Research Article

Application of Concomitant Disease Scoring in Acute Cerebral Infarction

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Abstract

Background: Acute cerebral infarction (ACI) is a common cerebrovascular disease that seriously endangers human health. It is very important to carry out disease assessments to rescue patients who may suffer from preventable death.
Objectives: This study aimed to explore the predictive value of concomitant disease scoring for the prognosis of patients with ACI.
Methods: This is a respective observational study. A total of 399 patients with ACI from the Affiliated Hospital of North China University of Science and Technology, who met the inclusion criteria, were enrolled in 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, and the best survival/death cut-off value was determined.
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 compared to patients with a lower score.
Conclusions: The 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.

Keywords: Acute Cerebral Infarction, Prognosis, Receiver Operating Characteristic Curve, Illness Assessment

1. Background

Acute cerebral infarction (ACI) is a common cerebrovascular disease that seriously endangers human health, which has high morbidity and mortality, disability, and recurrence rate (1). Cerebral infarction is hypoxic and ischemic necrosis induced by insufficient blood supply of the local brain, which results from a blockage or narrowing in the arteries, and this blockage can be due to a thrombus, an embolus, or the atheromatous stenosis of one or more arteries. In recent years, the incidence of ACI has exhibited a significant upward trend. The majority of ACI patients would be complicated by pathological changes in other organs during the onset of ACI. Therefore, it is very important to carry out disease assessments to rescue patients who may suffer from preventable death. At present, regarding the development status in domestic cases and abroad, there are many evaluation criteria for stroke, but these have not been widely applied (2).

The major risk factors for cerebral infarction are generally the same as those for atherosclerosis, such as high blood pressure, diabetes mellitus, tobacco smoking, obesity, and dyslipidemia. These factors could influence the prognosis of ACI. However, at present, no previous studies have established a scoring system for assessing the concomitant disease of ACI, in order to predict the efficacy and prognosis.

In the present study, the concomitant disease score of patients with ACI was assessed to preliminarily investigate its effect on the prognosis of ACI. This would be beneficial for doctors to make timely and effective intervention measures.

2. Methods

The present study was conducted in accordance with the declaration of Helsinki and compliance with the Ethics Guidelines. Furthermore, the present study was approved

by the Ethics Committee of the Affiliated Hospital of North China University of Science and Technology. Written informed consent was obtained from the participants or their guardians.

2.1. Patient Selection

The present study was a retrospective observational study. A total of 399 patients with ACI, who were diagnosed in the Department of Neurology, Affiliated Hospital of North China University of Science and Technology from January 2012 to January 2016, were enrolled in the present study. All included patients were admitted to the hospital within three days after onset, and these patients met the diagnostic criteria established at the Fourth National Cerebrovascular Disease Conference of China. The diagnosis was further confirmed by craniocerebral computed tomography (CT) or magnetic resonance imaging (MRI).

Inclusion criteria: (1) patients who provided informed consent and volunteered to participate in the present study; (2) patients who met the diagnostic criteria for cerebrovascular disease in China.

Exclusion criteria: (1) patients with serious organic injuries or those who cannot take care of themselves; (2) patients with a previous history of cerebral stroke; (3) patients who could not communicate properly; (4) patients with atherosclerotic cerebral infarctions or cerebral embolisms.

2.2. Patients

The concomitant disease score of all patients was assessed within 24 hours after admission. This assessment was performed by two observers who underwent a unified training. In the current study, one month after admission was set as the observation deadline. Patients who died within one month were defined as dead patients, while patients who survived beyond one month were defined as survived patients (including patients in the vegetative state). Patients who were discharged early were confirmed by the follow-up.

2.3. Scoring Criteria

(i) Each of the following situations was scored as 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 as 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 as 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 as 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).

2.4. Statistical Analysis

The data were analyzed using SPSS 22.0 software (IBM Corp., Armonk, NY). Continuous variables were expressed as mean $\pm$ standard deviation (SD), while discontinuous variables were expressed in percentage (%). The variables were investigated using visual (plots/histograms) and analytical methods (Kolmogorov-Smirnov test) to determine whether these were normally distributed. For two comparisons, each normally distributed value was compared by *t*-test, while non-normally distributed continuous data were compared using non-parametric test. Counting data were tested by chi-square test. Fitting analysis was applied to evaluate the fitting of the death of patients with cerebral infarction and the concomitant disease scores. For the validity of the concomitant disease scoring system in predicting the prognosis of cerebral infarction, the receiver operating characteristic (ROC) curve of the concomitant disease score was drawn, and the areas under the ROC curve were calculated. The Youden's indexes (cut-off values) that corresponded to the points on the ROC curve were calculated to determine the sensitivity and specificity of the prognosis. The cutoff value that corresponded to the maximum Youden's index was used as the best cut-off value for evaluating the prognosis. $P < 0.05$ was considered statistically significant.

