

Correlation of Serum UCH-L1 and Del-1 Levels with Cerebral Infarction Size and Prognosis and Their Diagnostic Value in Patients with Acute Cerebral Infarction

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Abstract

Objective: To explore the correlation of serum ubiquitin C-terminal hydrolase L1 (UCH-L1) and developmental endothelial locus-1 (Del-1) levels with cerebral infarction size and prognosis and their diagnostic value in patients with acute cerebral infarction. **Methods:** 60 patients with acute cerebral infarction who received medical treatment in our hospital from January 2022 to March 2024 were selected as the diseased group, and the other 60 healthy people who underwent physical examination during the same period were selected as the healthy group. The diseased group was divided into small and medium area group (n = 46) and large area group (n = 14) according to the size of the cerebral infarction, and into good prognosis group (n = 38) and poor prognosis group (n = 22) in line with the modified Rankin Scale (mRS) score. Serum UCH-L1 and Del-1 levels, cerebral infarction size and mRS scores were compared among all groups. Spearman rank correlation analysis was used for correlation analysis, and area under receiver Operating characteristic (ROC) curve (AUC) was applied to analyze the diagnostic value of each parameter. **Results:** The serum UCH-L1 level was higher and the Del-1 level was lower in the diseased group than in the healthy group ($p < 0.05$). The cerebral infarction size and serum UCH-L1 level were lower while the Del-1 level was higher in the small and medium area group than those in the large area group ($p < 0.05$). mRS scores and serum UCH-L1 level were lower and Del-1 level was higher in the good prognosis group compared to poor prognosis group ($p < 0.05$). Serum UCH-L1 level was positively correlated while Del-1 level was negatively correlated with cerebral infarction size and mRS Score ($p < 0.05$). The AUC values of serum UCH-L1 and Del-1 alone and combined in predicting large area cerebral infarction were 0.782, 0.781 and 0.797, respectively, and the AUC values of serum UCH-L1 and Del-1 alone and combined in predicting poor prognosis were 0.739, 0.765 and 0.794, respectively, which were all greater than 0.7 ($p < 0.05$). **Conclusion:** Serum UCH-L1 level is positively, while Del-1 level is negatively correlated with cerebral infarction size and mRS Score in patients with acute cerebral infarction. The combined serum UCH-L1 and Del-1 has high diagnostic value and can be used as an indicator for clinical evaluation of acute cerebral infarction.



1 Introduction

Acute cerebral infarction is a common cerebrovascular disease in neurology, often arising from local cerebral blood supply disorders-induced ischemic necrosis or softening of brain tissue, with the elderly population as the main sufferer [1,2]. Acute cerebral infarction is characterized by a sudden onset, rapid disease progression, and high disability rate, with primary symptoms such as dizziness and hemiplegia, and it can lead to death in severe cases [3]. Therefore, finding indicators that can timely diagnose and assess the condition is of great significance for improving the clinical efficacy in patients with acute cerebral infarction and their prognosis.

In recent years, serum biomarkers have been increasingly used to assess the severity of brain damage and prognosis in patients with cerebral infarction [4,5]. Serum ubiquitin C-terminal hydrolase L1 (UCH-L1) is a multifunctional small molecule protein that is highly expressed in neurons of the brain and spinal cord, and its levels are related to the onset and progression of brain injury and neurodegenerative diseases [6]. UCH-L1 was confirmed significantly elevated in cerebrospinal fluid following controlled cortical impact traumatic brain injury and middle cerebral artery occlusion in rats, it suggest that UCH-L1 is a candidate brain injury biomarker detectable [7]. It has been reported that that in patients with acute cerebral infarction, the expression levels of serum UCH-L1 are significantly elevated, and there is a certain correlation with the severity of the cerebral infarction [8]. The expression level of serum UCH-L1 is linked to the infarct area, degree of neurological deficit, and prognosis in patients with acute cerebral infarction, and can be used as a clinical assessment indicator [9,10]. Moreover, serum developmental endothelial locus-1 (Del-1) can promote angiogenesis in various ischemic diseases, regulate the recruitment of inflammatory cells, and

limit neuroinflammation and demyelinating lesions, but few clinical studies have been performed on the assessment value of Del-1 in acute cerebral infarction [11-13].

