

# Application of concomitant disease scoring in acute cerebral infarction

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## Research article

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# Abstract

**Background:** This study aims to explore the predictive value of concomitant disease scoring for the prognosis of patients with acute cerebral infarction (ACI). **Methods:** A total of 399 patients with ACI, who met the inclusion criteria, were enrolled into the present study. The concomitant disease score was assessed within 24 hours after admission, and the risk degree of death was analyzed. Then, the goodness of fit test and validity analysis were carried out, the best survival/death cut-off value was determined, and its predictive value for the prognosis of ACI patients was assessed. **Results:** The area under the receiver operating characteristic (ROC) curve for the concomitant disease score was 0.700, the distinctiveness was relatively good, and the prediction cut-off value was 10 points. Furthermore, the mortality rate of patients with a higher score was significantly higher, when compared to patients with a lower score. **Conclusion:** This concomitant disease score has good predictive value for the prognosis of ACI patients, and is an ideal system for evaluating the condition of cerebral infarction. The survival/death cut-off value was 10 points.

## Background

Acute cerebral infarction (ACI) is a common cerebrovascular disease that seriously endangers human health, and has high morbidity, mortality, disability and recurrence rate.[1-3] Cerebral infarction is a hypoxic and ischemic necrosis induced by insufficient blood supply of the local brain, which results from a blockage or narrowing in the arteries, and the blockage can be due to a thrombus, an embolus or an atheromatous stenosis of one or more arteries.[4,5] Major risk factors for cerebral infarction are generally the same as for atherosclerosis: high blood pressure, Diabetes mellitus, tobacco smoking, obesity, and dyslipidemia.[6] In recent years, the incidence of ACI has exhibited a significant upward trend. The majority of ACI patients would be complicated with pathological changes in other organs during the onset of ACI. Therefore, it is very important to carry out disease assessment to rescue patients who may suffer from preventable death.[7] In the present study, the concomitant disease score of patients with ACI was assessed to preliminarily investigate its effect on the prognosis of ACI, which is beneficial for doctors to make timely and effective intervention measures.

## Methods

### 1.1 Patient selection

A total of 399 patients with ACI, who were admitted in the Department of Neurology, Affiliated Hospital of North China University of Science and Technology from 2012 to 2016, were enrolled in the present study. Among these patients, 278 patients survived and 121 patients died. Furthermore, among these patients, 221 patients were male and 178 patients were female. The average age of these patients was  $63.650 \pm 12.756$  years old. All included patients were admitted to the hospital within three days after onset, met the diagnostic criteria established at the Fourth National Cerebrovascular Disease Conference of China, and were confirmed by craniocerebral computed tomography (CT) or magnetic resonance imaging (MRI).

## 1.2 Methods

The concomitant disease score of all patients was assessed within 24 hours after admission. This assessment was performed by surveyors who underwent a unified training, strictly according to the scoring criteria. In the present study, one month after admission was set as the observation endpoint. Patients who died within one month were defined as death patients, while patients who survived within one month were defined as survival patients (including patients in the vegetative state). Patients who were discharged early were confirmed by follow-up.

### *Scoring criteria*

(i) Each of the following situations was scored 1 point: obesity, incidental premature systole, elevation of 1-2 items of blood lipids, and mild tracheitis.

(ii) Each of the following situations was scored 2 points: hypertension, cardiac enlargement, cardiac hypertrophy, premature systole (<5 times/minute), elevation of three items of blood lipids, fever at approximately 37.5°C for no more than three days, and cervical bruits.

(iii) Each of the following situations was scored 3 points: frequent premature systole (>15 times/minute), electrocardiogram (ECG) ST-T changes, hyperglycemia, bilateral lesions revealed by head CT scan, positive pyramid sign on the unaffected side (+), fever at or over 38°C for more than three days, and gastrointestinal bleeding (melena).

(iv) Each of the following situations was scored 4 points: myocardial infarction, dementia, pseudobulbar palsy, renal dysfunction, heart failure, bronchopneumonia for more than one week, pulmonary edema, atrial fibrillation, and gastrointestinal bleeding (hematemesis).

## 1.3 Statistical analysis

The linear trend  $\chi^2$ -test, *t*-test, and goodness of fit test were carried out for the data analysis.

