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Evaluate the elasticity of carotid artery in the type 2 diabetes mellitus patients with nonalcoholic fatty liver disease by two-dimensional strain imaging

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Abstract

To evaluate carotid elasticity by using two-dimensional strain imaging (2DSI) in type 2 diabetes mellitus (T2DM) patients with nonalcoholic fatty liver disease (NAFLD). 98 patients with T2DM diagnosed in our hospital were selected. All the patients were without carotid plaque, which were proved by carotid ultrasonography. According to the fatty liver classification standard, patients were divided into three groups. There were 35 cases without NAFLD in group A, 33 cases with mild NAFLD in group B and 30 cases with moderate to severe NAFLD in group C. By using two-dimensional and M-mode ultrasound to measure the left carotid intima-media thickness (IMT), common carotid arterial systolic diameter (Ds) and diastolic diameter (Dd). The systolic peak velocity was measured by spectral Doppler ultrasound. The systolic global peak circumferential strain (CS), early and late systolic global circumferential strain rate (CSr) were measured by 2DSI. The stiffness parameters β1 and β2 were calculated by M-mode ultrasound and 2DSI separately. Among three groups, the Ds, Dd and systolic peak velocity showed no significant difference (all $P > .05$). In group C, IMT and β1 were obviously increased than those of groups A and B (all $P < .05$). Compared groups A and B, there were no significant difference in IMT and β1 (all $P > .05$). β2 was higher in groups B and C than those in group A, CS, CSr were lower in groups B and C than those in group A (both $P > .05$). The carotid elasticity of T2DM patients with NAFLD can be evaluated by 2DSI.

Abbreviations: T2DM = type 2 diabetes mellitus, 2DSI = two-dimensional strain imaging, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = body mass index, CS = circumferential strain, CSr = circumferential strain rate, DBP = diastolic blood pressure, Dd = diastolic diameter, Ds = systolic diameter, FBG = fasting blood glucose, HbA1c = glycosylated hemoglobin, IMT = intima-media thickness, IR = insulin resistance, NAFLD = nonalcoholic fatty liver disease, NASH = nonalcoholic steatohepatitis, SBP = systolic blood pressure, TG = triglyceride.

Keywords: carotid elasticity, non-alcoholic fatty liver disease, two-dimensional strain imaging, type 2 diabetes mellitus

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is defined as at least 5% fat accumulate (steatosis) in hepatocytes, while patients have neither previous history of excessive alcoholic consumption nor any other liver diseases.[1,2] NAFLD is a serious metabolic abnormality. The pathological manifestations of NAFLD are massive accumulation of fat in the liver parenchyma and abnormal increase of liver enzymes. Both of them can lead to liver steatosis and inflammation, and cause liver cell injury and apoptosis. Due to the above pathological changes, the liver metabolism function will be reduced and the volume of liver will be enlarged. NAFLD, at present, has become one of the most crucial causes of chronic liver disease.[3] In addition, the prevalence and incidence of NAFLD in China are also increasing, which not only seriously affect people's health status, but also pose a certain burden to the economy. Due to the high prevalence of NAFLD across the country, more and more people pay attention to it. Type 2 diabetes mellitus (T2DM), insulin resistance (IR) and obesity is closely connected with the development of NAFLD.[4,5] With the improvement of the quality of life, the number of obese people is increasing. Obese individuals have abnormal increase of lipids in non-adipose tissues, which can lead to the dysfunction of obesity-related organs. Due to the metabolic abnormities, the incidence of cardiometabolic complications, such as T2DM and NAFLD, is higher in obese patients. And the risk of cardiovascular diseases is correspondingly increased. NAFLD often coexists with T2DM, Zobair M et al[6] suggested more than half of T2DM patients also have NAFLD all over the world. In addition to that, the view of NAFLD is a risk factor for T2DM have been revealed by some

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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studies.[7,8] Compare with normal controls, the prevalence of T2DM in NAFLD patients is 5 times increased, and NAFLD is also convinced to have a strong bi-directional relationship with T2DM.[7,8] NAFLD and T2DM can increase the risk of cardiovascular disease, which is the most common cause of death among patients with NAFLD.[9] Therefore, early assessment of cardiovascular disease risk in T2DM patients with NAFLD is particularly important.