Based on this, this study compared the levels of serum UCH-L1 and Del-1 in patients with acute cerebral infarction and healthy populations, as well as the differences in infarct area and prognostic indicators, to explore the application value of the two serum markers alone and in combination for the diagnosis of acute cerebral infarction, providing a reference for the clinical assessment of acute cerebral infarction.

2 Materials and methods

2.1 General information

60 patients with acute cerebral infarction who received medical treatment in our hospital from January 2022 to March 2024 were selected as the diseased group, and the other 60 healthy people who underwent physical examination during the same period were selected as the healthy group. The diseased group was divided into small and medium area group (n = 46) and large area group (n = 14) according to the size of the cerebral infarction, and into good prognosis group (n = 38) and poor prognosis group (n = 22) in line with the modified Rankin Scale (mRS) score. Area of cerebral infarction: if the maximum diameter of infarction ≤ 5 cm, it is classified as a small and medium area infarction; If the maximum diameter of the infarction > 5 cm, it is classified as a large area infarction; mRS score: mRS score ≤ 2 points is good prognosis, and > 2 points is poor prognosis [14]. The general information of all patients were collected and compared. This research has been approved by the hospital's ethics committee.

2.2 Inclusion and exclusion criteria

2.2.1 Inclusion criteria

(1) Meet the diagnostic criteria for acute cerebral

infarction, and confirmed by Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) examination [15]; (2) Age ≥ 60 years; (3) Time from onset to visit ≤ 48 h.

2.2.2 Exclusion criteria

(1) Unstable vital signs; (2) History of brain trauma or surgery; (3) Severe immune system diseases; (4) Other malignant tumors; (5) Coagulation dysfunction; (6) Organic lesions in important organs such as liver and kidneys; (7) Mental disorders, and poor treatment compliance; (8) Incomplete clinical data.

2.3 Methods

All patients' serum UCH-L1 and Del-1 levels were detected. 5 mL fasting peripheral venous blood was drawn from patients in the early morning, placed at room temperature for 30-60 min, and centrifuged at 3000 r/min for 10 min to separate the serum and store it at -20°C . The serum UCH-L1 level and Del-1 level were measured by enzyme-linked immunosorbent assay, with UCH-L1 (ml038357) and Del-1 (ml060559) kits from Shanghai MLBIO Biotechnology Co., Ltd.

2.4 Statistical methods

SPSS 26.0 software was used for statistical analysis. Count data were represented as percentage (%), and two-group comparisons were made using the χ^2 test. Measurement data were examined for normality using the Kolmogorov-Smirnov test and Shapiro-wilk test. Data that met the normal distribution were represented as mean $\pm$ standard deviation, and two-group comparisons were conducted using the independent samples t -test. Continuous variables that did not meet the normal distribution were expressed using the quartile method [M (P25, P75)], and two-group comparisons were performed using the Mann Whitney U test. Correlation analysis was achieved using Spearman's rank correlation analysis, and the diagnostic value of each parameter was

analyzed using the area under the receiver operating characteristic (ROC) curve (AUC). A difference with $p < 0.05$ was considered statistically significant.

3 Results

3.1 Comparison of general information between the two groups

There were no significant differences in gender, age, body mass index (BMI), drinking history, triglycerides, total cholesterol, low-density lipoprotein cholesterol, creatinine, and uric acid between the diseased group and the healthy group ($p > 0.05$). The proportion of smoking, diastolic pressure, systolic pressure, and glycosylated hemoglobin in the diseased group were all higher than those in the healthy group ($p < 0.05$, Table 1).

