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***Observational Study***

**Relationship between β-amyloid protein 1-42, thyroid hormone levels and the risk of cognitive impairment after ischemic stroke**

Mao L *et al*. Relationship between Aβ1-42, T3 and PSCI

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**Abstract**

***BACKGROUND***

Post-stroke cognitive impairment (PSCI) is not only a common consequence of stroke but also an important factor for adverse prognosis of patients. Biochemical indicators such as blood lipids and blood pressure are affected by many factors, and the ability of evaluating the progress of patients with PSCI is insufficient. Therefore, it is necessary to find sensitive markers for predicting the progress of patients and avoiding PSCI. Recent studies have shown that β-amyloid protein 1-42 (Aβ1-42) and thyroid hormone levels are closely related to PSCI, which may be the influencing factors of PSCI, but there are few related studies.

***AIM***

To investigate the relationship between serum levels of Aβ and thyroid hormones in acute stage and PSCI and its predicted value.

***METHODS***

A total of 195 patients with acute cerebral infarction confirmed from June 2016 to January 2018 were enrolled in this study. Baseline data and serological indicators were recorded to assess cognitive function of patients. All patients were followed up for 1 year. Their cognitive functions were evaluated within 1 wk, 3 mo, 6 mo and 1 yr after stroke. At the end of follow-up, the patients were divided into PSCI and non-PSCI according to Montreal cognitive assessment score, and the relationship between biochemical indexes and the progression of PSCI was explored.

***RESULTS***

Compared with patients with non-PSCI, the levels of Aβ1-42, triiodothyronine (T3) and free thyroxin were lower in the patients with PSCI. Repeated measures analysis of variance showed that the overall content of Aβ1-42 and T3 in PSCI was also lower than that of the non-PSCI patients. Further analysis revealed that Aβ1-42 (*r* = 0.348), T3 (*r* = 0.273) and free thyroxin (*r* = 0.214) were positively correlated with disease progression (*P* < 0.05), suggesting that these indicators have the potential to predict disease progression and outcome. Cox regression analysis showed that Aβ1-42 and T3 were important factors of PSCI. Then stratified analysis showed that the lower the Aβ1-42 and T3, the higher risk of PSCI in patients who were aged over 70, female and illiterate.

***CONCLUSION***

Aβ1-42 and T3 have the ability to predict the progression of PSCI, which is expected to be applied clinically to reduce the incidence of PSCI and improve the quality of life of patients.

**Key words:** Post-stroke cognitive impairment; Triiodothyronine; β-amyloid protein; Prognosis; Montreal cognitive assessment; Free thyroxin

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**Core tip:** Post-stroke cognitive impairment (PSCI) has become a deepening public health problem. PSCI diagnosis is mostly based on clinical manifestations, neuroimaging and a series of neuropsychological tests. However, early diagnosis is difficult because the implementation of the above-mentioned scheme depends on the cooperation of patients. Therefore, it is necessary to identify early biomarkers. Our study found that β-amyloid protein 1-42 and triiodothyronine can dynamically monitor the patient’s clinical status and correlates with progression of the disease. It is suggested that β-amyloid protein 1-42 and triiodothyronine have the ability to predict the progress of PSCI and can be broadly applied.

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**INTRODUCTION**

With its high morbidity, disability and mortality, stroke is one of the major health-threatening diseases[1-3]. Besides causing motor and sensory disorders, stroke can also result in cognitive impairment, including mild post-stroke cognitive impairment (PSCI) and dementia, which seriously affects the daily activities of patients and brings great burden to society[4,5]. Epidemiological data show that more than half of stroke patients have different degrees of PSCI, and about one-third of patients develop severe PSCI or even dementia at 3 mo after onset of the disease, but there is no specific treatment for this disease[6-8]. Thus, early detection and intervention of PSCI has become an important and urgent social need. Extensive experimental data show that the main factors affecting PSCI include hypertension, diabetes mellitus, hyperlipidemia and other vascular risk factors as well as demographic factors such as age and education level[9-11]. These high-risk factors suggest the occurrence of PSCI, but the relevant biochemical indicators are interfered by many factors and have low specificity, which is not suitable for early assessment and prediction of prognosis[12,13]. The Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination are the common neuropsychological scales of early screening and evaluating for PSCI and widely used in long-term follow-up of patients because of their good reliability and validity in PSCI large sample epidemiological studies and clinical trials[14,15]. However, different scales have their own limitations. It is difficult to perform accurate screening with a single application, and the combination of multiple scales will increase the burden on patients. Additionally, the neuropsychology scale has certain subjectivity and requires other clinical diagnostic indicators.