Two-dimensional strain imaging (2DSI), as a noninvasive ultrasound imaging technique, can track the movement of tissues in region of interest through the way of frame by frame, so it can achieve the purpose of evaluating tissular function and elasticity quantitatively.[10,11] Carotid atherosclerosis has a close association with the risk of cardiovascular disease. And because the position of carotid artery is shallow and fixed, it is easy to be detected and can be shown clearly by ultrasound. Arterial stiffness can be used to predict the risk of cardiovascular disease. Therefore, our study was aimed to evaluate the elasticity of carotid artery in the T2DM patients, by using 2DSI.

2. Methods

2.1. Study population

Inpatients who were diagnosed with T2DM in endocrinology department of our hospital from October 2020 to November 2021, and in line with following criteria at the same time, including without plaque in conventional examination of carotid ultrasound, intima-media thickness (IMT) ≤1.5 mm、ejection fraction ≥50% and T2DM duration is 5 to 10 years, were collected. The diagnostic criteria for NAFLD were conformed to the practical guidelines for the diagnosis and management of NAFLD, as issued by American association in 2017.[12] According to the guidelines for the diagnosis and treatment of NAFLD,[13] all NAFLD patients diagnosed by liver ultrasound were divided into three groups: there were 35 individuals without NAFLD in group A, including 20 males and 15 females, aged from 25 to 56 years with an average age of 45.8 ± 8.3 years, 33 individuals with moderate NAFLD in group B, including 21 males and 12 females, aged from 27 to 58 years with an average age of 48.3 ± 6.5 years, while 30 individuals with moderate to severe NAFLD in group C, including 18 males and 12 females, aged from 30 to 55 years with an average age of 46.2 ± 7.1 years.

Exclusion criteria included: patients with history of cardiomyopathy, congenital heart disease and other cardiovascular and cerebrovascular diseases; obese and hypertensive patients; patients with complications of diabetes; patients with severe liver and kidney dysfunctions such as cirrhosis and renal failure.

All participants were given written informed consent, and the study was approved by the local Ethics Committee.

2.2. Instruments and methods

2.2.1. General clinical parameters. All essential data of each selected patients were recorded, which involved sex, age, duration of diabetes, height, body mass, resting heart rate and blood pressure, and we calculated their body mass index (BMI). Venous blood samples were obtained in the morning for measuring fasting blood glucose (FBG). The following biochemical parameters were determined by automatic biochemical analyzer: glycosylated hemoglobin (HbA1c), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, triglyceride (TG), high density lipoprotein cholesterol, and low-density lipoprotein cholesterol.

2.2.2. Carotid ultrasound. The ultrasound diagnostic instrument of GE Vivid E9, equipped with a frequency ranged from 5.5 to 11.0 MHz vascular probe of 11 L, was used to measure IMT in this study, and it was connected with synchronous electrocardiogram. We asked participants to lie down in a supine position without pillow under their head, then head turned towards the right and tilted their head back as far as possible for fully exposing their necks. When the long axis image of the left common carotid was shown in two-dimensional, adjusted the probe until the intima-media was shown most clearly. Subsequently, we put the probe at the left common carotid artery within 1.0 to 1.5 cm of the bifurcation in the longitudinal plane, at the end of diastole, the thickness of posterior wall of the common carotid artery was measured. While the common carotid arterial systolic diameter (Ds), the common carotid arterial diastolic diameter (Dd) and the systolic peak velocity (PSV) were measured by M-mode and spectral Doppler ultrasonography, the vessel wall motility (△D, ΔD = Ds–Dd) and the stiffness parameter of carotid artery (β1, β1 = ln (SBP/diastolic blood pressure (DBP)/[(Ds–Dd)/Dd] were calculated by the above formula, where SBP and DBP are systolic and diastolic blood pressure, respectively). In this experiment, all of the data were rendered as the average values of three times.

