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Original Article

Prognostic value of thyroid Hormone T3 in patients with acute cerebral infarction

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Abstract: Objective: To explore the changes in thyroid T3 hormone levels and its prognostic value in patients with acute cerebral infarction. Methods: 58 patients with the first onset of acute cerebral infarction (B group) and 64 participants who underwent regular physical examination (A group) were recruited. According to the total T3 expression, the B group was further divided into two subgroups (normal- and low-expression groups). The 28-day survival rate was statistically analyzed using Kaplan-Meier survival curves. In addition, multi-variate Cox regression analysis was performed to validate independent prognostic factors of 28-day survival. The severity of patients' conditions in the normal- and low-expression subgroups was compared using the National Institutes of Health Stroke Scale. Results: T3 levels in A group were significantly higher than those in B group (P=*0.000*). There were 5, 11, and 14 patients with severe, moderate, and mild nerve function deficit in the group with normal T3 expression, respectively. While in the group with low T3 expression, the statistics were 14, 10, and 4, respectively and a statistically significant difference between the two groups was observed (P=*0.000*). Patients in the subgroup with low T3 expression had significantly lower 28-day survival rates than those in the subgroup with normal T3 expression (P=0.023). Single-variate Cox regression analysis showed that normal T3 expression levels, advanced age, and history of hypertension were prognostic factors, and the multifactor regression analysis revealed that normal T3 expression levels and age were independent prognostic factors for death resulting from acute cerebral infarction. Conclusion: In patients with acute cerebral infarction, the thyroid hormone level is downregulated in the blood and is considered an independent risk factor for 28-day survival.

Keywords: Acute cerebral infarction, serum, thyroid hormone, prognosis

Introduction

Acute cerebral infarction is the most common cerebrovascular disease in the aging population, and it is characterized by high morbidity, mortality, and disability rates [1, 2]. The major causes of acute cerebral infarction include the formation of a thrombus in the vessels that blocks the blood flow in the brain, which results in lesions and hypoxia in the blocked area, and this phenomenon contributes to the development of nerve dysfunction [3]. In the population aged between 15 and 54 years [4, 5], the mortality rate of cerebral infarction was as high as 49/1000000, and the incidence is gradually increasing, particularly in the aging population aged between 50 and 60 years. A variety of factors may induce the development of cerebral infarction, including the environment, diet, blood pressure, blood glucose levels, and fat in the blood [6]. Studies have shown that early diagnosis of patients with acute cerebral infarction can improve the patient's condition and prognosis [7, 8]. Thus, efficient diagnostic methods and an accurate judgment of the patients' condition are important for prognosis and improvement of the patients' health status.

The thyroid is the largest endocrine organ in the human body, and it can synthesize and release thyroid hormones via nerve stimulation on the receptor [9]. Evidence shows that thyroid hormone can promote growth and development as well as metabolism. Moreover, it can increase the excitability of the central nervous system and sympathetic nerves in humans [10]. Triiodothyronine (T3) and thyroxine (T4) are the major types of thyroid hormones, and mutual transformation sustains the dynamic equilibri-

um [11]. Recent studies have shown that changes in the thyroid hormone levels result in atrial fibrillation, cerebral venous thrombosis, hypertension, and moyamoya disease, which are risk factors of cerebral infarction [12, 13]. However, in the blood of individuals with acute cerebral infarction, the expression of T3 is significantly lower than that of healthy individuals [14]. However, whether T3 can be used as an indicator of prognosis in patients with acute cerebral infarction has not been reported in related literature.

Thus, this study aimed to investigate the changes in the T3 levels and its prognostic value in individuals with cerebral infarction, thus providing reference for clinical physicians.

Methods and materials

Clinical data of the patients

58 patients with the first onset of acute cerebral infarction but without thyroid diseases (B group) were recruited from January 2014 to May 2015. In B group, 39 patients were men and 19 were women aged between 47 and 82 years, and the average age was 61.84±6.30 years. All the patients underwent regular treatment. In addition, 64 participants aged between 45 and 80 years (with an average age of 62.29±5.11 years) who underwent regular physical examination during the same period were enrolled and included in A group. Of the participants in the control group (B group), 42 were men and 22 were women. All patients in B group were diagnosed in accordance with the diagnostic criteria revised during the Fourth National Cerebrovascular Diseases Conference [15]. This study had been approved by the ethics committee of Lanzhou University Second Hospital, and written informed consent was obtained from all the participants.