In order to evaluate the compatibility between these two observers in grading the concomitant disease score, the kappa co-efficiency [very good ($\kappa > 0.8$), good ($\kappa = 0.61$ - 0.8), moderate ($\kappa = 0.41$ - 0.6), low ($\kappa = 0.21$ - 0.4), and very low ($\kappa \leq 0.2$)] was calculated. Then, the compatibility between the two observers was calculated as 0.8939.

3. Results

3.1. Age and Gender Composition of the Survived and Dead Groups

From January 2012 to January 2016, a total of 521 patients with ACI were admitted to our hospital. Among these patients, 399 patients met the inclusion criteria and were included in the present study. Furthermore, among

these patients, 121 patients died, while 278 patients survived. In addition, among these patients, 221 patients were male and 178 patients were female, and their average age was 63.65 ± 12.76 years old. The differences in age and gender between the dead and survived groups were not statistically significant (Table 1). The score was 12.00 ± 6.54 in the dead group and 7.37 ± 4.79 in the survived group, and the difference in scores between the survived and dead groups was statistically significant (P < 0.05).

3.2. Qualitative Analysis of the Correlation Between the Concomitant Disease Score and In-Hospital Mortality in ACI Patients

The compatibility between the two observers in grading the concomitant disease score was good. 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).

3.3. Dose-Response Relationship Between the Concomitant Disease Score and In-Hospital Mortality in ACI Patients

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

3.4. Goodness of Fit Analysis

In order to evaluate whether there was good goodness of fit between the death and concomitant disease score of ACI patients, the investigators carried out goodness of fit test (Table 4). The test of Hosmer Lemeshow Goodness of fit revealed that there were no significant differences between the predicted risk degree of death and actual death rate.

3.5. The 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).

3.6. 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.
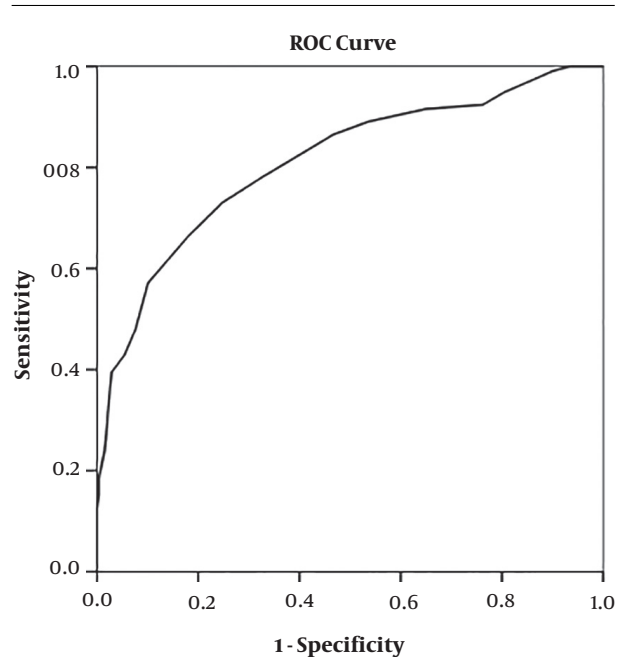

Figure 1. ROC curve of patients with acute cerebral infarction accompanied by some disease is depicted.

3.7. 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. The maximum Youden's index was 0.260. When the cut-off value was 10 points, sensitivity was 0.587, specificity was 0.673, the positive predictive value was 0.438 and the negative predictive value was 0.789.

