nivoi SCUBE1 i CLEC-2, bili viši. Višestruka logistička regresiona analiza pokazala je da su povišeni nivoi SCUBE1 i CLEC-2 povezani sa lošijom prognozom AIS pacijenata nakon IVT ($P<0,05$), dok su viši nivoi UCP2 bili zaštitni faktor od lošeg ishoda ($P<0,05$). Površine ispod krive (AUC) serumskih SCUBE1, CLEC-2 i UCP2 za predviđanje loše prognoze nakon IVT iznosile su 0,752, 0,694 i 0,776. Kombinacija sva tri markera imala je veći AUC od svakog pojedinačno (AUC=0,861), sa statistički značajnim razlikama (Z(3-kombinacija – SCUBE1)=2,358, Z(3-kombinacija – CLEC-2)=2,714, Z(3-kombinacija – UCP2)=2,591; P=0,018, 0,007, 0,010).

Zaključak: Kod AIS pacijenata sa lošom prognozom nakon IVT, nivoi serumskih SCUBE1 i CLEC-2 su povećani, dok je nivo UCP2 smanjen. Kombinovano određivanje ova tri pokazatelja ima visoku prediktivnu vrednost za procenu lošeg ishoda AIS pacijenata nakon IVT.

Ključne reči: SCUBE1, lektinu sličan receptor 2 C-tipa (CLEC-2), nevezani protein 2 (UCP2), akutni ishemijski moždani udar, intravenska tromboliza, prognoza

Introduction

Acute ischemic stroke (AIS) is a type of cerebrovascular disease in which the brain's blood supply is inadequate or cerebral blood vessels are damaged for a variety of reasons, leading to an imbalance of blood oxygen in brain cells and subsequently causing brain tissue necrosis. If not treated promptly after the onset of this disease, it can cause severe hypoxia in brain cells and easily result in patient death (1–3). The group affected by this disease is mostly middle-aged and older people. Clinically, this disease is generally believed to be caused by cerebral vascular embolism, the presence of many thrombi in the blood vessels, etc (4). This approach involves intravenous administration of thrombolytic drugs to promote vascular patency, restore regular blood oxygen supply to the brain, and, as much as possible, save brain cells that have died due to vascular blockage (5). However, due to differences in age, severity of stroke and other past medical history, some patients may have a poor prognosis (6). Therefore, predicting patients' prognosis after IVT can enable targeted, effective treatment. It is also widely present in thrombus cells and participates in thrombus formation (7). Platelet-activating C-type lectin-like receptor-2 (CLEC-2) is a member of the C-type lectin superfamily of cell surface receptors that participates in the formation and development of various thrombotic diseases (8). Uncoupling protein 2 (UCP2) is an endogenous antioxidant protein that is often used to reflect cellular dysfunction.

Acute ischemic stroke (AIS) has always been a significant public health challenge that endangers human health due to its high rate of occurrence, impairment, and death (9). In the hyperacute phase of AIS, intravenous recombinant tissue plasminogen activator (rt-PA) thrombolysis is currently recognised as an effective reperfusion therapy that can significantly improve neurological functional outcomes in some patients. However, in clinical practice, there are significant individual differences in patients' responses to thrombolytic therapy. Even if some patients successfully achieve vascular recanalisation, they may still experience adverse prognoses, such as no improvement in symptoms, early deterioration of neurological function, or even secondary hemorrhagic transformation (10–12). Accurate prediction of the clinical outcomes of AIS patients receiving thrombolytic therapy is crucial for the early identification of high-risk groups, optimisation of treatment plans, rational allocation of medical resources, and improvement of the long-term quality of life of patients. At present, the commonly used predictive tools rely mainly on the severity of baseline neurological deficits (such as the National Institutes of Health Stroke Scale (NIHSS) score) and imaging examinations (such as infarction core and ischemic penumbra assessment). However,

there are still limitations in terms of timeliness, convenience or specificity. There is an urgent need to find more sensitive, reliable and easily accessible biological markers. In recent years, numerous studies have focused on novel serum markers involved in key pathophysiological links of AIS, such as platelet activation, endothelial injury, the inflammatory response, oxidative stress and energy metabolism disorders (13). Among them, the signal peptide-CUB-EGF domain protein 1 (SCUBE1) mainly reflects platelet activation and endothelial function. Platelet activation, thrombus stability, and inflammatory modulation are all significantly impacted (14–16).