Inclusion and exclusion criteria

Inclusion criteria for patients in B group were as follows: patients aged >18 years; patients with no previous history of thyroid function disease, patients were diagnosed as ischemic stroke by head CT; the cerebral infarction occurred within 24 hours before seeking medical attention; patients had taken drugs that affected the thyroid within 2 months. Exclusion criteria were as follows: patients with malignant tumors, chronic infection, pulmonary thrombus, history of thyroid surgery, multiple endocrine diseases, taking thyroid or anti-thyroid drugs, gastrointestinal diseases; those who did not cooperate with the treatment or follow-up; and those with insufficient clinical data.

Examination items

Venous blood was drawn from the patients on the next day after onset, and the samples were then delivered to the clinical laboratory of Lanzhou University Second Hospital to determine serum T3 levels of the patients using radioimmunoassay. Low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) levels were measured using the Hitachi 7600 automatic biochemical analyzer, and white blood cell (WBC) count was assessed using the Sysmex XT-1800i hematology analyzer.

Outcome measures

Major outcome measures: The serum T3 levels of the patients in the two groups were assessed, and according to normal level values (0.92~2.79 nmol/L), B group was further divided into two subgroups (Normal- and low-expression groups) for statistical analysis of the 28-day survival rates and identification of the Kaplan-Meier survival curves. In addition, Cox regression analysis was performed to validate the independent prognostic factors for death resulting from acute cerebral infarction.

Other outcome measures: The severity of the patients' conditions in the normal- and low-expression subgroups was evaluated using the National Institute of Health Stroke Scale (NIHSS), and a score >15 indicated a severe nerve function deficit. Meanwhile, a score of 6-14 indicated a moderate deficit, and a score of 0-6 suggested a mild deficit [16].

Statistical analysis

The Statistical Package for the Social Science software, version 20.0, was used for data processing, and GraphPad Prism 7 was utilized for image preparation. Measurement data (mean ± standard deviation) of the two groups were compared with independent *t*-tests. Meanwhile, enumeration data and continuous variables

Table 1. Comparison of the clinical data between A and B group

Factor	A group (n=64)	B group (n=58)	t/χ^2	*P* value
Sex			0.036	0.850
Female	42 (65.63)	39 (48.15)		
Male	22 (34.38)	19 (32.76)		
Age (years)	61.84±6.30	62.29±5.11	0.431	0.668
BMI (kg/m^2)	22.54±1.35	22.68±1.48	0.546	0.586
Smoking history			6.405	0.011
Yes	32 (50.00)	42 (72.41)		
No	32 (50.00)	16 (27.59)		
History of alcoholism			0.544	0.461
Yes	8 (12.50)	10 (17.24)		
No	56 (87.50)	48 (82.76)		
History of hypertension			7.278	0.007
Yes	31 (48.44)	42 (72.41)		
No	33 (51.56)	16 (27.59)		
Diabetes history			0.581	0.446
Yes	32 (50.00)	25 (43.10)		
No	32 (50.00)	33 (56.90)		
WBC (10^9/L)	7.15±2.11	6.68±2.01	1.257	0.211
LDL-C (mmol/L)	1.82±0.48	3.15±0.86	10.675	0.000
TG (mmol/L)	1.20±0.15	1.57±0.22	10.940	0.000
TC (mmol/L)	2.88±0.84	4.95±0.65	15.109	0.000
HDL-C (mmol/L)	1.66±0.46	1.51±0.42	1.874	0.063

Table 2. T3 expression of A and B groups

Group	A group (n=64)	B group (n=58)	t value	*P* value
T3 (ng/mL)	1.84±0.38	0.99±0.46	11.166	0.000

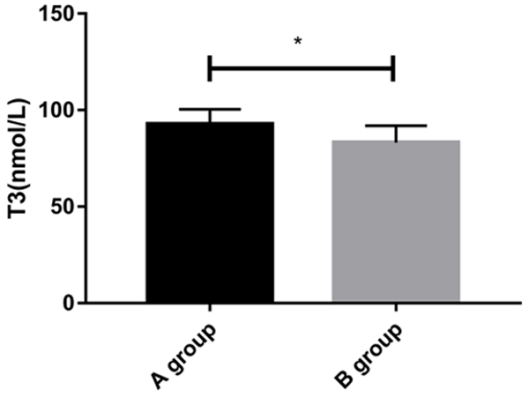

Figure 1. The T3 expression in the blood of A group was significantly higher than that of B group (P<0.05), indicating that there was a difference between the two groups (P<0.05).

were compared using chi-square tests and rank-sum tests, respectively. The Kaplan-Meier survival curves were identified to analyze the survival rates of the two groups with normal T3 expression and low T3 expression. We also performed one-way Cox regression analysis to validate the correlation between each potential variable and the mortality rate of the patients. In addition, multi-variate Cox regression analysis was performed to identify the independent prognostic variables that could be used to predict the mortality rate of the patients.