Recent research found that PSCI is closely related to the core pathological changes of Alzheimer’s disease, suggesting that both may have common diagnostic biomarkers[16,17]. β-amyloid protein (Aβ) is the main component of senile plaques characterized by Alzheimer’s disease[18]. Previous studies have suggested that serum Aβ may be an independent cerebrovascular risk factor, which can indicate vascular injury during dementia[19,20]. Yu *et al*[21] found that Aβ not only exists in Alzheimer’s disease but also has a close relationship with the progress of stroke. It shows a good application prospect in early diagnosis and judgment of the severity of dementia. Furthermore, the influence of metabolic factors such as thyroid hormone levels on PSCI has been observed[22]. Wang *et al*[23] confirmed that thyroid function may affect the cognitive level of patients by regulating brain energy metabolism and signal transduction. Nevertheless, little research has been done on the relationship between Aβ, thyroid hormone levels and PSCI, and further studies are needed to identify the value of these indicators assessing the risk of cognitive disorders after acute ischemic stroke.

Therefore, this study intends to analyze the relevant indicators of patients with acute cerebral infarction and to clarify the correlation between each index and PSCI.

**MATERIALS AND METHODS**

***Participants***

A total of 195 patients with acute cerebral infarction confirmed from June 2016 to January 2018 were enrolled in this study. There were 109 males and 86 females, aged from 60 to 80 years, and the average age was (69.38 ± 10.05) years. The diagnostic criteria were in line with the “Diagnostic Points for Various Cerebrovascular Diseases” formulated by the Fourth National Cerebral Vascular Disease Conference in 1995, and all patients were diagnosed by cranial magnetic resonance imaging or computed tomography. The inclusion criteria were: (1) acute ischemic stroke occurring within 7 d before admission; (2) right-handed; and (3) new cases. The exclusion criteria were: (1) aphasia, severe hearing or visual impairment; (2) thyroid disease and other endocrine diseases; (3) severe condition after cerebral infarction and unconsciousness unable to cooperate with examination and cognitive assessment; (4) with consciousness obstacle prior to the illness onset [the National Institutes of Health Stroke Scale (NIHSS) > 10] or other diseases associated with cognitive impairment in patients; (5) suffering from abnormal function of the heart, lungs, liver or systemic disease, estimated survival < 1 year; and (6) have a history of mental illness or behavioral disorders.

The patients and their guardians participated in the study voluntarily and provided written informed consent. The study was approved by the Ethics Committee of Changzheng Hospital, the PLA Naval Medical University.

***Clinical basic information***

Patient data were collected within 3-5 d after admission, including demographic data (gender, age, body mass index and education level), lifestyle (smoking and drinking) and health status (systolic blood pressure; diastolic blood pressure, atrial fibrillation, hypertension, hyperlipidemia, diabetes, history of stroke/transient ischemic attack and myocardial infarction). Meanwhile, NIHSS scale was used to determine the neural function of patients (the higher the score, the more severe the neurologic impairment).

***Imageology examination***

Patients with acute cerebral infarction were tested by Siemens MAGNETOM Skyra, (Germany) and their infarct location (anterior circulation infarction or posterior circulation infarction) was recorded (Figure 1). Pulliino formula was used to calculate the size of the lesion, and TOAST classification was performed.

***Biochemical tests***

Blood samples of patients were collected within 24 h of admission. Three milliliters of venous blood was collected after fasting, centrifuged at 3000 r/min for 10 min to collect serum and then stored at -80 °C. Biochemical indexes including total cholesterol, triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein, hypersensitive C-reactive protein and homocysteine were detected by AU-400 fall-automatic biochemical analyzer. ELISA was used to determine Aβ, and the kit was provided by Shanghai Hengfei Biotechnology Co., Ltd. Chemiluminescence immunoassay was applied to analyze the level of triiodothyronine (T3), thyroxin (T4), free triiodothyronine, free thyroxin (FT4) and thyrotropin, and the kit was purchased from Beijing Baioleibo Technology Co., Ltd.

***Scale measurement and definition of PSCI***

The cognitive function scale was measured using the MoCA within 1 wk, 3 mo, 6 mo and 1 yr after the onset of the disease. The assessment areas included visual spatial ability, executive function, short-term memory and recall, attention, language and direction. The MoCA, with a total score of 30, showed high sensitivity in screening for mild cognitive impairment, and patients should take no more than 10 min to complete the assessment.