2.2.3. 2DSI. We switched the equipment to M5S probe (frequency of 2.3–4.6 MHz), placed a 100 mL saline bag above the patients' left common carotid artery. The short axis images of left common carotid artery, 1.5 cm below the bifurcation, were collected and stored in the hard disk. The patients were required to hold their breath during the process of images acquisition. Besides, three cardiac cycles were recorded consecutively on each image. Then, under the offline condition, the Echo PAC software, which was equipped with the ultrasound equipment, was used for analyzing the images that we recorded before. Manually depicted the intima of the vessel and adjusted the width of the region of interest to make it consistent with the thickness of the vessel wall. The software can automatically track the motion of the blood vessel wall, so the curves of the systolic global peak circumferential strain (CS), the early and late systolic global circumferential strain rate (CSr) of the left common carotid artery can be obtained. Finally, the carotid stiffness parameter (β2) was calculated by the following formula: β2 = ln (SBP/DBP)/CS.

2.3. Repeatability test

Twenty-five patients were randomly selected from all participants. Two sonographers used 2DSI technique to measure the left carotid strain parameters, involved CS, early and late systolic global CSr in these patients. By one of the sonographers, the same measurements were taken again in these 25 patients, and the correlation coefficients between and within observers were calculated.

2.4. Statistical analysis

The statistical analysis of research was using the SPSS version 26.0, and quantitative data are manifested as the mean ± standard deviation. One-way analysis of variance was performed to test for significant differences among the three groups, and the comparisons of quantitative data among the three groups were compared by using the χ^2 test, while among the two groups were LSD t test. The parameters' correlation was assessed by Pearson correlation analysis. $P < .05$ was regarded as statistically significant.

3. Results

3.1. Clinical characteristics

Among three groups, there were no significant differences in age, sex, heart rate, SBP, DBP, FBG, total cholesterol, high density lipoprotein cholesterol, and low-density lipoprotein cholesterol (all $P > .05$). Compared with group A and group B, we found BMI

Table 1

Comparison of general clinical and biochemical parameters among 3 groups (__x ± s).

Clinical and biochemical parameters	Group A (n = 35)	Group B (n = 33)	Group C (n = 30)
Age (yr)	45.8 ± 8.3	48.3 ± 6.5	46.2 ± 7.1
Male/female ratio	20/15	21/12	18/12
Heart rate (rates/min)	72.86 ± 7.69	74.95 ± 9.47	77.04 ± 10.31
BMI (kg/m^2)	24.15 ± 2.16	25.78 ± 2.37	27.20 ± 3.26*,†
SBP (mm Hg)	126.03 ± 5.51	126.52 ± 5.83	127.5 ± 6.84
DBP (mm Hg)	75.80 ± 7.36	77.42 ± 5.53	77.83 ± 7.72
FBG (mmol/L)	8.49 ± 1.66	8.90 ± 1.79	8.92 ± 2.00
HbA1c (%)	7.99 ± 1.92	8.52 ± 2.14	9.91 ± 2.08*,†
ALT (U/l)	20.97 ± 6.24	33.95 ± 9.98*	52.20 ± 21.79*,†
AST (U/l)	17.52 ± 4.79	29.27 ± 5.24*	35.78 ± 11.02*,†
TC (mmol/L)	5.46 ± 1.06	5.42 ± 1.42	5.22 ± 1.36
TG (mmol/L)	1.53 ± 0.55	2.05 ± 1.11*	2.63 ± 1.28*,†
HDL-C (mmol/L)	1.55 ± 0.59	1.33 ± 0.47	1.32 ± 0.38
LDL-C (mmol/L)	2.78 ± 0.47	2.89 ± 0.86	3.10 ± 0.91

BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, FBG = fasting blood glucose, HbA1c = glycosylated hemoglobin, ALT = alanine aminotransferase, AST = aspartate aminotransferase, TC = total cholesterol, TG = triglyceride, HDL-C = high density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol.

*P < .05, compared with group A.

†P < .05, compared with group B.

and HbA1c in group C were increased (all P < .05), while there were no significant differences were shown between group A and B (all P > .05). The values of ALT, AST, and TG in three groups showed significant differences (all P < .05),and ALT, AST, and TG levels in group C were higher than those in groups A and B, these levels in group B were higher than those in group A (Table 1).

3.2. Conventional ultrasound parameters

Among three groups, the values of Ds, Dd, △D, and PSV showed no significant differences. Besides, the values of IMT and β1 in group C were higher than those in groups A and B (all P < .05), while no obvious differences were found between groups A and B (all P > .05) (Table 2).

