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ORIGINAL ARTICLE

Retrospective Study

Correlation between non-alcoholic fatty liver with metabolic risk factors and brachial-ankle pulse wave velocity

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Abstract

AIM: To assess the relationship between non-alcoholic fatty liver disease (NAFLD) with metabolic risk factors and brachial ankle pulse wave velocity (baPWV).

METHODS: A total of 8603 subjects (6662 males and 1941 females) were enrolled during an annual health check-up. Fatty liver was examined using a Philips HD 11 XE multi-function color Doppler diagnostic instrument, and baPWV was determined using a novel arteriosclerosis detection device. Blood pressure (BP), fasting plasma glucose (FPG), waist circumference (WC), plasma triglycerides (TG), high-density lipoprotein (HDL), total cholesterol (TC), low-density lipoprotein (LDL) and uric acid (UA) were measured using standard methods. The relationship between fatty liver with metabolic risk factors and baPWV was analyzed using regression analysis and the χ^2 test.

RESULTS: The values and abnormal rates of baPWV were significantly different between NAFLD patients and non-NAFLD subjects ($P < 0.001$). In addition, the values of baPWV were different by gender between NAFLD patients and non-NAFLD subjects. The OR values in females, males, and the entire population were 3.33, 1.67, and 2.13, respectively ($P < 0.001$). The incidence of high baPWV increased with increasing degree of NAFLD (levels 0, 1, 2, and 3) ($P < 0.001$), which was 45.9%, 54.5%, 60.2%, and 71.4% in males

and 27.0%, 49.1%, 55.60%, and 60.0% in females ($P < 0.001$), respectively. Logistic regression analysis showed that the OR value for baPWV in the non-metabolic syndrome group and the metabolic syndrome group was 1.28 *vs* 1.14 (males) and 2.55 *vs* 0.98 (females). The OR values for baPWV in the non-high-BP and high-BP, non-high-WC and high-WC, non-high-FPG and high-FPG, non-high-TG and high-TG, non-high-HDL and high-HDL, non-high-TC and high-TC, non-high-LDL and high-LDL, non-high-UA and high-UA groups were 3.38 *vs* 1.19, 3.50 *vs* 1.44, 2.80 *vs* 2.30, 3.29 *vs* 1.88, 3.03 *vs* 3.28, 3.35 *vs* 2.70, 3.93 *vs* 1.66, and 3.20 *vs* 2.34, respectively, in females ($P < 0.001$), and were 1.37 *vs* 1.34, 1.56 *vs* 1.26, 1.51 *vs* 1.28, 1.49 *vs* 1.52, 1.71 *vs* 1.61, 1.59 *vs* 1.74, 1.76 *vs* 1.47, and 1.73 *vs* 1.54, respectively, in males ($P < 0.01$). The OR value for baPWV was still higher than 1.2 (1.21 in males and 1.40 in females) after adjustment for the metabolic component (0, 1, 2, 3, 4, 5, 6 and above) ($P < 0.01$).

CONCLUSION: NAFLD is closely correlated with baPWV, particularly in females. NAFLD has a large impact on baPWV, no matter whether the metabolic index is increased or not. NAFLD may be a useful indicator for assessing early arteriosclerosis.

Key words: Non-alcoholic fatty liver; Metabolic risk factors; Brachial ankle pulse wave velocity

Core tip: Non-alcoholic fatty liver disease (NAFLD) is emerging as an independent risk factor for the occurrence and progression of ischemic cardiovascular disease. However, the association between NAFLD and arterial stiffness is not fully elucidated. This study showed that NAFLD is closely related to brachial ankle pulse wave velocity. NAFLD has a noticeable impact when considering gender in the metabolic risk factor group, especially in females. NAFLD may be a useful indicator for assessing early arteriosclerosis.