***Follow-up and quality control***

The patients were treated routinely and followed up for 1 year, starting at 14 d after treatment and then followed monthly. All investigators were trained uniformly, and pre-survey was conducted before formal investigation. The data records were independently conducted by two individuals. The endpoint was defined as the patient with a MoCA score < 26 were the PSCI group), and the patients with a MoCA score < 26 were the non-PSCI group (+ 1 was added to the patient’s for an education level below 12 years).

The progress of the patient’s condition was evaluated compared with the baseline. If the MoCA score decreased by more than 4 points, then progress was noted as aggravation. If the MoCA score decreased by less than 3 points, then progress was noted as stable. If the MoCA score increased by more than 4 points, then progress was noted as improvement. All ischemic stroke outcomes were assessed by a professional neurologist.

***Statistical analysis***

The data were analyzed by SPSS16.0 statistical software. Continuous variables conforming to normal distribution and homogeneity of variance were tested by independent sample *t* test, and the composition ratio was analyzed by Chi-square test/Fisher exact probability method. Repeated measures analysis of variance was used to compare the biochemical indicators in the two groups within 1 wk, 3 mo, 6 mo and 1 yr after stroke. The relationship between the biochemical indicators and the progression of the disease was evaluated by Spearman correlation analysis. Cox regression analysis was used to calculate the relative risk of each influencing factor.

**RESULTS**

***Baseline data analysis of two groups***

At the end of follow-up, a total of seven cases were lost to follow-up. According to the MoCA score, 72 cases with mild cognitive impairment were regarded as the PSCI group, while the remaining 116 cases were regarded as the non-PSCI group. Analysis of baseline data of admission between the two groups showed that there were more patients who were female, had a history of stroke/transient ischemic attack and had atrial fibrillation in the PSCI group than in the non-PSCI group (*P* < 0.05). In addition, compared with the non-PSCI group, age, TG, LDL and the NIHSS score at admission were higher in the PSCI group, while the education level, Aβ1-42, T3 and FT4 were lower in the PSCI group than in the non-PSCI group. The difference was significant (*P* < 0.05, Table 1).

***Changes of biochemical indexes in two groups at different time points***

The follow-up results showed that 15 out of 188 patients had PSCI at the 14th day after treatment, and the highest incidence was observed at 3 mo. In the PSCI group, 48 patients suffered from PSCI, which was significantly relieved at 6 mo and continued to recover at the end of the follow-up.

The results of repeated measures analysis of variance showed that the levels of Aβ1-42 and T3 in the PSCI group decreased first and then increased at different time points, reaching a low level at 3 mo, stabilizing at 6 mo after stroke and then slowly increasing. By contrast, the levels of Aβ1-42 and T3 in the non-PSCI group continuously, steadily and slowly increased. Aβ1-42 and T3 reached the highest level within 1 wk of onset, and then decreased slightly, showing a steady trend. The level of Aβ1-42 and T3 in the PSCI group were lower in the 3rd and 6th month after onset. The overall levels of Aβ1-42 (*FBetween groups* = 4.782, *PBetween groups* = 0.011) and T3 (*FBetween groups* = 6.069, *PBetween groups* < 0.001) in the PSCI group was also lower than those in the non-PSCI group. The changes of FT4 level in the two groups were analyzed, and the results revealed that the FT4 content of both groups increased continuously with time, but there was no significant difference between the two groups as a whole (*FBetween groups* = 1.724, *PBetween groups* = 0.195, Table 2).

***Relationship between Aβ1-42, thyroxine levels and disease progression***

During the follow-up period, the progression of the disease was aggravated in 77, stable in 65 patients and improved in 46 patients. The relationships between Aβ1-42, T3, FT4 and disease progression (improvement, stabilization, and aggravation) were analyzed by Spearman rank correlation analysis, and the results are shown in Table 3. Aβ1-42, T3 and FT4 were positively correlated with disease progression (*P* < 0.05). Patient’s condition improved with the increase of Aβ1-42, T3 and FT4 levels (*P* < 0.05).

Comparing the correlation degree of the above indicators, the correlation between Aβ1-42 and disease progression was better (*r* = 0.348), followed by T3 (*r* = 0.273).