3.3. 2DSI parameters

The carotid artery 2DSI parameters of Cs, the early and late systolic global CSr in group C were significantly decreased, when compared with groups A and B (all P < .05). In addition, the carotid stiffness values (β2) in groups B and C were higher than those in group A, and compared with group B, β2 in group C displayed higher stiffness values (Table 3, Figs. 1 and 2).

3.4. Correlation analysis

The systolic global peak CS, the early and late systolic global CSr and β2 in three groups were expressed negative correlations

Table 2

Comparison of carotid artery conventional ultrasound parameters among 3 groups (__x ± s).

Parameters	Group A (n = 35)	Group B (n = 33)	Group C (n = 30)
IMT (mm)	0.64 ± 0.12	0.66 ± 0.14	0.83 ± 0.19*,†
Ds (mm)	6.95 ± 0.52	7.05 ± 0.48	7.14 ± 0.39
Dd (mm)	6.40 ± 0.45	6.49 ± 0.41	6.54 ± 0.39
D (mm)	0.60 ± 0.11	0.57 ± 0.09	0.59 ± 0.10
β1	5.55 ± 1.72	5.60 ± 1.44	6.02 ± 1.24*,†
PSV (cm/s)	59.87 ± 11.23	58.43 ± 10.94	58.52 ± 10.56

IMT = intima-media thickness, Ds = systolic diameter, Dd = diastolic diameter, D = systolic diameter (Ds) - diastolic diameter (Dd), PSV = systolic peak velocity.

*P < .05, compared with group A.

†P < .05, compared with group B.

Table 3

Comparison of two-dimensional strain parameters of carotid artery in 3 groups (__x ± s).

Parameters	Group A (n = 35)	Group B (n = 33)	Group C (n = 30)
CS(%)	8.57 ± 1.90	6.99 ± 1.91*	5.43 ± 1.30*,†
The early systolic global CSr (s^{-1})	1.01 ± 0.34	0.82 ± 0.27*	0.69 ± 0.16*,†
The late systolic global CSr (s^{-1})	−0.45 ± 0.10	−0.39 ± 0.10*	−0.35 ± 0.12*,†
β2	0.06 ± 0.02	0.08 ± 0.02*	0.09 ± 0.01*,†

CS = circumferential strain, CSr = circumferential strain rate.

*P < .05, compared with group A.

†P < .05, compared with group B.

(r = −0.807, −0.611, −0.510, P < .01). The stiffness parameters of β1 and β2 were positively correlated (r = 0.504, P < .01). Among three groups, the value of CS, CSr were negatively correlated with HbA1c (r = −0.425, −0.448, −0.405, P < .01). However, there were no correlation among the value of CS, CSr, and IMT among 3 groups (all P > .05).

3.5. Repeatability test

The intra-observer intraclass correlation coefficient values of carotid strain parameter CS, early and late systolic global CSr, which we obtained by 2DSI, is 0.829 to 0.922, and interobserver intraclass correlation coefficient values is 0.794 to 0.899 (Table 4).

4. Discussion

NAFLD can be divided into two types, one is defined as non-alcoholic fatty liver, the triglycerides exceedingly accumulate in the liver parenchyma is the feature of it, while there was no liver cell injury and inflammation, and the other one is more severe, may evolve into cirrhosis, liver cancer and liver failure, defined as non-alcoholic steatohepatitis (NASH).[14] NAFLD and its subtype NASH are common in adults and even children. As a progressive disease, NAFLD can evolve into NASH, which undergoes a slow process and then evolve into liver fibrosis. And compare to NAFLD, NASH patients often have more severe carotid atherosclerosis. For these reasons, NASH, the more severe phenotype of NAFLD, is gradually turn into the leading cause of liver transplantation. There is a complex bidirectional relationship between NAFLD and T2DM, NAFLD can increase