# Results

### *2.1 Age and gender composition of the survival group and death group*

A total of 399 patients were included in the present study. Among these patients, 121 patients died, while 278 patients survived. Furthermore, among these patients, 221 patients were male and 178 patients were female. The differences in age and gender between the death group and survival group were not statistically significant (Table 1). The score was  $12.00 \pm 6.54$  in the death group and  $7.37 \pm 4.79$  in the survival group, and the difference in score between the survival group and death group was statistically significant ( $P < 0.05$ ).

### *2.2 Qualitative analysis of the correlation between the concomitant disease score and in-hospital mortality in ACl patients*

With the concomitant disease score of 15 points as the cut-off value, these ACI patients were divided into two groups: high score and low score groups. Then, the risk of death was compared between these two groups. The results revealed that the risk of death was higher in the high score group than in the low group (Table 2).

### *2.3 Dose-response relationship between the concomitant disease score and in-hospital mortality in ACI patients*

The linear trend  $\chi^2$ -test was used to analyze the association strength between the concomitant disease score and in-hospital mortality. The results revealed that as the concomitant diseases score increased, the in-hospital mortality increased (Table 3).

### *2.4 Goodness of fit analysis*

In order to evaluate whether there was a good goodness of fit between the death and concomitant disease score of ACI patients, the investigators carried out a goodness of fit test (Table 4).

### *2.5 Correlation between the concomitant disease score and in-hospital mortality in ACI patients*

With the increase in concomitant disease score, the in-hospital mortality of patients with ACI significantly increased. The higher the score was, the more serious the condition became, and the higher the risk of death was. Conversely, when the condition improved and the score decreased, the risk of death decreased (Table 5).

### *2.6 Validity of the concomitant disease scoring system in predicting the prognosis of cerebral infarction*

With the 1-month death or survival of ACI patients as the observation endpoint, the sensitivity and specificity of each point of concomitant disease score were calculated, and the receiver operating characteristic (ROC) curve of the concomitant disease score at admission was constructed (Figure 1). Then, the area under the curve (AUC) was calculated, which was 0.700. The AUC was compared between the concurrent disease score and baseline area (0.5), and the differences were statistically significant.

### *2.7 The best cut-off value of the concomitant disease scoring for the prognosis of ACI patients*

The AUC was 0.700, which has good validity in predicting the prognosis of patients with cerebral infarction. On the basis of its sensitivity, specificity and predicted value (Table 6), it can be concluded that the best cut-off value of the concomitant disease score in predicting cerebral infarction was 10 points. When the cut-off value was 10 points, sensitivity was 0.667 and specificity was 0.700.

## **Discussion**

ACI is a common disease in the elderly, and is also a frequently occurring disease in neurology [8], which causes great harm to human health. The quantization of the prognosis of patients with cerebral infarction can more accurately assess the severity of the disease, and predict the risk of death of

patients. This score can be used to judge the conditions of disease, predict the mortality of population-based patients more reliably, provide an objective basis for doctors, family members and society to make medical decisions, be helpful in correctly formulating treatment plans and explaining the conditions to the family members [9].

A large number of epidemiological studies have confirmed that hypertension is one of the important and independent risk factors for cerebral infarction, and this has been accepted by scholars both at home and abroad. Increased blood pressure can alter the structure and function of vascular endothelial cells, and cause damage to endothelial cells. Low density lipoprotein cholesterol (LDL-C) enters into the arterial wall, and stimulates the proliferation of vascular smooth muscle cells, causing atherosclerosis and inducing angiostegnosis, and subsequently, cerebral infarction. Especially in patients with diabetes, the complications of hypertension and diabetes are risk factors for stroke. When it is constantly subjected to high-pressure blood flow, the inner walls of arteries easily form microaneurysm, which allows lipids in plasma to enter into the endarterium and form hyaline depositions. This would cause fibrous necrosis of the arterial wall, which could easily cause cerebrovascular disease. Increased blood lipids can cause increased blood viscosity, slow blood flow and increased platelet activating factor. These promote vascular endothelial cell injury and proliferation, and cause angiostegnosis and thrombosis, inducing tissue ischemia and hypoxia. Hyperlipidemia can damage vascular endothelial cells, make platelets adhere to the walls of blood vessels, reduce the activity of the fibrinolytic enzyme system, and facilitate the formation of thrombus [10]. Furthermore, hyperlipidemia can damage blood vessels, and promote the occurrence of atherosclerosis. Arteriosclerosis is the most important basis for cerebral infarction. Hyperlipidemia patients are often in a hypercoagulable state, in which blood coagulation and viscosity increases, and platelet adhesion and aggregation increases. These are all factors for cerebral infarction [11]. Glycation in diabetic patients causes hypoxia and ischemic injury in vascular endothelial cells, which can cause atherosclerosis, and induce the thickening and degeneration of the basement membrane of small vessels. All of these increase the risk of cerebrovascular disease to a certain extent [12]. Moreover, a study revealed that [13] a large amount of glycated hemoglobin (HbA1c) can also increase free radicals in the body. Dyslipidemia is also a pathological basis for atherosclerosis, which can cause the disorder of local cerebral blood circulation. In addition, intravascular endometrial injury can cause stenosis of the cerebral artery, which subsequently causes ischemia, anoxia and necrosis of brain tissues, and accordingly lead to the occurrence of cerebral infarction [14-16]. Diabetic patients have a certain degree of insulin resistance, and insulin resistance is involved in the pathological and physiological processes of cerebral arteriosclerosis and cerebral infarction [17,18]. A history of diabetes can affect cell metabolism in brain tissues in the hyperglycemic state, and increase oxidative stress and inflammatory response, aggravating the conditions [19-21]. In addition, for patients with angiostegnosis induced by the progression of diabetes and patients combined with intracranial artery stenosis, the establishment of collateral circulation is difficult, and thrombus expansion easily occurs after cerebral infarction [22].