***Cox analysis of the effect of Aβ1-42 and thyroxine levels on PSCI***

Whether the patient has PSCI or not was taken as a dependent variable (MoCA score < 26 points = 1, ≥ 26 = 0), and Aβ1-42, T3 and FT4 levels were included in the Cox regression equation. The degree of influence of the above indicators on the risk of PSCI in univariate Cox (unadjusted), Model I (adjusted for age and gender), Model II (adjusted for age, gender, body mass index, education levels, smoking, drinking and history of disease) and Model III (adjusted for NIHSS, LDL and TG in addition to the confounders that were adjusted for in Model II) was calculated.

Univariate Cox regression analysis showed that Aβ1-42, T3 and FT4 had an effect on the occurrence of PSCI in patients and that they were protective factors. After adjusting age and gender, these above indicators were still important as influencing factors for the occurrence of diseases (*P* < 0.05). There was a regression relationship between Aβ1-42, T3 and cognitive function of patients in Model III (*P* < 0.05). After further adjustment for NIHSS score, LDL, TG and other factors, we found that the increase of Aβ1-42 and T3 could reduce the risk of PSCI (*P* < 0.05, Table 4).

***Stratified analysis of Aβ1-42, T3 and risk of PSCI***

As shown in Table 5, the relationship between Aβ1-42, T3 and PSCI were further analyzed in different age, gender and educational level groups. After adjustment for age, gender, education level, body mass index, smoking, drinking, history of disease, NIHSS, LDL and TG, the results showed that the lower the Aβ1-42 and T3 levels, the higher the risk of PSCI in patients who were aged over 70, female and illiterate.

**DISCUSSION**

Currently, comprehensive treatment is the main treatment for PSCI in the clinic. Traditional rehabilitation training is suitable for patients with early and mild illness. Those with severe illness can be treated with adjuvant drugs. However, most drugs are aimed at people with Alzheimer’s disease and vascular cognitive impairment, and there are few drugs that specifically target PSCI[24]. It is worth noting that PSCI itself has a high heterogeneity. The disease tends to develop dynamically, and the early symptoms are not obvious and easy to ignore. Therefore, the search for sensitive predictive markers and early detection of PSCI are essential for the improvement of PSCI patients.

In this study, we compared the baseline data of the PSCI patients with that of the non-PSCI patients and found that Aβ1-42, LDL, TG, T3 and FT4 levels were closely related to the risk of PSCI, which had the potential to evaluate the prognosis of stroke patients. Aβ1-42 is one of the important markers of the development of Alzheimer’s disease and vascular dementia. A large accumulation of Aβ1-42 in the brain can cause apoptosis and cognitive impairment, leading to a cascade of neuron injury and death and amplifying inflammation[25]. An increasing amount of evidence indicates that Aβ is closely related not only to Alzheimer's disease but also to cerebral ischemia, suggesting that Aβ may be a risk factor for stroke and play an important role in the process of PSCI.

Previous studies have also reported that atrial fibrillation is associated with the degree of severity of stroke, poor prognosis and mortality during long-term follow-up of stroke patients[26-28]. Even in atrial fibrillation patients without a history of stroke, their cognitive function sharply declines. Therefore, appropriate cardiac assessment and anticoagulation therapy should be given priority to these patients. This study also showed that the location and cause of the lesion had no statistically significant effect on the occurrence of PSCI. It may be due to the disease subtype, the time of cognitive assessment and other factors, which affect the credibility of the index[29,30]. It is limiting to analyze the prognosis of stroke patients only by the location of stroke, and comprehensive analysis should be made in combination with factors such as stroke volume and number.

A longitudinal study showed that the prevalence of severe cognitive impairment at 2 wk, 3 mo and 6 mo after stroke was 16.3%, 32.0%, and 13.6%-31.8%, respectively[31]. Studies from Britain and France found that the incidence of cognitive impairment 3 mo after stroke was 39% and 47.3%, respectively[32,33]. After a 1-year follow-up of stroke patients in this study, we also found that the incidence rate was the highest at 3 mo after onset of the disease and gradually recovered at 6 mo, which accorded with the above conclusion. This suggests that the management of patients should be strengthened 3 to 6 mo after stroke in order to identify and prevent the occurrence of PSCI as soon as possible. Moreover, the results of repeated measurements of variance analysis suggested that the overall content of Aβ1-42 and T3 in the PSCI group was lower than that in non-PSCI group, suggesting that the changes in Aβ1-42 and T3 after stroke may be related to disease progression, and both of them can dynamically monitor and evaluate the risk of disease for a long time. However, due to the impact of subsequent changes in indicators, there is a need to expand the analysis.