3.2 Comparison of serum UCH-L1 and Del-1 levels between the diseased group and the healthy group

The serum UCH-L1 level in the diseased group was higher than that in the healthy group ($p < 0.05$, Table 2), while the Del-1 level was lower than that in the healthy group ($p < 0.05$, Table 2).

3.3 Comparison of serum UCH-L1 and Del-1 levels and cerebral infarction area between small and medium area group and large area group

The cerebral infarction area and serum UCH-L1 level were lower and Del-1 level was higher in the small and medium area group ($p < 0.05$, Table 3), relative to those in large area group ($p < 0.05$, Table 3).

3.4 Comparison of serum UCH-L1 and Del-1 levels and mRS scores between good prognosis group and poor prognosis group

The mRS score and serum UCH-L1 level in the good prognosis group were lower ($p < 0.05$, Table 4) and the Del-1 level was higher than those in the poor prognosis group ($p < 0.05$, Table 4).

Table 1 Comparison of general information between the two groups.

Project	Diseased group (n = 60)	Healthy group (n = 60)	χ^2	p
Gender [case (%)]			0.586	0.444
Male	37 (61.67)	41 (68.33)		
Female	23 (38.33)	19 (31.67)		
Age (years)	69.30 ± 3.52	69.03 ± 2.66	0.468	0.641
BMI (kg/m ²)	23.85 ± 2.44	24.65 ± 3.52	-1.450	0.150
History of smoking [case (%)]			5.076	0.024
No	31 (51.67)	43 (71.67)		
Yes	29 (48.33)	17 (28.33)		
History of drinking [case (%)]			1.677	0.195
No	43 (71.67)	49 (81.67)		
Yes	17 (28.33)	11 (18.33)		
Diastolic pressure (mmHg)	86.75 ± 6.93	81.23 ± 5.16	4.945	< 0.001
Systolic pressure (mmHg)	129.72 ± 13.38	117.02 ± 7.81	6.350	< 0.001
Triglyceride (mmol/L)	1.80 (1.31, 2.32)	1.68 (1.31, 2.00)	-1.331	0.183
Total cholesterol (mmol/L)	4.76 ± 0.92	4.47 ± 0.87	1.743	0.084
Low density lipoprotein cholesterin (mmol/L)	2.51 ± 0.80	2.68 ± 0.66	-1.278	0.204
Glycosylated hemoglobin (%)	6.89 ± 1.34	6.31 ± 1.03	2.649	0.009
Creatinine (mmol/L)	78.92 (57.95, 93.40)	72.81 (64.41, 85.59)	-0.341	0.733
Uric acid (mmol/L)	5.81 (3.95, 6.97)	5.13 (4.61, 6.21)	-0.205	0.838

Table 2 Comparison of serum UCH-L1 and Del-1 levels between the diseased group and the healthy group (mean ± standard deviation).

Group	Case	UCH-L1 (µg/L)	Del-1 (µg/L)
Diseased group	60	0.65 ± 0.28	3.76 ± 1.11
Healthy group	60	0.21 ± 0.12	4.46 ± 0.89
t		11.340	-3.813
p		< 0.001	< 0.001

Table 3 Comparison of serum UCH-L1 and Del-1 levels and cerebral infarction area between small and medium area group and large area group.

Group	Case	Cerebral infraction area (cm ²)	UCH-L1 (µg/L)	Del-1 (µg/L)
Small and medium area group	46	6.00 (4.00, 12.00)	0.62 (0.43, 0.75)	4.02 ± 0.96
Large area group	14	16.00 (12.00, 27.75)	0.88 (0.82, 1.06)	2.93 ± 1.19
t/Z		-4.151	-3.173	3.523
p		< 0.001	0.002	< 0.001

Table 4 Comparison of serum UCH-L1 and Del-1 levels and mRS scores between good prognosis group and poor prognosis group.

