Int J Clin Exp Med 2021;14(2):1025-1032
www.ijcem.com /ISSN:1940-5901/IJCEM0122110

Original Article

Ultrasonic detection of pathological characteristics and influencing factor analysis in diabetic patients with carotid atherosclerosis

Yanyan Zhao, Shibin Lin, Kailiang Chen, Die Chen, Jineng Lai

Department of Ultrasound, The First Affiliated Hospital of Hainan Medical University, Haikou 570102, Hainan, China

Received September 10, 2020; Accepted November 6, 2020; Epub February 15, 2021; Published February 28, 2021

Abstract: Objective: This study aimed to measure the incidence rates and detect the pathological characteristics of intracranial and extracranial atherosclerosis using color Doppler ultrasound in elderly patients with type 2 diabetes mellitus (T2DM). Methods: A total of 96 T2DM patients without cerebral ischemia diagnosed in our hospital were selected and divided into the observation group (n = 47, receiving atorvastatin) and control group (n = 49, receiving placebo). Sound Doppler ultrasound and carotid ultrasound were performed to detect the pathological characteristics of intracranial atherosclerosis (stenosis analysis), extracranial atherosclerosis and carotid artery plagues followed by the analysis of influencing factors on T2DM patients. The blood lipid levels, vascular endothelial function, carotid artery intima-media thickness (IMT) and detection rates of carotid atherosclerotic plaque before and after treatment in the two groups were recorded. Results: The detection rates of isolated intracranial or extracranial atherosclerosis were 8.34% and 35.41% respectively; the detection rates of intracranial atherosclerotic stenosis with extracranial atherosclerosis and combined intracranial and extracranial atherosclerosis were 16.67% and 58.34% respectively; the incidence rates of cerebral artery stenosis were 17.0%, accounting for 58.5% of all arterial stenosis. The number of cases for extracranial atherosclerosis, stenosis, and plaque was 47 (48.95%). The leading causes of intracranial and extracranial atherosclerosis were shown to be diabetes and hypertension from logistic regression analysis; the sizes of carotid atherosclerotic plaques were reduced, the vascular endothelial function was significantly improved, TC and LDL-C levels were significantly decreased, and HDL-C levels were significantly increased after treatment ($P < 0.05$). Conclusion: All T2DM patients diagnosed with out cerebral ischemia after hospitalization were shown to have carotid artery atherosclerosis, and the main risk factor of carotid atherosclerosis was the combination of hypertension and diabetes. Treatment with atorvastatin can improve vascular endothelial function and delay the progression of atherosclerosis in patients.

Keywords: Type 2 diabetes, intracranial and extracranial carotid atherosclerosis, ultrasound, atorvastatin

Introduction

With the improvement of living standards in recent years, the incidence rates of diabetes mellitus (DM) has significantly increased, and 1/4 to 1/2 of all patients have a family history [1]. DM can lead to chronic complications that affect many organ systems, which critically endanger the life and health of the patients. According to the Guidelines for the Prevention and Treatment of Type 2 Diabetes in China (2017 edition), the incidence rates of T2DM in adults is as high as 10.4% and the incidence rates in patients ≥60 years old are 20% [2]. The increase of blood glucose levels in DM patients led to abnormalities in cardiomyocytes, resulting in cardiac hypofunction and induced heart failure, which seriously affects the quality of lives in DM patients [3]. Diabetes is classified into type 1 and type 2 based on the different pathologies of islet cells. T2DM is also known as adult-onset diabetes in clinical practice and accounts for more than 90% of all types of diabetes [4]. Studies have found that macroangiopathy is the leading cause of mortality and disability in T2DM patients. Early detection of macroangiopathy and prompt clinical treatment can effectively reduce the incidence rates of disability and mortality in patients [5]. With the continuous development

of ultrasonic technology in recent years, the application of ultrasonic detection of carotid atherosclerosis has been widely used in clinical practice. Color Doppler ultrasound is frequently used in clinics for detecting intracranial and extracranial atherosclerosis. The results of a clinical study on 90 patients with suspected carotid atherosclerosis showed that the diagnostic accuracy and sensitivity of color Doppler ultrasound in carotid atherosclerosis were as high as 98.16% and 89.11%, respectively [6]. However, there are few reports on its combination with carotid ultrasound to detect intracranial and extracranial atherosclerosis in patients with T2DM. Some studies have indicated that atorvastatin has a significant effect in the treatment of atherosclerosis by reducing platelet aggregation, regulating blood lipid levels, and improving vascular endothelial function [7]. In this study, 96 patients diagnosed with T2DM in our hospital were selected as research subjects, and the characteristics of lesions and disease distribution were analyzed by color Doppler ultrasound combined with carotid ultrasound, in order to provide clinical reference for improving the prognosis of such patients.