After further evaluation of the relationship between Aβ1-42, T3, FT4 and the disease progression, Spearman analysis showed that each index correlated with the patient’s disease progression and had a certain clinical value in indicating the severity of the disease and prognosis. Then, we performed a regression analysis of the relationship between each indicator and the risk of PSCI. Because of the high correlation among independent variables, multiple models were used to correct the related factors. The results show that both Aβ1-42 and T3 were important influencing factors for the occurrence of the disease, regardless of whether the confounding factors were adjusted or not. This indicates that Aβ1-42 and T3 had a good application prospect in evaluating the occurrence and development of PSCI.

According to the conclusion of Chen *et al*[34], the mechanism of T3 changes after stroke may be that the decrease of cerebral perfusion damages the blood-brain barrier and affects the level of organic anion transporting polypeptide in epithelial cells, causing the decline of peripheral thyroid hormone responsible for transporting, which changes the content of T3 in brain[34]. Conversely, the decrease of thyroid hormone level will also affect cerebral blood flow perfusion, energy metabolism and so on, leading to diffuse neurological dysfunction and cognitive decline[35]. A stratified analysis of the level Aβ1-42, T3 and risk of PSCI found that the lower the Aβ1-42 and T3 levels, the higher risk of PSCI in patients who were aged over 70, female and illiterate. Those studies at home and abroad have confirmed that the age, gender and education level are high risk factors for stroke, which is consistent with this result.

A prospective research method was applied in this study, and the collected data had good reliability and persuasiveness. However, the weaknesses of this study are a short follow-up time, small number of included research factors and insufficient extrapolation.

In conclusion, Aβ1-42 and T3 have the ability to predict progression of PSCI and are expected to be applied clinically to reduce the incidence of PSCI and improve the quality of life of patients.

**ARTICLE HIGHLIGHTS**

***Research background***

Acute ischemic stroke is the second most common cause of cognitive impairment and dementia in recent years. According to statistics, more than 64% of the patients after stroke show different degrees of cognitive impairment, and about 25% of stroke survivors suffer from dementia within 12 mo after stroke. Early monitoring is very important for clinical assessment of the severity and prognosis of ischemic stroke. Recent studies and epidemiological investigations have shown that the deposition of β-amyloid protein (Aβ) is associated with vascular risk factors and plays an important role in the development of post-stroke cognitive impairment. In addition, it has the advantages of invasiveness, small variability and good stability and has a good application prospect. However, the conclusions of the relationship between Aβ and post-stroke cognitive impairment (PSCI) have not been unified, and there are few related studies.

***Research motivation***

The commonly used tools for detecting cognitive function include neuropsychological scales, related imaging and cerebrospinal fluid examinations. Neuropsychological scales are limited by their clinical application due to a variety of factors and the need for higher expertise. The cost of imaging examination is relatively high, and its accuracy is related to the level of medical facilities. Therefore, the discovery of effective biomarkers may increase the efficiency of diagnosis and treatment of PSCI. Aβ is considered to be the common pathway of vascular dementia induced by various causes, which can lead to a cascade reaction of neuron injury. More and more studies have shown that Aβ1-42 is associated with PSCI, but there is no direct correlation between the two.

***Research objectives***

The purpose of this study is to explore the relationship between serum Aβ1-42, thyroid hormone level and PSCI and its predictive effect on this disease and to understand the influence of other possible risk factors on PSCI.

***Research methods***

A total of 195 patients with acute cerebral infarction were followed up for 1 year and grouped according to the Montreal Cognitive Assessment score. We analyzed the difference of clinical data and Aβ1-42 and thyroid hormone between the two groups. The changes of Aβ1-42 and thyroid hormone with time after onset were analyzed by repeated measurement variance analysis, and the relationship between the above indicators and the progression of the disease was explored. COX regression and stratified analysis were used to evaluate the effects of Aβ1-42 and thyroid hormone on PSCI and other possible risk factors.

***Research results***

Our results showed that the prevalence of PSCI was highest at 3 mo after stroke and gradually decreased at 6 mo after stroke. We found that Aβ1-42, triiodothyronine (T3) and free thyroxin in patients with PSCI were lower than those with non-PSCI, and the above indicators were correlated with disease progression. Furthermore, Cox regression analysis revealed that Aβ1-42 and T3 were the factors influencing the development of disease, and the higher the Aβ1-42 and T3 levels, the lower the risk of disease.