A study conducted by Chinese scholars revealed that [23] abnormal blood lipid, diabetes, carotid atherosclerosis, coronary heart disease and hypertension were the main risk factors for acute extensive cerebral infarction. Age and blood pressure are important indicators of the prognosis of stroke [24]. The

incidence of hypertension is relatively high in stroke patients. The reason is that hypertension is an important factor for stroke. On the other hand, stroke can lead to stress-associated elevated blood pressure. Deying Kang *et al.* pointed out that [25] the in-hospital mortality of admitted patients with stroke was correlated to age and hypertension. Xiaoqiu Wu *et al.* revealed that [26] the incidence of common clinical complications of acute stroke was significantly higher in hypotension patients. Furthermore, they also pointed out that in order to improve the cure rate, reduce the disability rate and improve the prognosis of stroke patients, the complications should be actively prevented and treated. Another study pointed out that [27] electrolyte disturbance in stroke is a marker of poor prognosis, and clinicians should actively seek the cause of these electrolyte disorders, as well as its prevention and treatment, in order to take precautions against danger. If the body temperature increases within 24 hours after stroke, the 3-month infarct size and mortality rate would increase [28].

A previous study revealed that there are certain synergic factors in the process of progressive cerebral infarction caused by hypertension, such as high homocysteine [29] and diabetes. The incidence of hypertension is significantly higher in diabetic patients with cerebral infarction than in patients with cerebral infarction alone [30]. Hyperglycemia can promote cerebral infarction in hypertensive patients, and promote the progression of cerebral infarction [31].

Patients with cerebral infarction are often complicated with pulmonary infection during hospitalization, and the incidence is 7-22% [32]. The reason may be that the dysfunction of the thalamic autonomic nervous system results in pulmonary arterial hypertension and pulmonary capillary damaged, subsequently inducing pulmonary edema and respiratory failure [33]. A study revealed that [34] the combination of pneumonia and pulmonary infection is a risk factor for in-hospital mortality in elderly patients with cerebral infarction. The cause is that after the pulmonary infection or pneumonia occurred in patients with cerebral infarction, the gas exchange was affected, blood oxygen saturation decreased, and the body temperature increased. These increase in oxygen consumption of the body aggravates the brain hypoxia, and the increase in brain damage aggravates the cerebral infarction. This conclusion is basically consistent with the results reported in literatures [35-39].

Atrial fibrillation can significantly reduce cardiac output, and affect the cardiac function of patients, such patients who are easily complicated with heart failure. This further reduces cerebral blood flow, and causes the insufficiency of blood supply for brain tissues, aggravating cerebral infarction. This conclusion is basically consistent with the results reported in literatures [40-43].

Previous studies have revealed that cerebral artery stenosis is one of the risk factors for progressive cerebral infarction [40,44]. Zhiwu Wu *et al.* revealed that [45] the risk of severe cerebral infarction increased in patients with severe cerebral artery stenosis. The assessment of stroke risk should be combined with vascular assessment, and individual intervention measures should be carried out, which can more effectively prevent stroke. It is of great clinical significance to assess vasculopathy in patients with cerebral infarction by imaging examination.