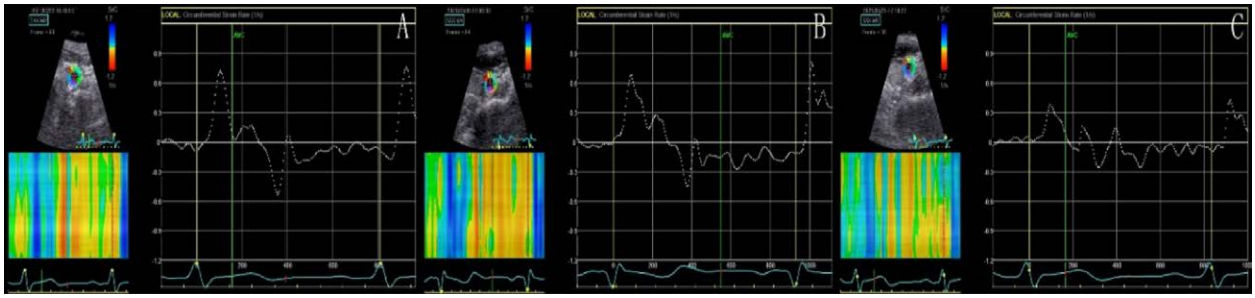

Figure 1. The early and late systolic global CSr curves of CCA in group A, B, and C. CSr = circumferential strain rate.

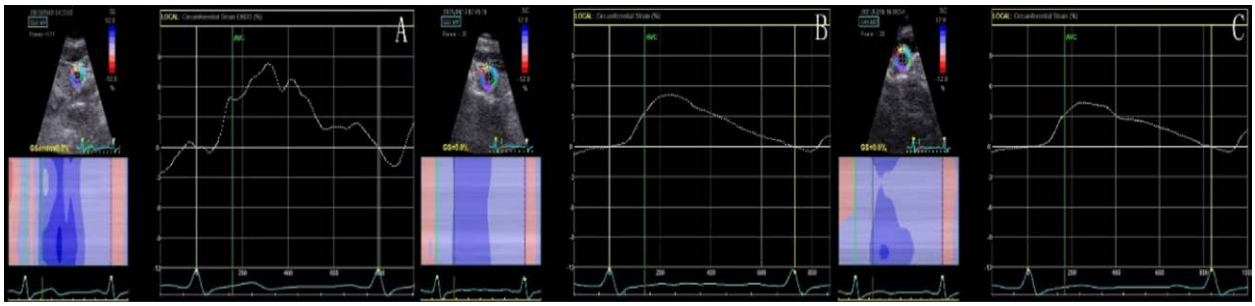

Figure 2. The systolic global peak CS curves of CCA in group A, B, and C. CS = circumferential strain.

Table 4

Reliability analysis of two-dimensional strain measurement of carotid artery.

	Intra-observer			Inter-observer		
Parameters	**ICC**	**95% consistency limit**	***P***	**ICC**	**95% consistency limit**	***P***
CS	0.922	0.831–0.965	<.001	0.899	0.784–0.954	<.001
The early systolic global CSr (s^{-1})	0.878	0.742–0.944	<.001	0.848	0.685–0.930	<.001
The late systolic global CSr (s^{-1})	0.829	0.650–0.921	<.001	0.794	0.586–0.904	<.001

CS = circumferential strain, CSr = circumferential strain rate, ICC = intraclass correlation coefficient.

the incidence of T2DM by IR, so about 75% of T2DM patients suffer from NAFLD.[15,16] In addition, T2DM is an important risk factor in the progression of NASH evolve into cirrhosis and hepatocellular carcinoma, and prediabetes may be a sign of further development of NAFLD. Although NAFLD mainly occurs in the liver, it can also cause multiple organ diseases, such as cardiovascular disease, T2DM and a variety of endocrine diseases et al.[15,17,18] The patients with T2DM and NAFLD are more likely to occur cardiovascular diseases, because both of them are closely associated with the development of atherosclerosis, which is an important pathophysiological factor in the occurrence of cardiovascular diseases, and the carotid is a common site of atherosclerosis.[19–21]

Carotid atherosclerosis is common in patients with T2DM, and patients with T2DM are more prone to suffer from cardiovascular complications. Metabolic syndrome is a risk factor for atherosclerosis, and the hepatic manifestation of this syndrome is NAFLD. NAFLD can lead to endothelial dysfunction, which result in increased cardiovascular morbidity and mortality in patients with NAFLD. When carotid atherosclerosis occurs, lots of fat accumulate in the wall of arteries, which lead to a series of pathological changes, including vascular endothelial dysfunction, fibrous thickening of the vascular wall and the formation of plaque. These changes then result in carotid artery stenosis and reduce its elasticity.[22] The maker of atherosclerosis is carotid IMT, it not only has certain significance for early diagnosis of atherosclerosis, but also is considered as an independent predictor of cardiovascular risk.[23] Targher et al[24] found that the cervical artery IMT in NAFLD patients was significantly thicker than that in the control group. And the results of research conducted by Kamran et al[25] also showed that patients with NAFLD were more likely to have the thickening IMT compared with general population. Although, in our study, there were no statistical differences in IMT between groups A and B, IMT in group C was thicker than that in groups A and B. It showed that the thickening of carotid IMT is a progressive process, when T2DM is combined with NAFLD, carotid IMT will be gradually thickened with the aggravation of NAFLD.