***Research conclusions***

Aβ1-42 and T3 play an important role in the development of PSCI. Low levels of Aβ1-42 and T3 at the acute phase of ischemic stroke is the predictor of PSCI, and a higher education level may help to reduce the risk of PSCI.

***Research perspectives***

Currently, most of the studies on the biological markers of cognitive impairment are related to cerebrospinal fluid markers, and most of them are single predictive indicators. Therefore, there are some disadvantages in clinical practicability, sensitivity and specificity. This study analyzed the predictive ability of serum Aβ1-42 and thyroid hormone levels in cognitive impairment after ischemic stroke, improving the diagnostic rate of patients with PSCI. It provided reference for the prevention and treatment of PSCI and has potential clinical application value.

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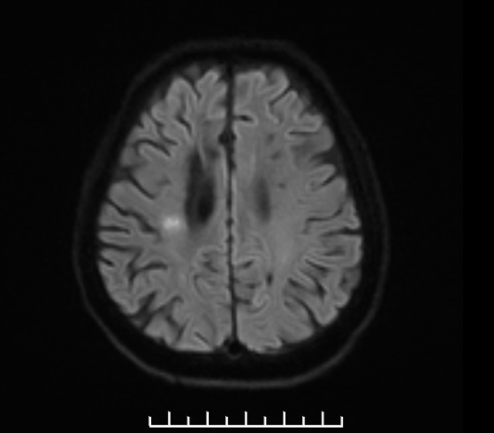
Grade A (Excellent): 0

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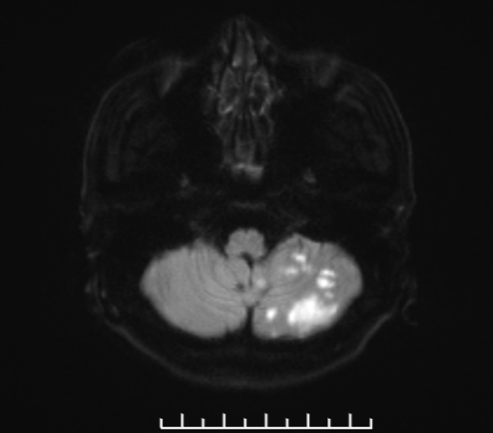
Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0



A



B

**Figure 1 Magnetic resonance imaging images of the infarct location of the patient with cerebral infarction.** A: Patient with anterior circulation infarction; B: Patient with posterior circulation infarction.