Group	Case	mRS score (score)	UCH-L1 (µg/L)	Del-1 (µg/L)
Good prognosis group	38	2.00 (2.00, 2.00)	0.57 ± 0.27	4.14 ± 1.04
Poor prognosis group	22	3.00 (3.00, 3.00)	0.79 ± 0.24	3.12 ± 0.92
<i>t/Z</i>		-7.090	-3.182	3.812
<i>p</i>		< 0.001	0.002	< 0.001

3.5 The correlation between serum UCH-L1 and Del-1 levels with cerebral infarction area and mRS score

The serum UCH-L1 level was positively, while Del-1 level was negatively correlated with cerebral infarction area and mRS score ($p < 0.05$, [Table 5](#)).

Table 5 Correlation between serum UCH-L1 and Del-1 levels with cerebral infarction area and mRS score.

Variables	Cerebral infarction area		mRS score	
	rs	<i>p</i>	rs	<i>p</i>
UCH-L1	0.386	0.002	0.427	< 0.001
Del-1	-0.357	0.005	-0.461	< 0.001

3.6 The ROC curves of serum UCH-L1 and Del-1 levels alone or in combination in evaluation of cerebral infarction area and prognosis

The AUC values of serum UCH-L1 and Del-1 alone and combined in predicting large area cerebral infarction

were 0.782, 0.781 and 0.797, respectively ($p < 0.05$, [Table 6](#), [Figure 1](#)), and the AUC values of serum UCH-L1 and Del-1 alone and combined in predicting poor prognosis were 0.739, 0.765 and 0.794, respectively ($p < 0.05$, [Table 6](#), [Figure 2](#)).

Table 6 The ROC curves of serum UCH-L1 and Del-1 levels alone or in combination in evaluation of cerebral infarction area and prognosis.

Indicator	AUC	95% CI	<i>p</i>	Optimum cutoff value	Jorden index	Sensitivity	Specificity
Prediction: large area infarct area							
UCHL1	0.782	0.608-0.956	0.002	0.815	0.634	0.786	0.848
Del-1	0.781	0.626-0.936	0.002	3.405	0.525	0.786	0.739
Combined detection	0.797	0.646-0.947	< 0.001	0.257	0.525	0.786	0.739
Prediction: poor prognosis							
UCHL1	0.739	0.609-0.869	0.002	0.720	0.536	0.720	0.763
Del-1	0.765	0.642-0.888	< 0.001	3.465	0.510	0.773	0.737
Combined detection	0.794	0.683-0.906	< 0.001	0.249	0.560	0.955	0.605