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a clinicopathologic syndrome with pathological changes in liver tissue similar to alcoholic fatty liver disease, but without a history of excessive alcohol consumption. It is a manifestation of the metabolic syndrome in the liver[1]. Many studies have shown that NAFLD can co-exist with metabolic risk factors; it is closely related to atherosclerosis and can cause early changes in the function of arterial wall. NAFLD is accompanied by the release of a variety of proinflammatory molecules also implicated in cardiovascular disease (CVD) and metabolic syndrome (MetS), and it is an early stage in the process of systemic endothelial damage[2]. In a long-term follow-up study, Rafiq *et al*[3] concluded that NAFLD was not only a sign of atherosclerosis, but may also be involved in the development of early atherosclerosis; the prognosis of NAFLD is mainly associated with the occurrence of acute coronary events and stroke events. NAFLD is associated with coronary plaque, independent of traditional cardiovascular diseases[4]. Brachial-ankle pulse wave velocity (baPWV) is currently well recognized as an ideal indicator for assessing early atherosclerosis[5]. Metabolic risk factors are defined as a cluster of multiple cardiovascular risk factors[6]. The current study was designed to analyze the relationship between NAFLD and baPWV and explore the potential impact of NAFLD and metabolic risk factors on early changes in the function of arterial wall, in order to provide evidence for the early assessment of cardiovascular diseases.

MATERIALS AND METHODS

Subjects

A total of 9613 subjects (7180 males and 2433 females) who received health check-ups in our hospital from January 2013 to June 2014 were enrolled in this study. Metabolic risk factors, NAFLD, and baPWV were determined in these subjects. The inclusion criteria were as follows: (1) healthy residents in Zhejiang Province, China; and (2) subjects aged 25-75 years. The exclusion criteria were: (1) subjects with cardiovascular disease, other types of viral hepatitis and liver disease, abnormal liver function, drug-induced hepatitis, decompensated cirrhosis, autoimmune liver disease, hyperthyroidism, or cancer; or (2) subjects with a history of heavy drinking (equivalent of 40 g ethanol intake per week). Excluding 1010 subjects who were lost to follow-up, a total of 8603 subjects (6662 males and 1941 females) were eventually included with informed consent. This study was approved by the Medical Ethics Committee in Sir Run Run Shaw Hospital. All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Detection of metabolic risk factors, NAFLD and baPWV

NAFLD was diagnosed by examining fatty livers using a Philips HD 11 XE multi-function color Doppler diagnostic instrument (Philips Ultrasound, United States). Subjects were then divided into the non-fatty liver group (group 0) and the fatty liver groups (including the mild, moderate, and severe fatty liver groups which were labeled as groups 1, 2, and 3).

The baPWV was determined using a novel arterio-

sclerosis detection device VP-1000 (BP-203RPE Ⅲ) (Omron Corporation, Japan). The subjects were asked to rest quietly before taking three deep breaths in the spinal position, then remain quiet for another 5 min, and the pulse wave at the brachial-ankle artery was measured, and the baPWV value and its abnormal change rate were determined[7]. Here, the "abnormal change rate" refers to the percentage of the changed baPWV values relative to the reference values in subjects of the same gender and age. The means at the left and right sides were obtained, and then the median and values higher than the median were determined in the increased group.

The metabolic risk factors (closely related to fatty liver) were selected according to the guidelines for metabolic syndrome, hyperlipidemia and hyperuricemia prevention. The metabolic risk factors were determined, including: blood pressure (BP), waist circumference (WC), fasting plasma glucose (FPG), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and uric acid (UA). BP was measured using the standard method recommended in the 2010 Chinese Guidelines for the Management of Hypertension. WC was measured using the World Health Organization (WHO) standard method (the subjects were asked to stand and breathe normally, and the WC at the midpoint between the lowest rib and the iliac crest was measured). TG and TC were measured using the oxidase method, and HDL and LDL were measured using direct homogeneous methods. Uric acid (UA) was measured using enzymatic colorimetric method.

Diagnostic criteria

Criteria for assessing NAFLD: Ultrasonography was performed to assess NAFLD in accordance with the Diagnostic Criteria of Non-alcoholic Fatty Liver Disease by the Chinese Society of Hepatology in 2010[8]. Fatty liver was defined as "diffuse" if it met two of the following three criteria: (1) there was diffuse enhancement of near-field echo in the hepatic region, with the echo stronger than that in the kidneys; (2) the intrahepatic ductal structures were not clearly shown; and (3) the far-field echo in the hepatic region gradually became attenuated. According to the NALFD grading proposed by the Chinese Society of Hepatology and those described in a national document[9], we categorized the degree of echo attenuation in the posterior field, the intensities of hepatic dotted echoes, and the clarity of intrahepatic portal vein into Ⅰ (low), Ⅱ (intermediate), and Ⅲ (high). The posterior-field echo attenuation in fatty liver patients was further graded: degree Ⅰ, attenuated by < 1/3; degree Ⅱ, attenuated by 1/3-2/3; and degree Ⅲ, attenuated by > 2/3.