Uncoupling protein 2 (UCP2) mainly regulates mitochondrial function and energy balance, and reduces oxidative stress damage. All three have been preliminarily confirmed to have potential biological significance in the pathogenesis and progression of AIS (17). After intravenous thrombolysis, it is unknown how useful the three together are as predictive markers for AIS patients. To explore the dynamic changes in serum SCUBE1, CLEC-2 and UCP2 levels at different time points after intravenous thrombolysis in AIS patients and to systematically evaluate their value alone and in combination in predicting the recovery of neurological function and the risk of hemorrhagic transformation after thrombolysis (18–20). This study is expected to provide a new and valuable combination of serological biomarkers to establish a more accurate, individualised prognosis prediction model after thrombolysis in AIS patients, thereby guiding clinical decision-making and improving the precise management of AIS thrombolysis therapy.

At present, relatively few studies have examined the prognostic value of SCUBE1, CLEC-2, and UCP2 in AIS patients after IVT. Therefore, this study analysed the predictive value of SCUBE1, CLEC-2, and UCP2, providing a reliable basis for the treatment of AIS patients.

Materials and Methods

General information

A total of 116 AIS patients who underwent IVT treatment at our facility between June 2023 and October 2024 were included in the study.

Inclusion criteria: (1) Met the diagnostic criteria for AIS; (2) Complete clinical data; (3) Aged >50 years; (4) Met the treatment requirements for IVT; (5) First onset. Exclusion criteria: (1) Bridge thrombectomy after IVT; (2) Cerebral haemorrhage; (3) Other cardiovascular and cerebrovascular diseases; (4) An immune system disorder; (5) Mental illness and inability to communicate normally; (6) The presence of malignant tumours; (7) Follow-up visits.

There were 58 males and 58 females in the observation group. The average age was 60.39±7.96 years. The body mass index (BMI) was 23.29±3.79 kg/m^2. In the control group, there were 52 males and 64 females. The average age was 61.38±6.74 years. The BMI was 23.14±4.13 kg/m^2.

All patients or their families provided informed consent, and the study was reviewed and approved by our hospital's Medical Ethics Committee [No. XXXX].

Detection of serum SCUBE1, CLEC-2 and UCP2 levels

On the morning of the second day after admission for IVT treatment and on the day of physical examination for healthy individuals, 10 mL of fasting venous blood was collected. The serum was separated from the blood by centrifuging it for 10 minutes at 3,000 rpm. The levels of SCUBE1 (catalogue no. PA5-20990), CLEC-2 (catalogue no. PA5-97313), and UCP2 (catalogue no. MA5-31945) were found. Thermo Fisher Scientific, USA, supplied all ELISA kits, and the protocols were strictly followed in accordance with the kit instructions. First, the required strips were removed, and standard wells and specimen wells were set up. The standard wells were filled with 100 microliters of various standard material concentrations; the sample wells were filled with 100 microliters of the sample to be analysed, and the detection antibody was filled with 100 microliters. After sealing the reaction wells with sealing film, they were incubated for 60 minutes at 37 °C (in a water bath or constant-temperature box). Then, 100 μL of the detection antibody mixture was added, and the mixture was incubated for 60 minutes. 100 μL of the detection enzyme-linked avidin-horseradish peroxidase working mixture was added; the mixture was incubated for 30 minutes, thoroughly washed, and then the substrate mixture was added for colour development.