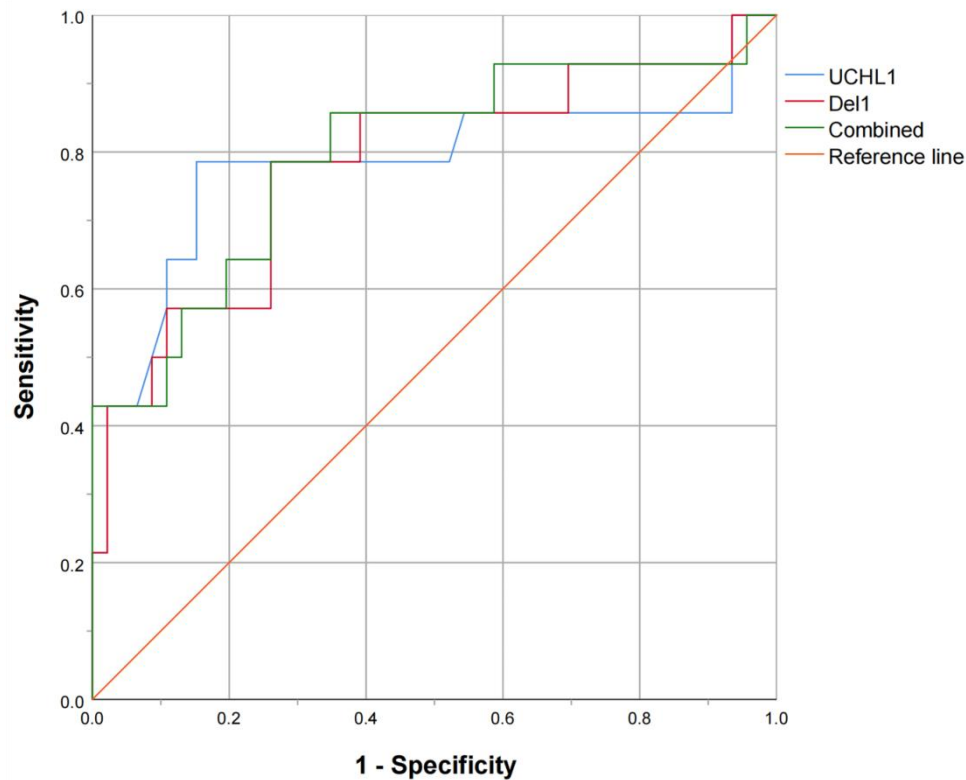


Figure 1 The ROC curves of serum UCH-L1 and Del-1 levels alone or in combination in evaluation of cerebral infarction area.

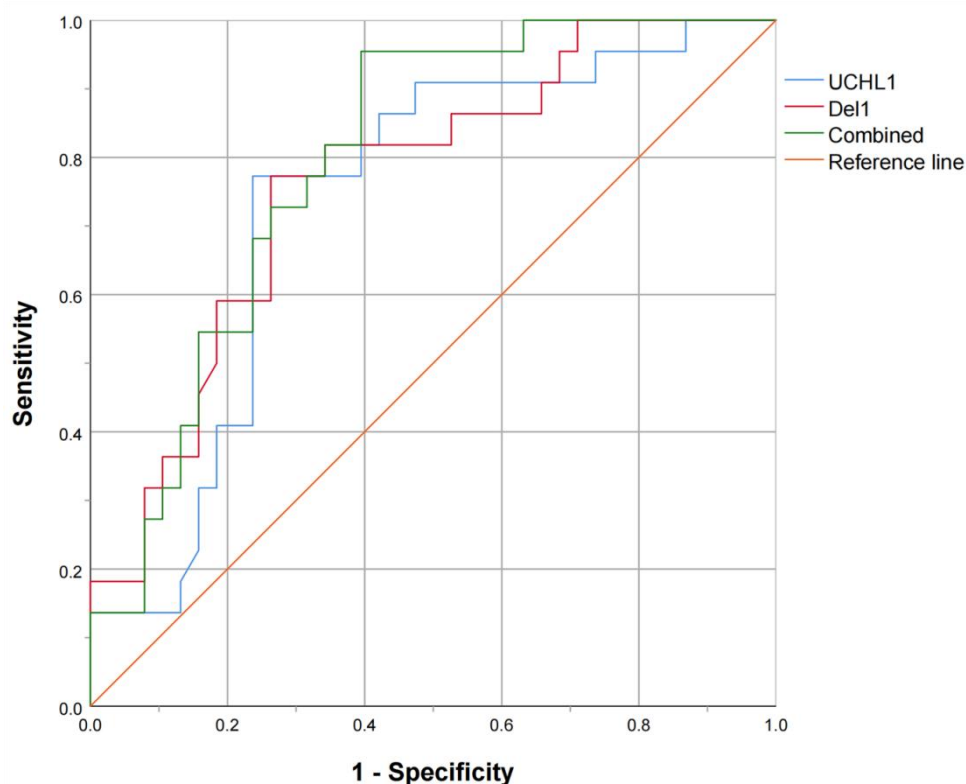


Figure 2 The ROC curves of serum UCH-L1 and Del-1 levels alone or in combination in evaluation of prognosis.

4 Discussion

To improve the assessment accuracy of acute cerebral

infarction condition, this study explored the application value of serum UCH-L1 and Del-1 levels alone and combined in diagnosis. The results showed

that serum UCH-L1 and Del-1 levels may be associated with the cerebral infarction area and prognosis of patients with acute cerebral infarction, possessing certain diagnostic value.

