Logistic Regression Analysis of the Influencing Factors of Cryptogenic Stroke with Positive c-TCD

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Abstract: **Objective:** To explore the influencing factors and logistic regression characteristics of cryptogenic stroke in patients with positive transcranial doppler bubble test (c-TCD). **Methods:** A total of 134 cases of cryptogenic stroke that were diagnosed by Tianshui First People's Hospital from November 2018 to April 2020 were selected according to the TOAST (Trial of ORG 10172 in Acute Stroke Treatment) classification criteria. According to c-TCD results, there were 70 cases of right to left shunt that were included in the positive group and 64 cases without right to left shunt in the negative group. Gender, age, smoking, diabetes, hypertension, and factors affecting the positive rate of foam were analyzed. According to the abnormal embolism scale scores, logistic regression equation was used to analyze the independent influencing factors. **Results:** The influencing factors of cryptogenic stroke in patients with positive c-TCD were correlated with age, gender, and abnormal embolism scale scores ($p < 0.05$). For each grade increase in age, the proportion of positive foam test was calculated to be 3.21 times, and the proportion of female to male was calculated to be 2.25 times. For each grade increase in the scores, the proportion of positive foam test was calculated to be 2.55 times. **Conclusion:** Female, older age, and higher scores in the abnormal embolism scale are the influencing factors for cryptogenic stroke in patients with positive c-TCD.

Keywords: Positive c-TCD; Cryptogenic stroke; Influencing factors; Logistic regression

1. Introduction

In recent years, many studies have shown that cryptogenic stroke is closely related to patent foramen ovale, where about 44% of cryptogenic stroke patients have patent foramen ovale. Contrast-enhanced transcranial doppler (c-TCD) is a new investigation method at the present stage. It has the advantage of being accurate and quick in the screening of patent foramen ovale [1,2]. In this study, 135 patients with cryptogenic stroke were selected to analyze the influencing factors of c-TCD positive patients.

2. Material and methods

2.1. General information

A total of 134 patients that were diagnosed with cryptogenic stroke in Tianshui First People's Hospital from November 2018 to April 2020 were selected according to the TOAST classification criteria. The inclusion criteria were patients that had conformed to the TOAST classification standard and signed the informed consent form. The exclusion criteria were those who refused or did not meet the conditions for c-TCD and those who were not able to perform the Valsalva maneuver.

2.2. Methods

The blood flow of the left middle cerebral artery was temporarily measured by Delikai's transcranial

doppler ultrasound monitor. 9 ml of normal saline was fully mixed with 1 ml of air and a drop of blood, and then injected through the vein in the elbow. The venous state and the number of microembolic signals in the patients within 30 seconds after Valsalva maneuver were observed. The diagnosis according to the International Consensus Criteria (ICC) included: Negative – no microembolic signal detected; Grade I – a small degree of shunting with 1~10 microembolic signals detected; Grade II – medium volume diversion with more than 10 but less than 25 microembolic signals detected; Grade III – more than 25 but less than 60 microembolic signals detected in the case of a large degree of shunting; Grade IV – more than 60 microembolic signals detected; Positive – Grade I~IV, i.e. with right to left shunt; Negative – microembolic signals negative without right to left shunt. The single and multiple factors affecting the positive rate of c-TCD were analyzed.

2.3. Observation indicators

Age, gender, underlying diseases, smoking history, and abnormal embolism scale scores were observed. The scores of the abnormal embolism scale were assessed by the RoPE (Risk of Paradoxical Embolism) scale. The total score that can be obtained from the scale was 10 points; one point each for no smoking history, no TIA or stroke history, no history of diabetes, no history of hypertension, and cortical infarct on imaging while patients of 18-29 years old were appointed 5 points, 4 points for those 30-39 years old, 3 points for 40~49 years old, 2 points for 50-49 years old, 1 point for 60-69 years old, and 0 point for ≥ 70 years old.

2.4. Statistical analysis

Logistic regression analysis was performed by Statistical Package for the Social Sciences (SPSS) version 18.0. The difference is considered statically significant if $p < 0.05$.

3. Results

3.1. Clinical analysis

According to the c-TCD results, among 134 patients with cryptogenic stroke, 70 patients were complicated with right to left shunt and 43 patients were the intrinsic type. After Valsalva maneuver, 27 patients were complicated with right to left potential type, including 33 patients with grade I shunt, 10 patients with grade II shunt, and 27 patients with grade III shunt. Among the 134 patients with cryptogenic stroke, 64 patients had no right to left shunt. The gender and age of the two groups were comparable ($p > 0.05$).

3.2. Single factor analysis

The influencing factors of cryptogenic stroke in patients with positive c-TCD were correlated with age, gender, and abnormal embolism scale scores ($p < 0.05$) (**Table 1**).