Carotid ultrasound can be used to judge the degree of carotid artery stenosis. It plays a momentous role during the process of screening carotid artery stenosis. So, the measurement of carotid IMT by ultrasound is widely used to evaluate the severity of carotid atherosclerosis in clinic, due to the noninvasive and convenient advantages of ultrasound. In recent years, ultrasound is also in continuous development and progress, providing a lot of help to clinical diagnosis. On the basis of these advantages, 2DSI overcomes the angle dependence of Tissue Doppler and provides new parameters for assessing tissular elasticity and function.[26] Previously, 2DSI was used to assess cardiac function, and it has demonstrated its advantages of measuring the function of atrium and ventricle. For the past few years, 2DSI has been more and more applied to arterial elasticity assessment, because it can assess the circumferential, radial and longitudinal strain, and perform segmental analysis of carotid artery.[27] In addition,

2DSI has great reproducibility for assessing carotid artery.[28] IR can decrease the body's sensitivity to insulin, NAFLD and T2DM are significantly correlated with it. IR is not only an important feature of T2DM, but also a main pathogenesis of NAFLD.T2DM and NAFLD can accelerate the occurrence and development of carotid atherosclerosis under the mechanism of IR.[29] The carotid artery is composed of three layers, namely intima, media and adventitia. And intima lesions are the first to occur in atherosclerosis.[30] IR can lead to hyperinsulinemia, and result in increased lipid content in vascular smooth muscle cells and fibroblasts.[31] Second, IR can release inflammatory factors, damage vascular endothelial cells, reduce arterial elasticity, then cause the increase of arterial wall stiffness.[32,33] Taharboucht S. et al[34] compared 213 NAFLD patients with a control group which was composed of 213 patients, the results showed that patients with NAFLD were had higher incidence of carotid atherosclerosis plaque than the control group, and there was a remarkable correlation between NAFLD and carotid atherosclerosis. In our study, the CS, the early and late systolic global CSr of groups B and C were lower than those of group A, and these parameters in group C were lower than those in group B. But IMT was within the normal range, suggested that the decrease of carotid elasticity occurred earlier than the thickening of carotid intima-media in T2DM combined with NAFLD patients. In addition, M-mode ultrasound measurements showed that carotid artery stiffness parameter β1 was increased in group C compared with groups A and B, and β1 in group A showed no significant difference when compared with that in group B. Compared the carotid artery parameter of β2 among three groups, the 2DSI measurements showed that β2 of group C was higher than that of groups A and B, and β2 was higher in group B than in group A, differences were found between groups A and B. Correlation analysis revealed that CS, the early and late systolic global CSr were negatively correlated with β2 in each group, demonstrated that in patients of T2DM with NAFLD, 2DSI can assess the changes of carotid elasticity earlier than M-mode ultrasound.

T2DM patients with NAFLD often have increased IR and glucose metabolism disorders.[35] ALT is an indicator, which can reflect the liver function. NAFLD patients are usually accompanied by increased ALT level, and the increase of ALT is not only closely related to the higher risk of NAFLD, but also associated with hepatic steatosis.[36] Increased ALT activity is the main manifestation of NAFLD patients. In a study of 524 obese children and adolescents conducted by Lianhui Chen et al[37] showed that in obese boys, the incidence of carotid IMT increased with the increase of HbA1c, and use HbA1c as a diagnostic criterion for diabetes may be helpful in early identification of macrovascular complications. There is a certain correlation between the occurrence of cardiovascular disease and abnormal HbA1c level in T2DM patients.[38] In patients of T2DM with NAFLD, abnormal blood glucose metabolism will be more prominent, and HbA1c level will be further increased. HbA1c has a close association with the elevation of FBG due to IR, higher levels of HbA1c may thicken carotid IMT through IR mechanisms, and then lead to atherosclerosis.[39] There were significant differences in ALT, AST, TG, BMI and HbA1c levels among three groups, and these parameters in group C were higher than those in groups A and B. Correlation analysis among the three groups demonstrated that CS, the early and late systolic global CSr and HbA1c were negatively correlated, indicated that HbA1c could promote the occurrence of carotid atherosclerosis in T2DM patients with NAFLD.