Laboratory testing equipment and reagents

Serum samples were collected at predetermined time points after enrollment. Centrifugation was used to separate the serum for 10 minutes at 3000 × g and 4°C via a centrifuge with a temperature control function (Model Centrifuge 5424 R from Eppendorf, Germany). After being aliquoted, the samples were immediately stored in a -80 °C ultralow-temperature refrigerator (Thermo Fisher Scientific, USA, model Thermo Scientific™ Forma™ 900 Series) for testing, and repeated freezing and thawing were avoided. All target biomarkers: The quantitative determination of the serum concentrations of the signal peptide CUB-EGF domain protein 1 (SCUBE1), C-type lectin-like receptor 2 (CLEC-2), and uncoupling protein 2 (UCP2) was conducted.

The detection of the serum SCUBE1 level was performed with the human SCUBE1 (Signal peptide) from Cusabio Company in the United States. The detection of serum CLEC-2 levels was carried out via the Human CLEC1B/CLEC-2 DuoSet ELISA Development Kit (catalogue number DY1394) of R&D Systems in the United States. The detection of serum UCP2 levels was carried out via the Human Uncoupling Protein 2 (UCP2) ELISA Kit (Product No. ml058399) from Shanghai Enzyme-Linked Biotechnology Co., Ltd.

Prognosis assessment

Prognosis assessment was conducted 2 months after discharge. Patients in the excellent-prognosis group had mRS scores less than 3, whereas those in the poor-prognosis group had mRS scores greater than 3.

Statistical analysis

SPSS 25.0 was used to analyse the data. The χ^2 test was used to compare groups, and count data are presented as percentages or counts. The independent-samples t-test was employed to compare the two groups, and $\bar{x}\pm s$ denotes the measurement data with a normal distribution. Using multivariate logistic regression, the factors influencing the poor prognosis of AIS patients after IVT were investigated. Serum SCUBE1, CLEC-2, and UCP2 were evaluated for their prognostic significance in AIS patients following IVT using receiver operating characteristic (ROC) curves.

Results

Comparison of serum SCUBE1, CLEC-2 and UCP2 levels between the observation group and the control group

Serum SCUBE1 and CLEC-2 levels were higher in the observation group than in the control group. However, serum UCP2 levels were considerably lower in the observation group than in the control group ($P<0.05$) (*Table I*).

Patients with acute ischemic stroke (AIS) undergoing intravenous thrombolytic therapy and the healthy control group had significantly different levels of three serum biomarkers. The serum SCUBE1 level in patients in the observation group before thrombolysis (baseline) was substantially greater than that in the healthy control group. Similarly, the baseline serum CEC-2 level also significantly increased in the observation group, suggesting that during the acute phase of AIS, it is actively involved in thrombosis and the inflammatory response. The baseline serum UCP2 level in the observation group was significantly lower than in the healthy control group, suggesting that patients with acute AIS have disturbances in energy metabolism and mitochondrial dysfunction.

Comparison of clinical information between the groups with bad and favourable prognoses

There were 41 patients in the poor-prognosis group and 75 patients in the good-prognosis group. No statistically significant differences were observed between the groups in terms of sex, age, BMI, stroke distribution, or the prevalence of comorbidities, including hypertension, diabetes, hyperlipidemia, smoking, or drinking ($P>0.05$). The proportion of patients with infarction areas >4 cm was also comparable between the groups. Patients in the poor-prognosis group exhibited lower serum UCP2 levels, whereas serum SCUBE1 and CLEC-2 levels were higher compared with those in the good-prognosis group. These differences were statistically significant ($P<0.05$) (*Table II*).

Analysis using multivariate logistic regression of AIS patients' poor prognosis following IVT

Taking the prognosis of AIS patients after IVT (poor prognosis =1, good prognosis =0) as the dependent variable and the infarct area (>4 cm × 1, ≤4 cm × 0), SCUBE1 (original value input), CLEC-2 (original value input), and UCP2 (original value input) as independent variables, multivariate logistic regression analysis was conducted. Elevated levels of serum UCP2 were protective factors against poor prognosis following IVT in AIS patients ($P<0.05$), while levels of serum SCUBE1 and CLEC-2 were risk factors for poor prognosis following IVT in AIS patients ($P<0.05$) (*Table III*).