The present study suggests that the concomitant disease score was closely correlated to in-hospital mortality. With the increase in the concomitant disease score, the in-hospital mortality of patients with cerebral infarction significantly increased. The higher the score was, the more serious the condition became, and the higher the risk of death was. Conversely, when the condition improved, the score decreased, and the risk of death also decreased. The ROC curve analysis is a basic identification tool in the field of clinical medicine [42,46]. An ideal predictor is that there is no overlap in the upper and lower limits between the survival group and death group, and both sensitivity and specificity were 100%. Furthermore, the AUC was also 100% or 1. A worthless predictor is that since it is a random guess, both the sensitivity and specificity were 50%, and the ROC was 0.5. The larger the area difference, the greater the prediction effectiveness. The investigators constructed a ROC curve for the concomitant disease scores for patients with cerebral infarction, and the AUC was calculated. Then, this was compared with the baseline AUC (0.5). The present study revealed that the ROC of concomitant disease scores for cerebral infarction was 0.700. Hence, the concomitant disease scores had good validity for evaluating the prognosis of patients with cerebral infarction.

## Conclusions

The present preliminary study suggests that the concomitant disease score has a relatively satisfactory predictive value for the prognosis of patients with ACI. At present, the present study is merely a preliminary study. Hence, further in-depth studies with an expanded sample size are needed to confirm these results.

## Abbreviations

acute cerebral infarction: ACI

receiver operating characteristic: ROC

computed tomography: CT

magnetic resonance imaging: MRI

Electrocardiogram: ECG

area under the curve: AUC

Low density lipoprotein cholesterol: LDL-C

## Declarations

Ethics approval and consent to participate: This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Affiliated Hospital of

North China University of Science and Technology. Written informed consent was obtained from the participants.

Consent for publication: obtained from the participants.

Availability of data and material: The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests: all authors declare that they have no competing interests.

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Authors' contributions: 1) Xiao-Jing Zhao, Substantial contributions to the conception and design of the work, and draft the work; And 2) Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, Fu-Xia Zheng, the acquisition, analysis, and interpretation of data for the work; And 3) Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, Fu-Xia Zheng, revising it critically for important intellectual content; AND 5) Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, Fu-Xia Zheng, final approval of the version to be published; AND 6) Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, Fu-Xia Zheng, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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## Tables

Table 1 age and gender of patients in the death group and survival group

Age	The survive group (n= 278)		Total	The death group (n= 121)		Total
	Male	Female		Male	Female	
≤60 years old	67	45	112	17	19	36
>60 years old	88	78	166	49	36	85
Total	155	123	278	66	55	121

Note: gender: ( $\chi^2=0.622$ ,  $P=0.430$ ); age: ( $\chi^2=0.141$ ,  $P=0.707$ ).

Table 2 comparison of the risk of death between the high score and low score groups

	The number of deaths	The number of survivals	OR(95%CI)
High score group	47	34	4.558(2.794-7.436)
Low score group	74	244	

Table 3 the risk of death in the concomitant disease scoring groups

Items	concomitant disease scoring groups					
	0	5	10	15	20	25
The number of the died	15	29	30	25	12	4
The number of the survival	81	93	70	21	1	1
OR value		1.684	2.314	6.429	64.800	21.600

Cerebral infarction:  $\chi^2=61.700$ ,  $P<0.001$ .

Table 4 Hosmer Lemeshow Goodness of fit analysis of concomitant disease score

Groups	The survival		The death	
	Actual frequency	Theoretical frequency	Actual frequency	Theoretical frequency
1	35	37.998	7	4.002
2	28	26.161	2	3.839
3	18	20.225	6	3.775
4	25	24.648	5	5.352
5	28	32.118	13	8.882
6	40	37.164	11	13.836
7	33	26.663	7	13.337
8	31	28.227	16	18.773
9	20	20.696	21	20.304
10	7	11.100	27	22.900

Note: the test of Hosmer Lemeshow Goodness of fit showed that there were no significant difference between the predicted risk degree of death and actual death rate.