Material and methods

Clinical material

A total of 96 patients diagnosed with type 2 diabetes in our hospital from May 2018 to May 2019 was selected, including 52 males and 44 females, aged 55-80 years old with an average age of (86.5±11.8) years old. The patients had a disease duration of 3-35 years with a median disease duration of 5.6 years. The included patients all met the 1999 diagnostic criteria of the World Health Organization (WHO) [8]. All the 96 patients did not have transient ischemic attack (TIA) or histories of ischemic stroke. Among the 96 patients, 33 patients had hyperlipidemia (34.37%), 22 patients consumed alcohol (22.92%), 52 patients had hypertension (54.16%), and 30 patients smoked cigarettes (31.25%). The patients were notified of this study and signed an informed consent during the carotid artery ultrasound and color Doppler ultrasound. Exclusion criteria: Patients with severe anemia, congestive heart failure, hyperthyroidism, and poor detection results of TCD Doppler ultrasound through the trans-temporal window were excluded. This study was approved by The First Affiliated Hospital of Hainan Medical University.

Diagnostic methods

Clinical diagnosis of extracranial carotid stenosis or plaque: The GE Logiq 9 ultrasound system and Philips iU 22 color doppler ultrasound were used, with the transducer frequencies of: 5.0-12.0 MHz. Diagnosis of plaque: a focal thickening with Intima-media thickness (IMT) of ≥1.3 mm. Definition of arterial stenosis: the arterial stenosis was defined as ≥50% diameter reduction. The cases of extracranial carotid stenosis or arterial occlusion with the plaque were counted.

Diagnosis of intracranial arterial stenosis: The degree of arterial stenosis in 96 T2DM patients was determined from color Doppler ultrasound, and ≥50 was considered as intracranial artery stenosis. The intracranial arteries involved in stenosis were: bilateral superior cerebellar artery (SCA), bilateral basilar artery (BA), bilateral middle cerebral artery (MCA), bilateral anterior cerebral artery (ACA), and bilateral posterior cerebral artery (PCA). After risk factor analysis, 96 patients were divided into an observation group of 47 patients and a control group of 49 patients. All patients were on 0.1 g/d aspirin. The observation group was given 20 mg atorvastatin once, every night and the control group was given placebo with identical dosing. The treatment lasted for 24 weeks.

Measurement of various blood biochemistry parameters: Venous blood samples were taken from the hospitalized patients who were in a fasted state for 10-12 hours and were collected in the morning, and the glycated hemoglobin (HBAlc) level, total cholesterol (TC) level, fasting blood glucose (FBG) level, triglyceride (TG) level, apolipoprotein a level, high density lipoprotein cholesterol (HDL-C) level, and low density lipoprotein cholesterol (LDL-C) level in patients were measured using a biochemical sensor.

Statistical methods

The data statistical analysis was performed using SPSS 13.0 software. The measurement data were expressed as x ± sd and assessed by *t* tests; the median value of minimum-maximum was used for measurement data with skewed distribution and assessed by Mann-

Table 1. The blood biochemistry of included patients and comparison of the clinical data (x ± s)/[n (%)]