Table I Comparison of serum SCUBE1, CLEC-2, and UCP2 levels.

Group	n	SCUBE1 (ng/mL)	CLEC-2 (ng/L)	UCP2 (ng/mL)
Observation Group	116	58.43±7.58	496.09±63.43	226.16±33.31
Control group	116	28.32±4.31	314.68±42.57	398.74±42.30
t		37.191	25.577	-34.523
P		<0.001	<0.001	<0.001

Table II Comparison of clinical data between the poor prognosis group and the good prognosis group [n(%) or $\bar{x}\pm s$].

Group	n	Gender		CLEC-2 (ng/L)	UCP2 (ng/mL)	SCUBE1 (ng/mL)
		male	female			
Poor prognosis	41	25 (60.98)	16 (39.02)	524.76±63.04	206.50±28.42	62.63±8.05
Good prognosis	75	33 (44.00)	42 (56.00)	480.42±57.70	236.91±30.62	56.13±6.20
χ^2/t		3.056		3.829	-5.242	4.846
P		0.08		≤0.001	<0.001	<0.001

Group	n	Smoking		Age (years)	BMI (kg/m^2)	Drinking alcohol	
		yes	no			yes	no
Poor prognosis	41	22 (53.66)	19 (46.34)	61.37±8.64	23.52±3.42	16 (39.02)	25 (60.98)
Good prognosis	75	31 (41.33)	44 (58.67)	59.86±7.13	23.17±3.15	32 (42.67)	43 (57.33)
χ^2/t		1.6		1.011	0.555	0.145	
P		0.2		0.314	0.580	0.703	

Group	n	Infarct area		Distribution of stroke		Combined with hypertension	Combined with diabetes	Combined with hyperlipidemia
		≤4 cm^3	>4 cm^3	Precirculation	Postcirculation			
Poor prognosis	41	13 (31.71)	28 (68.29)	27 (65.85)	14 (34.15)	18 (43.90)	20 (48.78)	19 (46.34)
Good prognosis	75	40 (53.33)	35 (46.67)	37 (49.33)	38 (50.67)	36 (48.00)	38 (50.67)	43 (57.33)
χ^2/t		4.996		2.925		0.179	0.038	1.287
P		0.025		0.087		0.672	0.846	0.257

Table III Multivariate logistic regression analysis of poor prognosis in AIS patients after IVT.

Factor	β	SE	Wald χ^2	P	OR	OR 95% CI
Infarct area	0.021	0.213	0.010	0.922	1.021	0.673 1.550
SCUBE1	0.364	0.153	5.658	0.017	1.439	1.066 1.942
CLEC-2	0.744	0.298	6.231	0.013	2.104	1.173 3.773
UCP2	-0.36	0.113	10.123	0.001	0.698	0.559 0.871

Table IV The predictive value of serum SCUBE1, CLEC-2 and UCP2 for poor prognosis in AIS patients after IVT.

Indicator	AUC	Optimal cutoff value	AUC 95% CI	Sensitivity (%)	Specificity (%)	Youden Index
SCUBE1	0.752	58.71 ng/mL	0.663 0.827	75.61	72.00	0.476
CLEC-2	0.694	483.23 ng/L	0.602 0.776	78.05	62.67	0.407
UCP2	0.776	208.04 ng/mL	0.689 0.848	63.41	88.00	0.514
Three joint projects	0.861	-	0.785 0.918	73.17	90.67	0.638