This study demonstrated that compared to healthy controls, patients with acute cerebral infarction have higher serum UCH-L1 levels and lower Del-1 levels. The reason may lie in that UCH-L1 is highly expressed in neurons, and its level changes are closely associated with axonal integrity and function. When acute cerebral infarction occurs or the condition progresses, the brain experiences ischemia and hypoxia, a large number of neuronal cells undergo apoptosis, and UCH-L1 is released and enters the bloodstream through cerebrospinal fluid or a damaged brain-blood barrier, ultimately causing upregulation of serum UCH-L1 [16,17]. Del-1 is a multifunctional protein that can regulate immune plasticity in tissue-specific environments [18]. In patients with acute cerebral infarction, brain tissue damage results in the production of massive pro-inflammatory cytokines, inducing endothelial cells to express adhesion molecules, inhibiting Del-1 expression, promoting neutrophil recruitment, and aggravating inflammatory response [18]. Therefore, serum UCH-L1 and Del-1 levels may have certain diagnostic value for patients with acute cerebral infarction.

In this study, as the infarct area and the mRS score increased, the serum UCH-L1 levels in patients were upregulated and Del-1 levels were downregulated. Moreover, serum UCH-L1 levels were positively while Del-1 levels were negatively correlated with the infarct area and mRS score. UCH-L1 is highly sensitive to diffuse neuronal lesions, and when the infarct area in patients increases or the prognosis worsens, the extent of brain tissue ischemia and hypoxia expands, neuronal axon injury becomes more severe, and heaps of nerve cells experience necrosis and apoptosis, leading to further upregulation of serum UCH-L1 levels

[17]. It has been documented that the larger volume of brain tissue damage and the poorer prognosis are associated with the higher serum UCH-L1 levels [19,20], which is consistent with the results of this study. In patients with increased infarct area or worsened prognosis, cerebral ischemic injury and neurologic dysfunction continue to aggravate, considerable immune cells accumulate around the ischemic tissue, the blood-brain barrier is severely damaged, the levels of circulating neutrophils and inflammatory mediators rise, inflammation is exacerbated, and serum Del-1 levels further decrease [21]. Therefore, in patients with acute cerebral infarction, serum UCH-L1 levels were positively, and Del-1 levels were negatively correlated with the infarct area and mRS score, which can be used as clinical indicators for the assessment of acute cerebral infarction.

Furthermore, this study tested serum UCH-L1 and Del-1 level in all patients with acute cerebral infarction and calculated that the combined diagnosis of serum UCH-L1 and Del-1 levels had a high accuracy rate for large area cerebral infarction and poor prognosis, which also had higher value than individual diagnosis. However, due to the limited sample source and size in this study, there may be biases in data analysis, and the study results are insufficient to represent the situation of all patients with acute cerebral infarction. In the future, it is necessary to conduct further research covering a wider range and involving more samples to explore this issue. In addition, the combined diagnostic efficacy of serum UCH-L1 and Del-1 levels needs further trials and exploration to refine relevant theoretical research.

To conclude, serum UCH-L1 levels in patients with acute cerebral infarction are positively and Del-1 levels are negatively correlated with the infarct area and mRS score. Serum UCH-L1 and Del-1 in combination has high diagnostic value and can serve as clinical

indicators for the assessment of acute cerebral infarction.

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Not applicable.

Conflicts of Interest

The authors declare no conflict of interest.

Author Contributions

Substantial contributions to conception and design: Y.L. Data acquisition, data analysis and interpretation: J.L. Drafting the article or critically revising it for important intellectual content: All authors. Final approval of the version to be published: All authors.

Ethics Approval and Consent to Participate

This study was approved by Medical Ethics Committee, and patients were informed and agreed.

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Availability of Data and Materials

The analyzed data sets generated during the study are available from the corresponding author on reasonable request.

Supplementary Materials

Not applicable.

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