Factors	Isolated intracranial arterial stenosis	Isolated extracranial carotid atherosclerosis	Intracranial arterial stenosis with extracranial carotid atherosclerosis	Non-disease
Cases	6	34	16	40
Age (years old)	49.2±10.3	57.8±9.0	64.9±6.4	51.3±13.2
Male (cases, %)	4 (66.67)	18 (54.5)	6 (37.50)	24 (60.00)
Course of diabetes (years)	7 (0-17)	10 (3-35)	14 (7-30)	6 (0-30)
Hypertension (cases, %)	6 (100.00)	20 (60.6)	12 (75.00)	15 (37.50)
Hyperlipidemia (cases, %)	2 (33.33)	9 (27.3)	9 (56.25)	12 (30.00)
Smoking (cases, %)	2 (33.33)	8 (24.2)	5 (31.25)	16 (40.00)
Alcohol consumption (cases, %)	2 (33.33)	5 (15.2)	2 (12.50)	12 (30.00)
FBG (mmol/L)	10.2±3.4	8.1±2.5	7.4±2.3	8.5±3.0
HbAlc (%)	9.1 (5.8-11.6)	8.3 (6.0-11.8)	9.2 (5.8-12.3)	9.5 (6.2-14.3)
TC (mmol/L)	4.93±1.31	5.32±1.41	5.30±1.46	4.79±1.04
HDL-C (mmol/L)	1.12±0.26	1.24±0.35	1.31±0.37	1.18±0.27
LDL-C (mmol/L)	3.06±0.99	3.34±0.98	3.09±1.10	3.03±0.90
TG (mmol/L)	1.77 (1.38-5.96)	1.55 (0.59-12.10)	1.41 (0.50-23.30)	1.38 (0.47-6.83)
Lipoprotein (mg/L)	150 (34-306)	134 (17-1659)	315 (13-730)	111 (5-704)

Whitney U test. The count data were expressed by frequency and percentage and assessed by chi-squared test. The related parameters of intracranial and extracranial atherosclerosis were analyzed by backward stepwise multiple logistic regression, with $P < 0.05$ considered as statistically significant.

Results

Distribution characteristics and incidence rates of intracranial and extracranial atherosclerosis

The detection rates of intracranial and extracranial atherosclerosis in T2DM patients were 58.34% (56/96), with isolated intracranial artery stenosis of 6.25% (6/96), isolated extracranial atherosclerosis was 35.41% (34/96), and intracranial atherosclerotic stenosis with extracranial atherosclerosis was 16.67% (16/96). No intracranial or extracranial atherosclerosis was detected in 40 T2DM patients via TCD and carotid ultrasound examination (**Table 1**). The detection rate of intracranial artery stenosis and extracranial atherosclerosis or stenosis was 23.95% and 3.20% ($X^2 = 16.68$, $P < 0.01$) respectively; the detection rate of MCA atherosclerosis was 16.67% (16/96); the detection rate of extracranial carotid plaque or stenosis was 48.95% (47/96); the detection rate of atherosclerosis in vertebral and basilar arteries was 5.20% (5/96) which was significantly lower than that in intracranial internal carotid arteries that were 20.83% (20/96) ($X^2 = 10.40$, $P < 0.01$) (**Figure 1**).

Comparison of blood biochemistry and basic data between groups with and without intracranial and extracranial carotid atherosclerosis

Significantly fewer T2DM patients in the non-disease group were found to have the coexistence of diabetes and hypertension compared to the group with intracranial and extracranial carotid atherosclerosis, and the difference is statistically significant ($P < 0.05$). Differences in parameters such as age, gender, hyperlipidemia, smoking, FBG, HbAlc, TC, HDL-C, LDL-C, TG, and lipoprotein levels had no statistical significance ($P > 0.05$) (**Table 2**).

Multiple logistic regression analysis

Variable risk factors such as gender, course of the disease, hyperlipidemia, disease course of diabetes, smoking, alcohol consumption in 96 patients were included in the backward stepwise logistic regression analysis. Logistic regression analysis indicated that the combination of hypertension and diabetes was the main risk factor of intracranial and extracranial carotid atherosclerosis (**Table 3**).