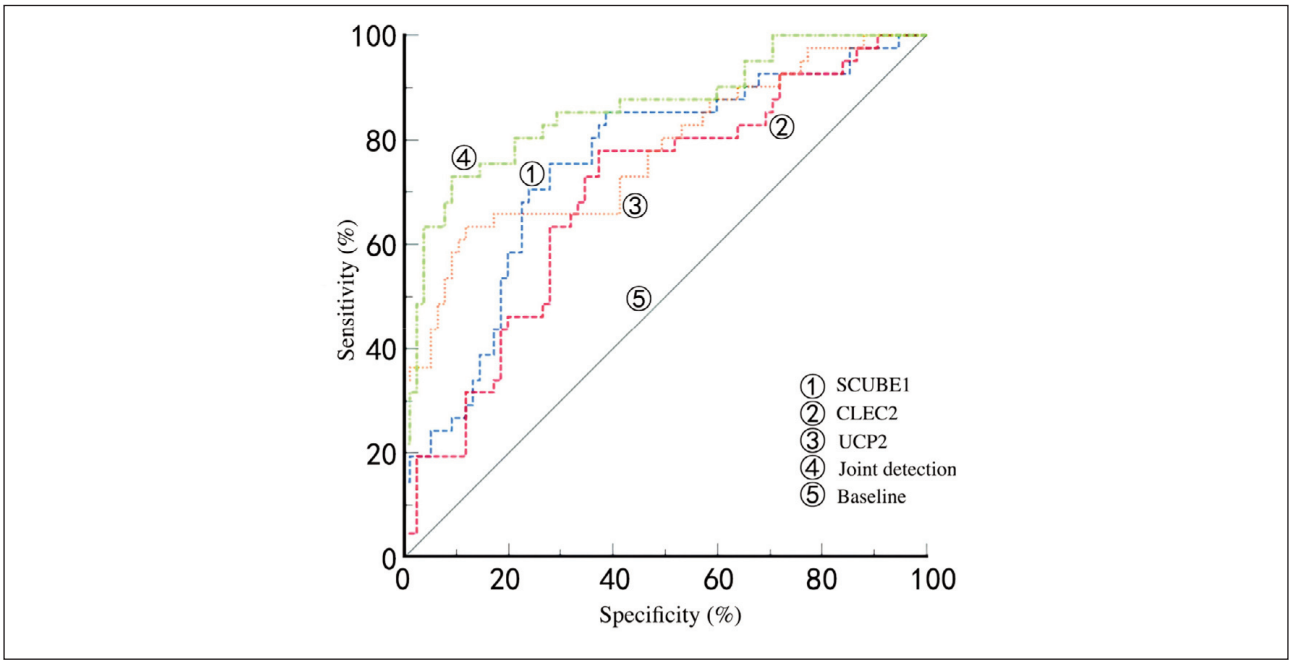

Figure 1 ROC curves of serum SCUBE1, CLEC-2 and UCP2 for poor prognosis in AIS patients after IVT.

Predictive value of serum SCUBE1, CLEC-2 and UCP2 for the poor prognosis of AIS patients after IVT

ROC curve analysis was performed, with the poor-prognosis group as the positive control and the good-prognosis group as the negative control. Serum SCUBE1, CLEC-2, and UCP2 alone had area under the curve (AUC) values of 0.752, 0.694, and 0.776, indicating a poor prognosis following IVT in AIS patients. When the three indicators were combined, the projected AUC was 0.861, and the AUC predicted by the combination was greater than those of SCUBE1, CLEC-2, and UCP2. The AUC predicted separately (Z3 combined -SCUBE1=2.358, Z3 combined -CLEC-2=2.714, Z3 combined -UCP2=2.591, P=0.018, 0.007, 0.010) (*Table IV* and *Figure 1*).

Discussion

With increasing life pressure, irregular schedules and changes in dietary structure, the incidence and mortality rates of AIS have been growing annually. AIS is a disease characterised by necrosis or damage to brain cells due to cerebral ischemia (21–23). Clinically, it often manifests as sudden numbness and weakness in the limbs, facial loss of control, language expression disorders, and inability to think, which significantly affects the everyday life of patients. At present, IVT treatment is often chosen in clinical practice (24). This method can dissolve thrombi in cerebral blood vessels through drugs and restore the normal blood oxygen supply to non-dead cells, thereby achieving the therapeutic goal. However, some patients have a poor prognosis, and currently there are no drugs that can significantly improve it (25–27). Therefore, predicting the prognosis of AIS patients after IVT is essential for the treatment of AIS patients.