Table 1. Age and Gender of Patients in the Dead and Survived Groups[a]

Age	The Survived Group (N= 278)			The Dead Group (N=121)		
	Male	Female	Total	Male	Female	Total
$\leq$ 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

[a]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	

4. Discussion

ACI is a common disease in the elderly and is also a frequently occurring disease in neurology (3), which causes great harm to human health. In the present study, the results revealed that the 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 concomitant disease score system is mainly based on the complications and risk factors of patients with acute cerebral infarction. The score items include hypertension, blood lipid, hyperglycemia, body temperature and pulmonary infection. Blood pressure is an important indicator of the prognosis of stroke (4). Kang et al. (5) reported that the in-hospital mortality of admitted patients with stroke was correlated to age and hypertension. Wu et al. (6) reported that the incidence of common clinical complications of acute stroke was significantly higher in hypotension patients. Furthermore, they also noted 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. A previous study revealed that there are certain synergic factors in the process of progressive cerebral infarction caused by hypertension, such as high homocysteine and diabetes (7). The incidence of hypertension is significantly higher in diabetic patients with cerebral infarction than in patients with cerebral infarction alone (8). Hyperglycemia can promote cerebral infarction in hypertensive patients, and promote the progression of cerebral infarction (9).

Patients with cerebral infarction are often complicated with pulmonary infection during hospitalization, and its incidence ranges within 7 - 22% (10). The reason may be that the dysfunction of the thalamic autonomic nervous system results in pulmonary arterial hypertension and pulmonary capillary damage, subsequently inducing pulmonary edema and respiratory failure (11). A study (12) revealed that the combination of pneumonia and pulmonary infection is a risk factor for in-hospital mortality in elderly patients with cerebral infarction. After pulmonary infection or pneumonia occurs in patients with cerebral infarction, the gas exchange would be affected, blood oxygen saturation would decrease, and the body temperature would increase. If the body temperature increases within 24 hours after stroke, the 3-month infarct size and mortality rate would increase.

Atrial fibrillation can significantly reduce cardiac output, and affect the cardiac function of 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 the cerebral infarction. This conclusion is basically consistent with the results reported in literature (13-16).

Cerebral artery stenosis is another risk factor for progressive cerebral infarction (14). Zhiwu Wu et al. (17) reported that 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 the vasculopathy in patients with cerebral infarction by imaging examination.

The present study suggests that the concomitant disease score closely correlates with in-hospital mortality. With the increase in 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 (18). An ideal predictor is that there was no overlap in the upper and lower limits between the

Table 3. The Risk of Death in the Concomitant Disease Scoring Groups[a]

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	

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

Table 4. Hosmer Lemeshow Goodness of Fit Analysis of Concomitant Disease Score[a]

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

[a]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						χ^2	P
	0~	5~	10~	15~	20~	25~		
Percent	15.63	23.77	30.00	54.35	100	100	61.700	< 0.001
Number of the death/Number of the survival	(15/81)	(29/93)	(30/70)	(25/21)	(12/0)	(4/0)		

Table 6. Sensitivity and Specificity of Concomitant Disease Scoring in Predicting the Prognosis of Patients with Cerebral Infarction

Value	Sensitivity	Specificity
8	0.710	0.502
9	0.673	0.570
10	0.667	0.700
11	0.579	0.714
12	0.542	0.776

survived and dead groups, 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 of patients with cerebral infarction. The present study revealed that the ROC of concomitant disease scores for cerebral infarction was 0.700. Hence, these concomitant disease scores have good validity for evaluating the prognosis of patients with cerebral infarction.

The present preliminary study suggests that the concomitant disease score has a relatively satisfactory predictive value for the prognosis of patients with ACI. However, the present study is merely a preliminary study. There were several limitations. First, the present study is a retrospective study, and the scale evaluation was influenced by subjective factors to a great extent. Second, the present study was not a randomized controlled trial. Third, the present study was only a single-center trial, and the sample size was not calculated before the study was carried out. Hence,

further in-depth studies with an expanded sample size are needed to confirm these results.

Footnotes

Authors' Contribution: Xiao-Jing Zhao: substantial contributions to the conception and design of the work, and drafting the work; Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, and Fu-Xia Zheng: the acquisition, analysis, and interpretation of data for the work; Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, and Fu-Xia Zheng: revising it critically for important intellectual content; Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, and Fu-Xia Zheng: final approval of the version to be published; Xiao-Jing Zhao, Qun-Xi Li, Ying Liu, Li-Sha Chang, Rui-Ying Chen, Hai-Yan Fan, and 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.

Conflict of Interests: All authors declare that they have no conflict of interest to disclose.

Ethical Approval: This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Ethics Committee of Affiliated Hospital of North China University of Science and Technology.

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