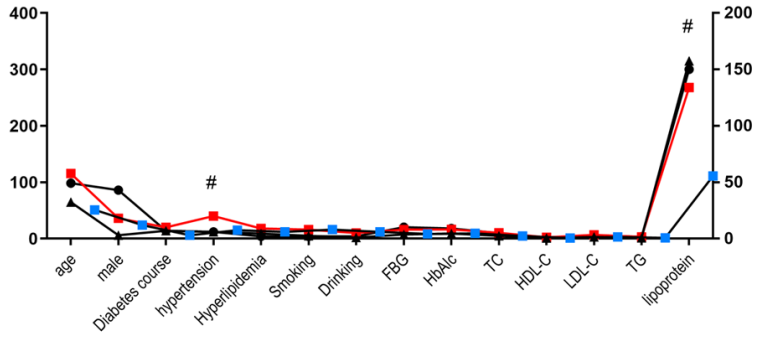

Figure 1. Comparison of clinical data between two groups of patients. The difference in the age and gender among patients with no atherosclerosis, isolated extracranial carotid atherosclerosis, intracranial arterial stenosis with extracranial carotid atherosclerosis, and isolated intracranial arterial stenosis was not statistically significant ($P > 0.05$); in the non-disease group, the incidence rates of diabetes combined with hypertension were lower than that of isolated extracranial carotid atherosclerosis, intracranial arterial stenosis with extracranial carotid atherosclerosis, and isolated intracranial arterial stenosis ($P < 0.05$). The difference in other indexes had no statistical significance ($P > 0.05$).

Change in blood lipid levels in two groups before and after treatment

The difference in TC, TG, HDL-C, and LDL-C levels between the observation group and the control group before the treatment was not statistically significant ($P > 0.05$). The difference in TC, TG, HDL-C and LDL-L levels between observation group and control group after treatment was statistically significant ($P < 0.05$) (**Figure 2**).

The change in vascular endothelial function before and after treatment in both groups

The difference in basal diameter of brachial artery, the change ratio of inner diameter after reactive hyperemia, and the change ratio of inner diameter after nitroglycerin intake between observation group and control group before treatment was statistically significant ($P > 0.05$). All parameters except basal diameter of the brachial artery were improved in both observation and control group after treatment, while the improvement in the observation group was more significant compared to that in the control group ($P < 0.05$) (**Figure 3**).

The detection rate of carotid atherosclerotic plaque and IMT in two groups after treatment

The difference in the detection rate of carotid atherosclerotic plaque and IMT between observation and control group before treatment was not statistically significant ($P > 0.05$). The detection rate of carotid atherosclerotic plaque in the observation group after treatment was significantly lower than that in the control group ($P < 0.05$), and the detection rate of IMT was lower than that in the control group ($P < 0.05$) (**Figure 4**).

Discussion

Many brain regions in diabetic patients are prone to macroangiopathy [9]. Prior studies have shown that there was a significant difference in the distribution of intracranial and extracranial atherosclerosis in T2DM patients via pathologic and angiographic analysis [10]. Currently, color Doppler ultrasound and magnetic resonance angiography are adopted for the diagnosis of arterial stenosis with high specificity and sensitivity [11]. Studies have indicated that the incidence rates of intracranial and extracranial stenosis in T2DM patients were 23.95% and 3.20% respectively, and 50% of the patients were found to have intracranial and extracranial atherosclerosis [12]. Many clinical researchers believed that the main cause of cerebral stroke is related to diabetes. However, the correlation between the development of cerebral stroke and intracranial and extracranial atherosclerosis is controversial [13]. Related studies have showen that diabetes is not the main risk factor of MCA stenosis [14, 15]. Studies have indicated that the increase rate of IMT in diabetic patients was more than twice of that in non-diabetic patients, which confirmed that diabetes could lead to accelerated carotid atherosclerosis [12].

Some studies have found that there was a correlation among the incidence rates of the carotid artery, the left anterior descending artery, and the brachial artery [16]. Besides, the vascular endothelial function of brachial artery could effectively indicate the degree of atherosclerosis, and significant morphological transformation could be observed in IMT during the development of atherosclerosis. The ultrasound examination indicated that there

Table 2. Comparison of medical history and blood biochemical indexes between disease and non-disease group (x ± s)/[n (%)]