SCUBE1 is mainly expressed in the vascular endothelium and is a biomarker of activated adherent platelets (28–30). Some studies (31–33) have noted that SCUBE1 is also produced and stored in thrombus cells, released on the cell surface, activated and subjected to protein hydrolysis to form thrombi, which may be one of the main determinants of thrombosis. Research indicates that SCUBE1 plays a significant role in the crucial stages of AIS development, platelet activation and inflammation, and can be used for the early diagnosis of AIS, predicting poor prognosis and lesion volume in AIS patients. Serum SCUBE1 level in the observation group was greater than that in the control group ($P<0.05$), suggesting that SCUBE1 is associated with the occurrence and development of AIS to a certain extent (34). AIS patients' poor prognosis was caused by an increase in platelet content, which in turn raised serum SCUBE1 levels.

CLEC-2 is a type C lectin receptor expressed on platelets that can bind to endogenous ligands and thereby participate in platelet activation. One study reported that elevated serum CEC-2 levels can promote platelet activation and are significantly associated with the progression of AIS and poor prognosis. The higher level of CLEC-2 can lead to adverse reactions or other complications in AIS patients, thereby increasing the mortality rate, and is an important factor affecting the poor prognosis of AIS patients. The results of this study revealed that the serum CLEC-2

level in the observation group was higher than that in the control group (P<0.05), suggesting that elevated CLEC-2 expression promotes platelet activation, causes thrombosis, and facilitates the occurrence and progression of AIS (35). The serum CLEC-2 level in the poor-prognosis group was higher than that in the good-prognosis group (P<0.05), suggesting a link between elevated CLEC-2 levels in AIS patients after IVT treatment and poor patient prognosis.

UCP2 is an anion transporter that reduces reactive oxygen species levels, which can regulate oxidative stress responses and thereby reduce cell damage. Some studies have reported that UCP2 is located on human chromosome 11 and is widely present in mammalian tissues. It can prevent damage to lipid membranes, proteins and DNA (36–38). Moreover, high UCP2 expression can reduce the risk of atherosclerosis and cerebrovascular injury. Related studies have indicated that elevated serum UCP2 levels can promote mitochondrial fusion and fission in the striatum of stroke-prone spontaneous hypertensive rats fed a high-sodium diet, reducing oxidative damage to cells and inflammatory responses in blood vessels (39). The serum UCP2 level in the observation group was lower than that in the control group (P<0.05), suggesting that reduced UCP2 expression may be associated with damage to cerebrovascular cells during the development of AIS (40, 41).

In AIS patients, serum SCUBE1 and CLEC-2 were risk factors for a poor outcome following IVT (P<0.05). However, after IVT, increased blood UCP2 levels were a protective factor against a poor outcome in AIS patients (P<0.05). SCUBE1, CLEC-2 and UCP2 are influencing factors for the poor prognosis of AIS patients after IVT. The AUC of the combined prediction of serum SCUBE1, CLEC-2, and UCP2 for poor prognosis after IVT in AIS patients was 0.861, which was greater than the AUC predicted separately by SCUBE1, CLEC-2, and UCP2 (Z3 combined -SCUBE1=2.358, Z3 combined -CLEC-2=2.714, Z3 combined) -UCP2=2.591, P=0.018, 0.007, 0.010), indicating that the prognosis of AIS patients following IVT can be predicted using SCUBE1, CLEC-2, and UCP2.

Conclusion

The combination of these three indicators has high predictive value for the poor prognosis of AIS patients after IVT. However, this study has several limitations. Due to funding and human resources constraints, dynamic monitoring of serum SCUBE1, CEC-2, and UCP2 levels was not conducted at multiple postoperative time points for patients. Moreover, the samples selected in this study were relatively simple. The sample size should subsequently be increased, and multiple time points of serum level monitoring should be performed to confirm the conclusions of this study further.

Authors' contribution

The first authors of this study are Chunying Sun, Zongmei Li, and Hongling Qin.

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Conflict of interest statement

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

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