Table 5 In-hospital mortality in the concomitant disease scoring groups (%)

Concomitant disease scoring groups							x <sup>2</sup>	P
	0	5	10	15	20	25		
15.63 (15/81)	23.77 (29/93)	30.00 (30/70)	54.35 (25/21)	100 (12/0)	100 (4/0)	61.700	<0.001	

Note: () means the number of the death/ the number of the survival

Due to technical limitations, Table 6 is only available as a download in the supplemental files section.

## Figures

# ROC Curve

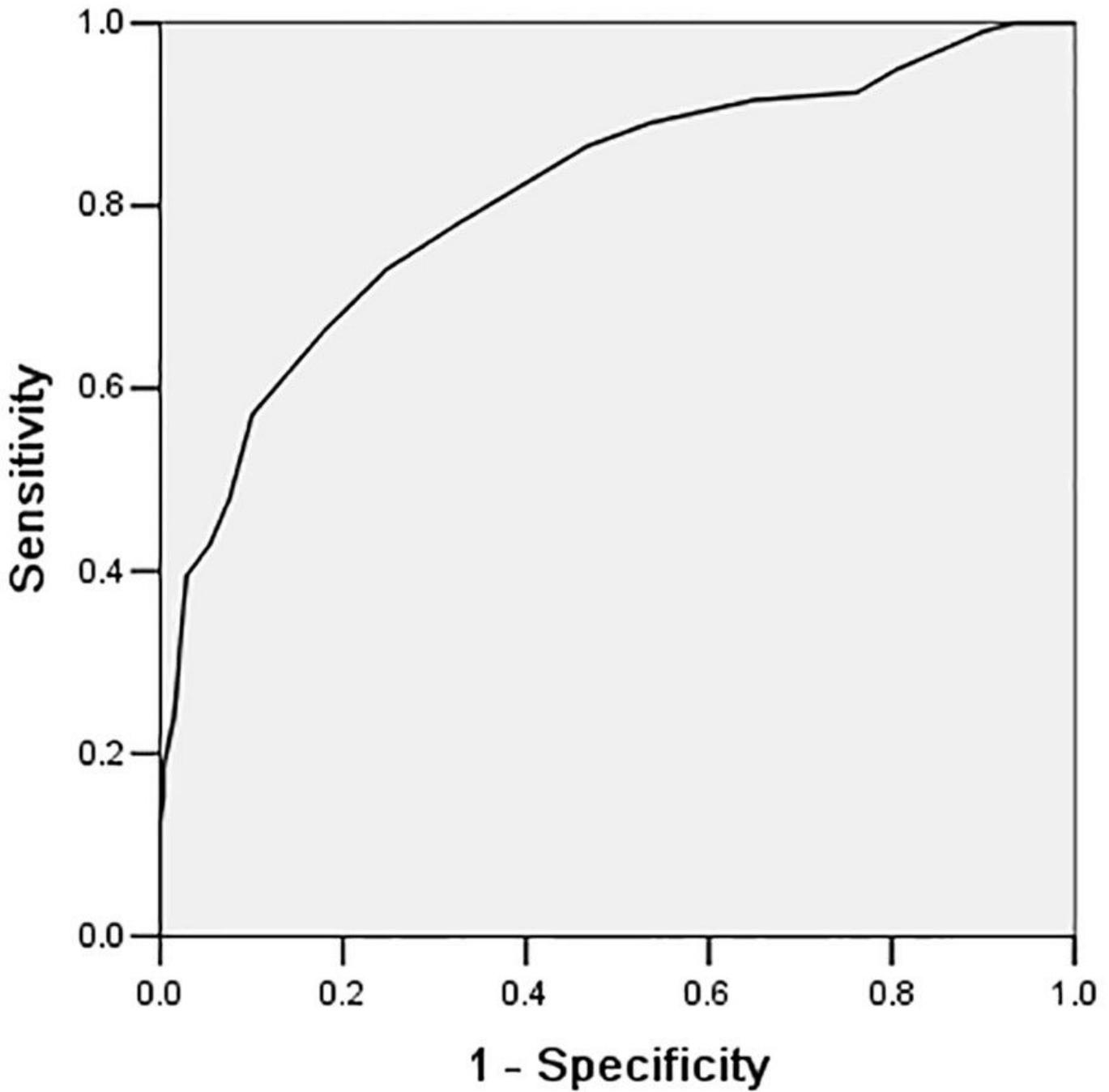


Figure 1

ROC curve of patients with acute cerebral infarction accompanied by some disease.

## Supplementary Files

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- [supplement1.jpg](#)