Factors	Intracranial and extracranial carotid atherosclerosis group (n = 56)	Non-disease group (n = 40)	t/X^2	*P* value
Age (years old)	58.61±9.81	51.13±13.12	3.197	0.002
Male (cases, %)	28 (50.00)	24 (60.00)	0.94	0.332
Course of diabetes (years)	11.21±0.34	6.45±0.98	33.679	< 0.001
Hypertension (cases, %)	38 (67.86)	15 (37.50)	8.696	0.003
Hyperlipidemia (cases, %)	20 (35.71)	12 (30.00)	0.343	0.558
Smoking (cases, %)	15 (26.78)	16 (40.00)	1.864	0.172
Alcohol consumption (cases, %)	9 (16.07)	12 (30.00)	2.649	0.104
FBG (mmol/L)	8.01±2.61	8.51±3.01	0.868	0.388
HbAlc (%)	8.91±0.81	9.67±0.45	5.367	< 0.001
TC (mmol/L)	5.27±1.39	4.79±1.04	1.845	0.068
HDL-C (mmol/L)	1.24±0.35	1.18±0.27	0.908	0.366
LDL-C (mmol/L)	3.24±1.00	3.03±0.90	1.057	0.293
TG (mmol/L)	1.55±0.31	1.38±0.21	3.008	0.003
Lipoprotein (mg/L)	164.48±20.19	111.28±10.29	15.394	< 0.001

Table 3. Multiple logistic regression analysis of risk factors of atherosclerosis in type 2 diabetes

Factors	OR value	95% confidence interval		*P* value
		Lower limit	Upper limit	
Course of diabetes	1.098	1.022	1.179	0.013
Combined with hypertension	3.685	1.452	9.355	0.006

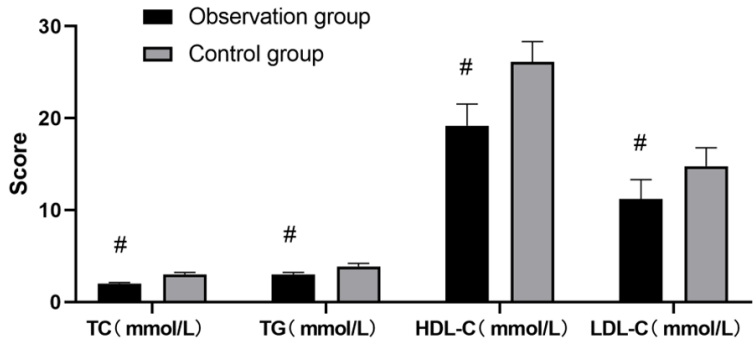

Figure 2. Comparison of changes in blood lipid levels before and after treatment in the two groups. After treatment, the levels of TC, TG, HDL-C, and LDL-C in observation group were significantly higher than those in control group, and the difference is statistically significant (P < 0.05); # indicates statistical differences in the same index between the groups.

was a significant correlation between IMT/plaque and atherosclerosis [17]. Studies have discovered statins could significantly lower blood lipid levels, improve vascular endothelial function, inhibit smooth muscle proliferation, and inhibit inflammatory reactions [18]. Studies have found that statins could effectively delay the progression of carotid and coronary artery atherosclerosis, and reduce the incidence rates of cardiovascular events [19].

In this study, different groups were established to analyze the characteristics of carotid atherosclerosis ultrasonography in diabetic patients, and results revealed that the incidence rates of intracranial and extracranial atherosclerosis in the disease group were significantly higher than that in the non-disease group, and diabetes was an independent factor causing intracranial and extracranial carotid atherosclerosis. In a comparative study of 50 cases of elderly diabetes patients with carotid atherosclerosis and 50 cases of healthy elderly individuals, it was found that the thickness of carotid intima in diabetic patients was significantly higher than that in normal elderly subjects, and the plaque detection rate of diabetic patients was significantly increased, suggesting that diabetes had a significant impact on the formation of atherosclerotic plaques [20]. The difference in the results of this study could result