4.1. Limitations

There are still some limitations in this study that we should not ignore. First of all, the sample size was insufficient. The moderate NAFLD and severe NAFLD were not grouped separately. So further study is needed to refine the grouping. Besides, the quality of two-dimensional images has certain influence on the accuracy of two-dimensional strain.

5. Conclusion

The results of our study indicate that 2DSI can effectively assess the carotid artery elasticity in T2DM patients with NAFLD at an early stage.

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References

[1] Cariou B, Byrne CD, Loomba R, et al. Nonalcoholic fatty liver disease as a metabolic disease in humans: a literature review. Diabetes Obes Metab. 2021;23:1069–83.
[2] Soto-Angona O, Anmella G, Valdes-Florido MJ, et al. Non-alcoholic fatty liver disease (NAFLD) as a neglected metabolic companion of psychiatric disorders: common pathways and future approaches. BMC Med. 2020;18:261.
[3] Lau LHS, Wong SH. Microbiota, obesity and NAFLD. Adv Exp Med Biol. 2018;1061:111–25.
[4] Cobbina E, Akhlaghi F. Non-alcoholic fatty liver disease (NAFLD) - pathogenesis, classification, and effect on drug metabolizing enzymes and transporters. Drug Metab Rev. 2017;49:197–211.
[5] Jahn D, Kircher S, Hermanns HM, et al. Animal models of NAFLD from a hepatologist's point of view. Biochim Biophys Acta Mol Basis Dis. 2019;1865:943–53.
[6] Younossi ZM, Golabi P, de Avila L, et al. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: a systematic review and meta-analysis. J Hepatol. 2019;71:793–801.
[7] Sung KC, Kim SH. Interrelationship between fatty liver and insulin resistance in the development of type 2 diabetes. J Clin Endocrinol Metab. 2011;96:1093–7.
[8] Muzurovic E, Mikhailidis DP, Mantzoros C. Non-alcoholic fatty liver disease, insulin resistance, metabolic syndrome and their association with vascular risk. Metabolism. 2021;119:154770.
[9] Caussy C, Aubin A, Loomba R. The relationship between type 2 diabetes, NAFLD, and cardiovascular risk. Curr Diab Rep. 2021;21:15.
[10] Yang J, Liu X, Jiang G, et al. Two-dimensional strain technique to detect the function of coronary collateral circulation. Coron Artery Dis. 2012;23:188–94.
[11] Pavlopoulos H, Nihoyannopoulos P. Strain and strain rate deformation parameters: from tissue Doppler to 2D speckle tracking. Int J Cardiovasc Imaging. 2008;24:479–91.
[12] Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67:328–57.
[13] Zeng MD, Fan JG, Lu LG, et al. Guidelines for the diagnosis and treatment of nonalcoholic fatty liver diseases. J Dig Dis. 2008;9:108–12.
[14] Khneizer G, Rizvi S, Gawrieh S. Non-alcoholic fatty liver disease and diabetes mellitus. Adv Exp Med Biol. 2021;1307:417–40.
[15] Muzica CM, Sfarti C, Trifan A, et al. Nonalcoholic fatty liver disease and type 2 diabetes mellitus: a bidirectional relationship. Can J Gastroenterol Hepatol. 2020;2020:6638306.
[16] Doycheva I, Patel N, Peterson M, et al. Prognostic implication of liver histology in patients with nonalcoholic fatty liver disease in diabetes. J Diabetes Complications. 2013;27:293–300.