**Table 1 Baseline clinical characteristics in non-post stroke cognitive impairment and post stroke cognitive impairment patients, *n* (%)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **PSCI, *n* = 72** | **Non-PSCI, *n* = 116** | | ***P* value** |
| Age in yr | 73 (66-80) | 65 (60-74) | | < 0.001 |
| Gender, male/female | 38/34 | 79/37 | | 0.027 |
| BMI as kg/m2 | 24.5 ± 2.6 | 23.8 ± 2.7 | | 0.081 |
| Education levels |  | |  | 0.011 |
| Illiterate | 26 (36.1) | 24 (20.7) | |  |
| Primary school | 32 (44.4) | 48 (41.4) | |  |
| Postsecondary school | 14 (19.4) | 44 (37.9) | |  |
| Smoking | 13 (18.1) | 26 (22.4) | | 0.449 |
| Drinking | 8 (11.1) | 17 (14.7) | | 0.448 |
| SBP as mmHg | 152 ± 24 | 147 ± 26 | | 0.189 |
| DBP as mmHg | 85 ± 12 | 83 ± 10 | | 0.219 |
| TC as mmol/L | 4.54 ± 0.78 | 4.58 ± 0.72 | | 0.720 |
| TG as mmol/L | 1.48 ± 0.57 | 1.31 ± 0.41 | | 0.019 |
| HDL as mmol/L | 1.19 ± 0.17 | 1.12 ± 0.22 | | 0.204 |
| LDL as mmol/L | 2.85 ± 0.71 | 2.34 ± 0.76 | | < 0.001 |
| Aβ1-42 as pg/mL | 363.0 ± 37.8 | 402.2 ± 35.3 | | < 0.001 |
| hs-CRP as mg/L | 4.8 ± 4.6 | 6.2 ± 7.1 | | 0.138 |
| Hcy as µmol/L | 15.8 ± 8.2 | 15.0 ± 8.6 | | 0.529 |
| T3 asnmol/L | 1.23 ± 0.59 | 1.47 ± 0.77 | | 0.025 |
| T4 asnmol/L | 117.2 ± 26.4 | 110.5 ± 21.4 | | 0.058 |
| FT3 aspmol/L | 4.68 ± 0.85 | 4.42 ± 0.93 | | 0.056 |
| FT4 as pmol/L | 13.03 ± 2.26 | 16.47 ± 3.84 | | <0.001 |
| TSH as mU/L | 1.22 ± 0.64 | 1.41 ± 0.75 | | 0.076 |
| History of disease | | | | |
| Hypertension | 25 (34.7) | 37 (31.9) | | 0.674 |
| Hyperlipidemia | 3 (4.2) | 9 (7.8) | | 0.284 |
| Diabetes | 16 (22.2) | 28 (24.1) | | 0.750 |
| Stroke/TIA | 19 (26.4) | 17 (14.7) | | 0.041 |
| Myocardial infarction | 2 (2.8) | 3 (2.6) | | 0.930 |
| Atrial fibrillation | 9 (12.5) | 5 (4.3) | | 0.037 |
| NIHSS score on admission | 7.2 ± 3.7 | 5.1 ± 2.9 | | < 0.001 |
| Cerebral infarction volume in cm3 | 11.14 ± 2.25 | 10.86 ± 1.98 | | 0.372 |
| Lesion location | | | | |
| Posterior circulation | 16 (22.2) | 33 (28.4) | | 0.313 |
| TOAST |  |  | | 0.890 |
| Large-artery atherosclerosis | 39 (54.2) | 58 (50) | |  |
| Cardioembolism | 6 (8.3) | 8 (6.9) | |  |
| Small-artery occlusion Lacunar | 21 (29.2) | 37 (31.9) | |  |
| Other determined etiology | 5 (6.9) | 9 (7.8) | |  |
| Undetermined etiology | 1 (1.4) | 4 (3.4) | |  |
| Medications during hospitalization | | | | |
| Hypoglycemic | 13 (18.1) | 23 (19.8) | | 0.759 |
| Antihypertensive | 35 (48.6) | 53 (45.7) | | 0.681 |
| Lipid-lowering drugs | 54 (75.0) | 81 (69.8) | | 0.411 |
| Antiplatelet | 65 (90.3) | 104 (89.7) | | 0.888 |

Data are presented as mean ± SD or median (interquartile range). PSCI: Post stroke cognitive impairment; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TC: Total cholesterol; TG: Triglyceride; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; Aβ1-42: β-amyloid protein1-42; hs-CRP: Hypersensitive C-reactive protein; Hcy: Homocysteine; T3: Triiodothyronine; T4: Thyroxin; FT3: Free triiodothyronine; FT4: Free thyroxin; TSH: Thyrotropin; TIA: Transient ischemic attack; NIHSS: National Institutes of Health Stroke Scale.

**Table 2 Difference of biochemical indexes in two groups at different time points**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable group** | **1st week** | **3rd month** | **6th month** | **1st year** |
| Aβ1-42 in pg/mL | | | | |
| PSCI, *n* = 72 | 363.0 ± 37.8 | 356.1 ± 37.5 | 360.7 ± 32.2 | 372.5 ± 38.6 |
| Non-PSCI, *n* = 116 | 402.2 ± 35.3 | 404.8 ± 32.6 | 411.4 ± 36.5 | 428.1 ± 40.9 |
| T3 in nmol/L | | | | |
| PSCI, *n* = 72 | 1.23 ± 0.59 | 1.17 ± 0.62 | 1.38 ± 0.55 | 1.45 ± 0.67 |
| Non-PSCI, *n* = 116 | 1.47 ± 0.77 | 1.49 ± 0.85 | 1.46 ± 0.72 | 1.52 ± 0.64 |
| FT4 in pmol/L | | | | |
| PSCI, *n* = 72 | 13.03 ± 2.26 | 13.15 ± 2.14 | 13.79 ± 1.57 | 14.28 ± 2.19 |
| Non-PSCI, *n* = 116) | 16.47 ± 3.84 | 16.23 ± 3.21 | 16.58 ± 4.04 | 17.67 ± 3.18 |

Data are presented as mean ± standard deviation. Aβ1-42: *FBetween groups* = 4.782, *PBetween groups* = 0.011; T3: *FBetween groups* = 6.069, *PBetween groups* < 0.001; FT4:*FBetween groups* = 1.724, *PBetween groups* = 0.195. PSCI: Post stroke cognitive impairment; Aβ1-42: β-amyloid protein1-42; T3: Triiodothyronine; FT4: Free thyroxin.