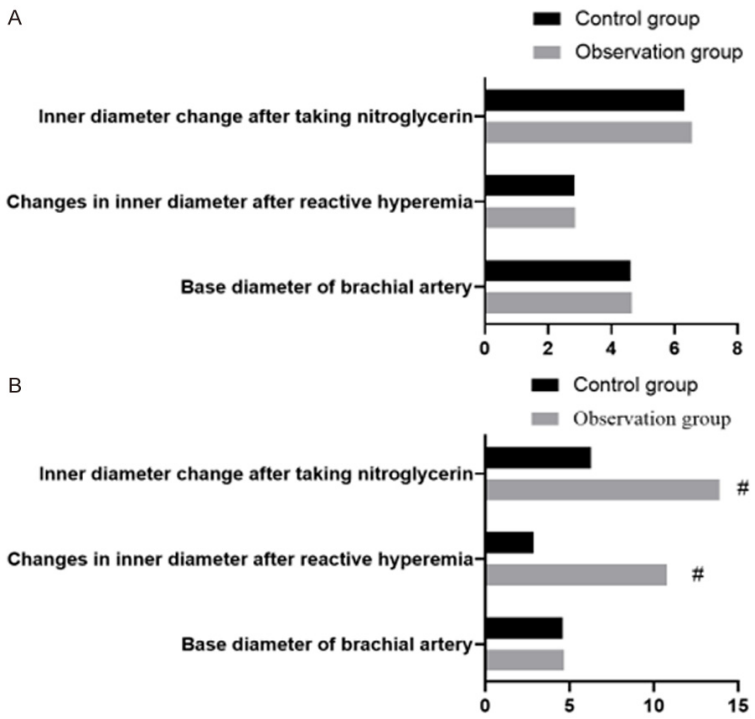

Figure 3. Comparison of vascular endothelial function between the two groups after treatment. After treatment, the change ratio of inner diameter after reactive hyperemia and the change ratio of inner diameter after nitroglycerin intake in the observation group were significantly higher than those in the control group, and the difference is statistically significant ($P < 0.05$). There was no statistically significant difference in the basic diameter of the brachial artery before and after treatment between two groups ($P > 0.05$). # indicates that the difference of the same index is statistically significant compared with the control group.

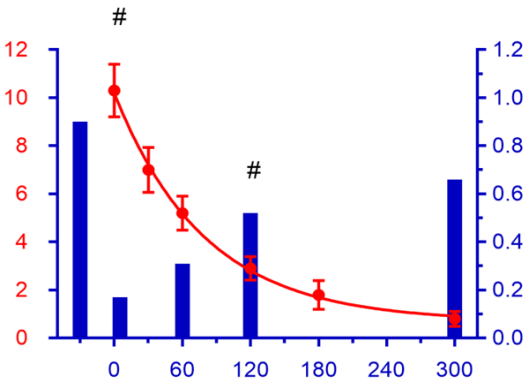

Figure 4. The change ratio in atherosclerotic plaque and IMT in two groups after treatment. The detection rate of plaque after treatment in observation group was 42.55% (20/47). The incidence rate of control after treatment in control group was 61.22% (30/49), and the difference is statistically significant ($X^2 = 4.12$, $P < 0.05$). The IMT was 1.18±0.12 (mm) in the observation group after treatment and 1.37±0.14 (mm) in control group after treatment ($X^2 = 5.56$, $P < 0.05$). # indicates that the difference is statistically significant compared with the control group.

from varied regulation of blood glucose level in patients. The HbAlc level was 9.4% in non-disease group and 8.8% in disease group, which indicated that poor regulation of HbAlc could increase the incidence rates of intracranial and extracranial atherosclerosis in diabetic patients. This study found that the percentage of patients with hypertension in the non-disease group was 38.5%, which was significantly lower than that (69.5%) in the disease group with intracranial and extracranial atherosclerosis ($P < 0.0$). A study also found that age is negatively correlated with the incidence rates of intracranial and extracranial atherosclerosis in T2DM patients, and hypertension is the main influencing factor causing intracranial and extracranial atherosclerosis [21]. There are many clinical studies on the risk factor analysis of intracranial and extracranial atherosclerotic lesions. A retrospective analysis of 894 patients with intracranial and extracranial atherosclerosis showed that hypertension, hyperglycemia, advanced age, and high-fat diet were all risk factors for intracranial and extracranial atherosclerosis, among which hypertension and hyperglycemia were independent risk factors, suggesting close attention needs to be paid to such patients clinically [22]. This study indicated that the size of the carotid plaques in all patients significantly reduced after 24 weeks of treatment with atorvastatin, and the IMT was significantly reduced after the treatment. This indicated that atorvastatin could effectively delay the progression of atherosclerosis in patients. This is consistent with the research results of other scholars. It has proved that atorvastatin is a commonly used lipid-lowering drug in clinical practice, which can inhibit the activity of HMG-CoA reductase, thereby reducing the synthesis of cholesterol in individuals and ultimately reducing the level of lipid [23]. Other studies indicated that atorvastatin was absorbed orally rapidly and inhibited the HMG-

CoA reductase for up to 30 h, showing a relatively obvious efficacy, which was consistent with the results of this study [24].