[17] Byrne CD, Targher G. NAFLD: a multisystem disease. J Hepatol. 2015;62(1 Suppl):S47–64.
[18] Adams LA, Anstee QM, Tilg H, et al. Non-alcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic diseases. Gut. 2017;66:1138–53.
[19] Sookoian S, Pirola CJ. Non-alcoholic fatty liver disease is strongly associated with carotid atherosclerosis: a systematic review. J Hepatol. 2008;49:600–7.
[20] Di Pino A, DeFronzo RA. Insulin resistance and atherosclerosis: implications for insulin-sensitizing agents. Endocr Rev. 2019;40:1447–67.
[21] Cernea S, Raz I. NAFLD in type 2 diabetes mellitus: still many challenging questions. Diabetes Metab Res Rev. 2021;37:e3386.
[22] Tschiderer L, Klingenschmid G, Seekircher L, et al. Carotid intima-media thickness predicts carotid plaque development: meta-analysis of seven studies involving 9341 participants. Eur J Clin Invest. 2020;50:e13217.
[23] Kul S, Dursun I, Sayin MR, et al. Presystolic wave is associated with carotid intima media thickness. Echocardiogr. 2019;36:237–42.
[24] Targher G, Bertolini L, Padovani R, et al. Relations between carotid artery wall thickness and liver histology in subjects with nonalcoholic fatty liver disease. Diabetes Care. 2006;29:1325–30.
[25] Lankarani KB, Mahmoodi M, Lotfi M, et al. Common carotid intima-media thickness in patients with non-alcoholic fatty liver disease: a population-based case-control study. Korean J Gastroenterol. 2013;62:344–51.
[26] Kurt M, Tanboga IH, Aksakal E. Two-dimensional strain imaging: basic principles and technical consideration. Eurasian J Med. 2014;46:126–30.
[27] Podgorski M, Grzelak P, Kaczmarska M, et al. Feasibility of two-dimensional speckle tracking in evaluation of arterial stiffness: comparison with pulse wave velocity and conventional sonographic markers of atherosclerosis. Vascular. 2018;26:63–9.
[28] Yuda S, Kaneko R, Muranaka A, et al. Quantitative measurement of circumferential carotid arterial strain by two-dimensional speckle tracking imaging in healthy subjects. Echocardiogr. 2011;28:899–906.
[29] Bansilal S, Farkouh ME, Fuster V. Role of insulin resistance and hyperglycemia in the development of atherosclerosis. Am J Cardiol. 2007;99:6B–14B
[30] Yao Y, Yang G, Chen Y. Carotid intima-media thickness and ankle-brachial index and their correlation with coronary artery dilatation in children with kawasaki disease. Evid Based Complement Alternat Med. 2021;2021:7372424.
[31] Ahn SK, Lee JM, Ji SM, et al. Incidence hypertension and fasting blood glucose from real-world data: retrospective cohort for 7-years follow-up. Int J Environ Res Public Health. 2021;18:2085.
[32] Wu S, Xu L, Wu M, et al. Association between triglyceride-glucose index and risk of arterial stiffness: a cohort study. Cardiovasc Diabetol. 2021;20:146.
[33] Adeva-Andany MM, Ameneiros-Rodriguez E, Fernandez-Fernandez C, et al. Insulin resistance is associated with subclinical vascular disease in humans. World J Diabetes. 2019;10:63–77.
[34] Taharboucht S, Guermaz R, Brouri M, et al. Subclinical atherosclerosis and arterial stiffness in nonalcoholic fatty liver disease: a case-control study in Algerian population. J Med Vasc. 2021;46:129–38.
[35] Bae JC, Cho YK, Lee WY, et al. Impact of nonalcoholic fatty liver disease on insulin resistance in relation to HbA1c levels in nondiabetic subjects. Am J Gastroenterol. 2010;105:2389–95.
[36] Ma X, Liu S, Zhang J, et al. Proportion of NAFLD patients with normal ALT value in overall NAFLD patients: a systematic review and meta-analysis. BMC Gastroenterol. 2020;20:10.
[37] Chen LH, Zhu WF, Liang L, et al. Relationship between glycated haemoglobin and subclinical atherosclerosis in obese children and adolescents. Arch Dis Child. 2014;99:39–45.
[38] Mo Y, Zhou J, Ma X, et al. Haemoglobin A1c variability as an independent correlate of atherosclerosis and cardiovascular disease in Chinese type 2 diabetes. Diab Vasc Dis Res. 2018;15:402–08.
[39] Mukai N, Ninomiya T, Hata J, et al. Association of hemoglobin A1c and glycated albumin with carotid atherosclerosis in community-dwelling Japanese subjects: the Hisayama Study. Cardiovasc Diabetol. 2015;14:84.