Results

Comparison of the clinical data between A and B groups

In this study, the clinical data of the two groups differed in terms of sex distribution, age, body mass index, history of smoking and drinking alcohol, hypertension, and diabetes mellitus (all P<0.05); however, LDL-C, TG, TC, and HDL-C levels were statistically different (P<0.05; **Table 1**).

T3 expression of A and B groups

Results showed that the expression of T3 in B group was significantly lower than that in A group. There was a difference between the two groups.t (P<0.05; **Table 2** and **Figure 1**).

NIHSS scores of the patients in B group

The average T3 expressions of B group was utilized to further classify them into two subgroups (normal-expression [n=30] group and low-expression [n=28] group). In the normal-expression group, 5, 11, and 14 patients presented with severe, moderate, and mild nerve function deficit, respectively. Meanwhile, in the low-expression group, 14, 10, and 4 patients had severe, moderate, and mild nerve function deficit, respectively; the difference was statistically significant (*P*<0.05; **Table 3**).

Table 3. NIHSS scores of the patients with normal and low T3 expressions (n [%])

Group	Severe neurological impairment	Moderate neurological impairment	Mild neurological impairment	χ^2	*P* value
Normal expression group (n=30)	5 (16.67)	11 (36.67)	14 (46.66)	9.640	0.002
Low expression group (n=28)	14 (50.00)	10 (35.71)	4 (14.29)		

Table 4. 28 day survival rates of patients with normal and low T3 expressions

Group	1 d	7 d	14 d	21 d	28 d
Normal expression group (n=30)	28 (93.33)	27 (90.00)	26 (86.67)	24 (80.00)	24 (80.00)
Low expression group (n=28)	25 (89.29)	20 (71.43)	19 (67.86)	19 (67.86)	14 (50.00)
χ^2	0.296	3.068	1.275	1.806	5.164
P value	0.586	0.080	0.259	0.179	0.023

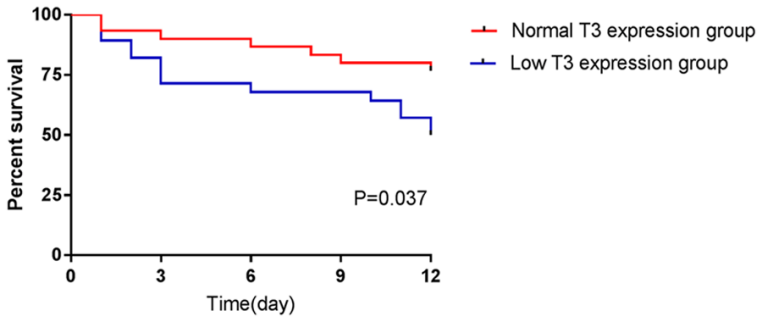

Figure 2. According to survival conditions, B group was further divided into the high- and low-expression subgroups. The survival condition of the high-expression subgroup was significantly higher than that of the low-expression subgroup (P<0.05), indicating that there was a difference between the two groups (P=0.023).

Analysis of the survival of patients

In the low-expression group, the patients had a significantly lower 28-day survival rate than those in the normal-expression group (P=0.023; **Table 4** and **Figure 2**).

Cox regression analysis

According to the one-way Cox regression analysis based on the collected data, normal T3 expression levels, advanced age, and hypertension were prognostic factors, and the multi-variate regression analysis showed that T3 levels (adjusted HR=2.325, 95% confidence interval [CI]: 1.848-2.846, P=0.023) and age (adjusted HR=7.229, 95% CI: 2.233-23.401, P=0.000) were independent prognostic factors (**Tables 4**-**6**).