In conclusion, 50% of the T2DM patients without cerebral ischemia had intracranial and extracranial atherosclerosis, and the incidence rates of intracranial carotid plaque were higher than that of T2DM with hypertension. The incidence rates of intracranial carotid stenosis were higher than that of extracranial carotid stenosis, and the SCA and MCA in intracranial arteries had high incidence rates. As a result, early detection with carotid ultrasound and color Doppler ultrasound can result in early intervention, which can delay the progression of intracranial and extracranial atherosclerosis, reduce the incidence rates of cerebral ischemia and, improve the long-term quality of life for diabetic patients. The innovation of this study is to select patients with different types of carotid atherosclerosis as the research subjects, and quantify the differences in ultrasound indications of patients with different lesions through comparative analysis. At the same time, the ultrasound indications of patients with atherosclerosis in different courses were analyzed and compared before and after treatment, which has a high reference value. The limitation of this study lies in the selection of fewer types of atherosclerotic lesions and limited coverage. In the next step, a clinical study with a larger sample size and more comprehensive diseases will be carried out.

Disclosure of conflict of interest

None.

Address correspondence to: Shibin Lin, Department of Ultrasound, The First Affiliated Hospital of Hainan Medical University, Haikou 570102, Hainan, China. Tel: +86-0898-66774347; E-mail: linshibin0909@163.com

References

[1] Bauer M, Caviezel S, Teynor A, Erbel R, Mahabadi AA and Schmidt-Trucksäss A. Carotid intima-media thickness as a biomarker of subclinical atherosclerosis. Swiss Med Wkly 2012; 142: w13705.

[2] Jia WP and Lu JM. Guidelines for the prevention and treatment of type 2 diabetes in China (2017 edition). Chin J Diabetes Mellitus 2018; 10: 2-67.

[3] Kim SK, Park SW, Kim SH, Cha BS, Lee HC and Cho YW. Visceral fat amount is associated with carotid atherosclerosis even in type 2 diabetic men with a normal waist circumference. Int J Obes (Lond) 2009; 33: 131-135.

[4] Wang X, Li W, Song F, Wang L, Fu Q, Cao S, Gan Y, Zhang W, Yue W, Yan F, Shi W, Wang X, Zhang H, Zhang H, Wang Z and Lu Z. Carotid atherosclerosis detected by ultrasonography: a national cross-sectional study. J Am Heart Assoc 2018; 7: e008701.

[5] Ye YC, Liu HM, Zhou Y and Zeng Y. Association between serum alkaline phosphatase and carotid atherosclerosis in a Chinese population: a community-based cross-sectional study. Biomed Environ Sci 2019; 32: 446-453.

[6] Zhao X, Zhao Q, Chu B, Yang Y, Li F, Zhou XH, Cai J, Cai Z and Yuan C. Prevalence of compositional features in subclinical carotid atherosclerosis determined by high-resolution magnetic resonance imaging in chinese patients with coronary artery disease. Stroke 2010; 41: 1157-1162.

[7] Chu CH, Chau AM and Lo EC. Current and future research in diagnostic criteria and evaluation of caries detection methods. Oral Health Prev Dent 2013; 11: 181-189.

[8] Kobayashi Y, Ishiguro H, Fujikawa T, Kobayashi H, Sumida K, Kagimoto M, Okuyama Y, Ehara Y, Katsumata M, Fujita M, Fujiwara A, Saka S, Yatsu K, Hirawa N, Toya Y, Yasuda G, Umemura S and Tamura K. Atherosclerosis of the carotid bulb is associated with the severity of orthostatic hypotension in non-diabetic adult patients: a cross-sectional study. Clin Exp Hypertens 2018; 1-8.

[9] Migdalis IN, Kalogeropoulou K, Karmaniolas KD, Varvarigos N, Mortzos G and Cordopatis P. Plasma levels of endothelin and early carotid atherosclerosis in diabetic patients. Res Commun Mol Pathol Pharmacol 2000; 108: 15-25.

[10] Oikawa M, Ota H, Takaya N, Miller Z, Hatsukami TS and Yuan C. Carotid magnetic resonance imaging. A window to study atherosclerosis and identify high-risk plaques. Circ J 2009; 73: 1765-1773.