**Table 3 Analysis of the correlation between indicators and disease progression**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Montreal Cognitive Assessment** | | | ***r*** | ***P* value** |
| **Aggravation, *n* = 77** | **Stable condition, *n* = 65** | **Improvement, *n* = 44** |
| Aβ1-42 in pg/mL | 358.6 ± 38.7 | 364.7 ± 33.9 | 392.5 ± 36.4 | 0.348 | < 0.001 |
| T3 in nmol/L | 1.19 ± 0.75 | 1.42 ± 0.66 | 1.48 ± 0.61 | 0.273 | < 0.001 |
| FT4 in pmol/L | 14.03 ± 2.86 | 15.15 ± 3.04 | 16.58 ± 2.42 | 0.214 | 0.005 |

Data are presented as mean ± standard deviation. Aβ1-42: β-amyloid protein1-42; T3: Triiodothyronine; FT4: Free thyroxin.

**Table 4 Effects of indicators on patients with post stroke cognitive impairment**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Aβ1-42** | **T3** | **FT4** |
| Unadjusted | | | |
| RR | 0.658 | 0.741 | 0.582 |
| 95% CI | 0.427-0.933 | 0.385-0.929 | 0.306-0.884 |
| *P* value | 0.022 | 0.036 | 0.017 |
| Model I | | | |
| RR | 0.932 | 0.895 | 0.918 |
| 95% CI | 0.852-0.936 | 0.876-0.982 | 0.923-0.994 |
| *P* value | 0.033 | 0.028 | 0.019 |
| Model II | | | |
| RR | 0.684 | 0.673 | 0.825 |
| 95%CI | 0.501-0.846 | 0.337-0.812 | 0.762-1.109 |
| *P* value | 0.009 | 0.017 | 0.092 |
| Model III | | | |
| RR | 0.282 | 0.430 | 0.748 |
| 95%CI | 0.258-0.833 | 0.332-0.918 | 0.747-1.116 |
| *P* value | 0.012 | 0.038 | 0.116 |

Model I: Adjusted for age and gender; Model II: Adjusted for age, gender, body mass index, education levels, smoking, drinking and history of disease; Model III: Adjusted for National Institutes of Health Stroke Scale, low-density lipoprotein, triglyceride in addition to the confounders that were adjusted for in Model II. Aβ1-42: β-amyloid protein1-42; T3: Triiodothyronine; FT4: Free thyroxin; RR: Relative risk; CI: Confidence interval.

**Table 5 Association between β-amyloid protein 1-42, triiodothyronine levels and post stroke cognitive impairment stratified by age, gender and education levels**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variable** | **Aβ1-42** | | | **T3** | | |
| **RR1** | **95%CI** | ***P* value** | **RR1** | **95%CI** | ***P* value** |
| Age in yr | | | | | | |
| < 70 | 0.982 | 0.437-2.188 | 0.173 | 0.371 | 0.208-0.663 | 0.001 |
| ≥ 70 | 0.416 | 0.290-0.612 | < 0.001 | 0.319 | 0.139-0.731 | 0.007 |
| Gender | | | | | | |
| Male | 0.794 | 0.328-1.901 | 0.075 | 0.618 | 0.249-1.527 | 0.298 |
| Female | 0.537 | 0.352-0.846 | 0.028 | 0.472 | 0.270-0.794 | 0.005 |
| Education levels | | | | | | |
| Illiterate | 0.682 | 0.511-0.853 | 0.034 | 0.151 | 0.056-0.403 | < 0.001 |
| Primary school | 0.945 | 0.875-0.998 | 0.047 | 0.786 | 0.414-1.495 | 0.464 |
| Postsecondary school | 0.853 | 0.640-1.066 | 0.089 | 0.937 | 0.625-1.403 | 0.256 |

1These statistical results were adjusted for age, gender, body mass index, education levels, smoking, drinking, history of disease, National Institutes of Health Stroke Scale, low-density lipoprotein and triglyceride. Aβ1-42: β-amyloid protein1-42; T3: Triiodothyronine; RR: Relative risk; CI: Confidence interval.