Table 1. Single factor influencing the positive rate of c-TCD in cryptogenic stroke patients

Factors		Total number	Positive number	Positive rate	χ^2/Z	p
Gender	Male	85	39	46%		
	Female	49	31	63%	3.764	0.039
Scores	< 4	17	6	35%		
	4-6	61	26	43%		
	> 6	56	38	68%	7.825	0.02
Age	< 40	16	9	56%		
	40-60	92	45	49%		
	> 60	26	16	62%	1.501	0.133
Hypertension	Yes	56	28	50%		
	No	78	42	54%	0.193	0.727
Diabetes	Yes	11	3	27%		
	No	123	67	54%	2.994	0.07
Smoking	Yes	63	28	44%	2.994	0.078

3.3. Logistic regression analysis

Using the logistic regression equation, it can be concluded that age, gender, and abnormal embolism scale scores are independent factors. With increasing age at each level, the proportion of positive foam test was calculated to be 3.21 times, and the proportion of positive foam test for female to male was calculated to be 2.25 times. The proportion of positive foam test was calculated to be 2.55 times with each grade increase in terms of the scores (**Table 2**).

Table 2. Logistic regression analysis

		B	S.E.	Wals	df	Sig.	Exp (B)	95% C.I. of exp (B) Lower limit	Upper limit
Step 1A	Age	1.189	.559	4.522	1	.033	3.284	1.098	9.829
	Gender	.851	.558	2.327	1	.127	2.342	.785	6.992
	Diabetes	-.733	.828	.783	1	.376	.480	.095	2.437
	Smoking	.025	.527	.002	1	.962	1.026	.365	2.878
	Scores	.835	.382	4.786	1	.029	2.305	1.091	4.870
	Constant	-5.133	2.037	6.349	1	.012	.006		
Step 3A	Age	1.166	.551	4.475	1	.034	3.209	1.089	9.451
	Gender	.810	.405	3.998	1	.046	2.249	1.016	4.977
	Scores	.937	.354	7.026	1	.008	2.552	1.277	5.103
	Constant	-5.304	1.696	9.784	1	.002	.005		

The incidence of complications among the patients in the research group was lower than that in the control group ($p < 0.05$) (**Table 3**).

4. Discussion

Exploring the etiology and pathogenesis of cryptogenic stroke can provide an important reference for its clinical diagnosis and treatment. In recent years, abnormal embolism and other factors have been gradually

found to be correlated to this disease. Abnormal embolism is the formation of thrombus at the right side of the heart or its distribution from the venous system. After falling off, it shunts from right to left and enters the systemic circulatory system through an abnormal arterial communicating branch or the atrioventricular notch, resulting in an embolism of the great arteries [3-4]. The causes of abnormal embolism include pulmonary arteriovenous malformation, atrial septal tumor, patent foramen ovale, etc. The early detection of the causes can reduce the incidence of stroke.

In this study, 134 patients with cryptogenic stroke were examined by c-TCD, and 70 cases showed positive results. This shows that c-TCD is a safe and an effective method to investigate cryptogenic stroke, which can significantly improve the detection rate of cryptogenic etiology, reduce the risk of misdiagnosis and missed diagnosis, as well as has a strong guiding significance for secondary prevention [5]. The analysis of c-TCD positive patients with cryptogenic stroke revealed that there was no difference in the positive rates of c-TCD between cryptogenic stroke and risk factors such as smoking, diabetes, and hypertension. However, in regard to gender difference and abnormal embolic scale scores, there was a significant difference in the positive rate of c-TCD [6]. In view of the results from this study, the influencing factors of cryptogenic stroke patients with positive c-TCD are related to age, gender, and abnormal embolism scale scores. For each grade increase in age, the proportion of positive foam test was calculated to be 3.21 times and the proportion of female to male was calculated to be 2.25 times. The proportion of positive foam test for the increase in scores for each grade was calculated to be 2.55 times. In other words, being female, older in age, and having a greater score in the abnormal embolism scale would result in a higher positive foaming test.

In the clinical diagnosis of cryptogenic stroke patients with suspected PFO, c-TCD can be performed first. After screening and determining the presence of PFO, transesophageal echocardiography can be carried out to determine the size of the gap and the anatomical relationship of the PFO. Moreover, c-TCD can be performed at bedside with high sensitivity, repeatability, and non-invasive advantages. It can be widely popularized in clinical practice as a screening method. It does not only reduce the pain experienced by patients to a large extent, but also increase their compliance.

In conclusion, female, old age, and higher scores obtained in the abnormal embolism scale are the influencing factors for cryptogenic stroke patients with positive c-TCD.

Project

The research belongs to the stage result of a project (Project plan number: 2021-SHFZKJK-5207).

Disclosure statement

The authors declare that there is no conflict of interest.

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