[11] Wada N, Sekiguchi M, Yoshioka N, Toyoshima H, Matsumoto A, Nomura M, Yanagisawa K, Ito T, Nishio T and Takeuchi J. Effect of probucol and pravastatin on common-carotid atherosclerosis in diabetic patients with hypercholesterolemia. J Jpn Diabetes Soc 2005; 48: 53-56.

[12] Migdalis IN, Gerolimou B, Kozanidou G, Voudouris G, Hatzigakis SM and Petropoulos A. Effect of gemfibrozil on early carotid atherosclerosis in diabetic patients with hyperlipidaemia. Int Angiol 1997; 16: 258-261.

[13] Katakami N, Kaneto H, Matsuhisa M, Shimomura I and Yamasaki Y. Effects of glimepiride and glibenclamide on carotid atherosclerosis in type 2 diabetic patients. Diabetes Res Clin Pract 2011; 92: e20-22.
[14] Gottsäter A, Rydén-Ahlgren A, Szelag B, Hedblad B, Persson J, Berglund G, Wroblewski M and Sundkvist G. Cardiovascular autonomic neuropathy associated with carotid atherosclerosis in type 2 diabetic patients. Diabet Med 2003; 20: 495-499.
[15] Belur AD and Mehta NN. Underestimation of risk of carotid subclinical atherosclerosis by cardiovascular risk scores in patients with psoriatic arthritis: how far are we from the truth? J Rheumatol 2018; 45: 150-152.
[16] Yan Y, Li W, Tang L and Feng Y. Evaluation of the neutrophil to lymphocyte ratio in newly diagnosed nondiabetic hypertensive patients with carotid atherosclerosis. South China J Cardiol 2018; 259-267.
[17] Sahadevan M, Chee KH and Tai MS. Prevalence of extracranial carotid atherosclerosis in the patients with coronary artery disease in a tertiary hospital in Malaysia. Medicine (Baltimore) 2019; 98: e15082.
[18] Mitevska IP, Baneva N, Bosevski M and Kostovska ES. Prevalence of risk factors and asymptomatic carotid atherosclerosis in diabetic patients screened for silent myocardial ischemia by SPECT myocardial imaging. Nucl Med Rev Cent East Eur 2017; 20: 3-9.
[19] Moumen A, Bouziane A, Meftah A, Errahali Y, Eljadi H, Elmoussaoui S and Belmejdoub G. Chronic kidney failure and carotid atherosclerosis in diabetic patient. Presse Med 2016; 45: e341-349.
[20] Jain A, Tantia P, Saini K, Sulemani AA, Sirohi P, Rizwani P and Agrawal RP. Ratio of waist-to-calf circumference and carotid atherosclerosis in patients of type 2 diabetes mellitus. J Assoc Physicians India 2016; 64: 32-35.
[21] Vasilkova V, Mokhort T and Naumenko E. OP0309 association of bone mineral density and carotid atherosclerosis in patients with diabetes type 2. Ann Rheum Dis 2016; 75 Suppl 2: 174.3-175.
[22] Revnic C, Voinea S, Pena C, Revnic F, Paltineanu B and Nica AS. The relationship between carotid stenosis and stroke in hyperthensive diabetic and non-diabetic patients. J Hypertens 2016; 34: e224.
[23] Mita T, Katakami N, Yoshii H, Onuma T, Kaneto H, Osonoi T, Shiraiwa T, Kosugi K, Umayahara Y, Yamamoto T, Yokoyama H, Kuribayashi N, Jinnouchi H, Gosho M, Shimomura I and Watada H. Alogliptin, a dipeptidyl peptidase 4 inhibitor, prevents the progression of carotid atherosclerosis in patients with type 2 diabetes: the study of preventive effects of Alogliptin on diabetic atherosclerosis (SPEAD-A). Diabetes Care 2016; 39: 139-148.
[24] Ménégaut L, Masson D, Abello N, Denimal D, Truntzer C, Ducoroy P, Lagrost L, Pais de Barros JP, Athias A, Petit JM, Martin L, Steinmetz E and Kretz B. Specific enrichment of 2-arachidonoyl-lysophosphatidylcholine in carotid atheroma plaque from type 2 diabetic patients. Atherosclerosis 2016; 251: 339-347.