Discussion

In this study, we assessed the serum T3 levels of patients with acute cerebral infarction, and results showed that the T3 levels in these patients were significantly lower than those in healthy individuals. Moreover, Jun et al. have found that T3 in the blood of patients with acute cerebral infarction is significantly down-regulated, which is also consistent with our results, and this may be caused by the blockage in the blood circulation of patients with acute cerebral infarction, inducing ischemia and hypoxia, which subsequently results in the massive release of cortisol and a decrease in 5'-deiodinase activity, inhibition of transformation of T4 to T3 in the peripheral organs, and down-regulation of T3 in the blood [14, 17]. Thus, T3 expression may be a potential observation index for patients with acute cerebral infarction.

The NIHSS is primarily used to evaluate the severity of the condition of a patient with cerebral stroke, and the NIHSS score is also a promising predictive indicator of cerebral stroke [18]. In this study, the average T3 expression in the blood of patients in the study group was used to further divide them into the normal- and low-expression subgroups to observe the distribution of the NIHSS scores in the patients of the two groups. Statistics showed that the ranked distribution of the NIHSS scores of the normal-expression subgroup was different from that in the low-expression subgroup, indicating that the patients with low T3 expression had poor prognosis. This is because the NIHSS score is positively correlated with the severity

Table 5. Cox single factor analysis

Factor	B	SE	Wald	Sig.	Exp(B)	95.0% CI
T3	1.155	0.444	6.778	0.009	3.175	1.331-7.577
Sex	0.204	0.483	0.178	0.673	1.226	0.476-3.160
Age	0.913	0.464	3.879	0.049	2.492	1.004-6.182
BMI	0.076	0.463	0.027	0.869	1.079	0.436-2.675
Smoking history	-0.484	0.450	1.157	0.282	0.616	0.255-1.489
History of alcoholism	0.444	0.513	0.750	0.386	1.559	0.571-4.259
History of hypertension	1.489	0.744	4.006	0.045	4.433	1.031-19.052
Diabetes history	-0.482	0.463	1.082	0.298	0.618	0.249-1.531
WBC	0.245	0.437	0.314	0.575	1.278	0.542-3.009
LDL	-0.371	0.441	0.706	0.401	0.690	0.291-1.639
TG	0.044	0.437	0.010	0.919	1.045	0.444-2.462
TC	0.192	0.437	0.192	0.661	1.211	0.514-2.853
HDL	0.376	0.441	0.727	0.394	1.457	0.613-3.460

Table 6. Cox multivariate analysis for survival rates

Factor	β	SE	Wald	Sig.	Exp(B)	95.0% CI
History of hypertension	1.182	0.758	2.432	0.119	3.260	0.738-14.399
Age	1.978	0.599	10.892	0.000	7.229	2.233-23.401
T3	2.190	0.593	4.254	0.023	2.325	1.848-2.846

of cerebral infarction, and increases with the severity of the patient's condition. However, we found that T3 expression also increased with the increase in NIHSS scores. Therefore, it is concluded that T3 is associated with the degree of disease in patients with cerebral infarction.

Glymour et al. have found that an NIHSS score >16 may indicate a significantly high mortality rate among patients with acute cerebral infarction patients [19]. Thus, we assessed the survival curves of the patients within 28 days and found that patients with low T3 expression had a higher mortality rate than healthy individuals with a high T3 expression. Thus, T3 expression is significantly correlated to the prognosis of patients with acute cerebral infarction. Hence, the one-way Cox regression analysis revealed that T3 level, age, and hypertension were prognostic factors. Meanwhile, according to the multi-variate Cox regression analysis, T3 level and age were independent prognostic factors, and this has been confirmed in the study of Scherrer et al. [20]. The main reason is that man's various organs and corresponding physiological functions are gradually declining, which slows down the metabolism of the body. Due to the aggravating trend of aging population in numerous developed and some developing countries, people have been focusing on the life and safety of the elderly population [21, 22]. Acute cerebral infarction is a common disease in the aging population, and precautions should be taken to prevent the development of the disease. The measurements of T3 in the blood of patients with acute cerebral infarction showed that T3 expression was an independent prognostic factor, which can be used as a novel potential index for evaluating prognosis.

However, this study had a small sample size. Whether the small sample size affects the correctness of our results remains to be verified. Secondly, we have not explored and identified the specific mechanisms, and did not conduct dynamic monitoring of T3 levels. Therefore, we will combine the data of multiple research centers for statistics, and dynamically monitor the T3 expression of patients, and improve the methods to explore its specific mechanism and verify the correctness of our study.

In conclusion, thyroid hormone level is downregulated in the blood of patients with acute cerebral infarction; thus, it can be used as an independent prognostic factor of acute cerebral infarction.

Disclosure of conflict of interest

None.

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