Diagnostic criteria for the metabolic syndrome and other metabolic risk factors: The diagnostic criteria for MS[10] established by the International Diabetes Federation in 2005 were adopted. More specifically, the subjects were determined to have MS if they had central obesity (waist circumference ⩾ 90 cm in males and ⩾ 80 cm in females) accompanied by two or more of the following features: (1) triglyceride (TG) level > 1.7 mmol/L; (2) systolic blood pressure (SBP) ⩾ 130 mmHg; or diastolic blood pressure (DBP) ⩾ 85 mmHg; or had been diagnosed with hypertension; (3) fasting plasma glucose (FPG) ⩾ 5.6 mmol/L, or had been diagnosed with type 2 diabetes; (4) high-density lipoprotein cholesterol (HDL-C) < 1.04 mmol/L in males and < 1.30 mmol/L in females. According to the diagnostic criteria proposed in the Guidelines on Adult Lipid Control in China (2007 Edition)[11], hypercholesteremia was defined as ⩾ 5.2 mmol/L and high LDL-C was defined as ⩾ 3.1 mmol/L; and (5) According to the diagnostic criteria of the American Rheumatism Association in 1997, hyperuricemia is defined as a serum uric acid level ⩾ 420 mmol/L in males or ⩾ 357 mmol/L in females.

Statistical analysis

All measurement data were entered into the database and then analyzed using SPSS 19.0 software. Data are presented as mean ± SD, categorical variables of medians, and percentages (%). *t* test was used for analysis of metabolic index and baPWV in non-alcoholic fatty liver and alcoholic fatty liver. The potential correlation between NAFLD and baPWV was analyzed using the logistic regression method. The potential impact of NAFLD on baPWV in subjects with high metabolic risk factors and in those with normal metabolic risk factors was also analyzed using the logistic regression method and multiple linear regression analysis. The increased percentage in baPWV in patients with different degrees of fatty liver was analyzed using the χ^2 test. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Demographic and clinical characteristics of study subjects

The baseline SBP, DBP, WC, FPG, body mass index, TG, HDL, TC, LDL, baPWV value, and rate of change in baPWV differed significantly between the fatty liver group and the non-fatty liver group (Table 1).

Relationship between brachial-ankle pulse wave velocity and NAFLD

High baPWV was defined as a value equal to or higher than the median [median baPWV value: 1321 cm/s (males) and 1219 cm/s (females), and 1302 cm/s (entire population)]. With NAFLD as the independent variable and high baPWV as the dependent variable, logistic regression and multiple linear regression analysis of the relationship between NAFLD and baPWV

Table 1 Demographic and clinical characteristics of study subjects in non-alcoholic fatty liver disease and no non-alcoholic fatty liver disease groups

Variables	NAFLD groups (n = 4025)	non-NAFLD group (n = 4578)	P value
Age (yr)	46.92 ± 9.12	45.67 ± 9.95	< 0.001
BMI (kg/m^2)	26.42 ± 2.83	22.93 ± 2.63	< 0.001
SBP (mmHg)	127.68 ± 15.49	119.46 ± 16.17	< 0.001
DBP (mmHg)	79.65 ± 11.38	72.78 ± 11.04	< 0.001
WC (cm)	90.70 ± 7.88	80.08 ± 8.23	< 0.001
FBG (mmol/L)	5.46 ± 1.36	4.97 ± 0.87	< 0.001
TG (mmol/L)	2.18 ± 1.64	1.25 ± 0.81	< 0.001
HDL-C (mmol/L)	1.12 ± 0.28	1.29 ± 0.29	< 0.001
TC (mmol/L)	5.02 ± 0.98	4.68 ± 0.89	< 0.001
LDL (mmol/L)	2.82 ± 0.78	2.65 ± 0.73	< 0.001
UA (mmol/L)	386.60 ± 88.75	319.00 ± 87.17	< 0.001
Mean baPWV value (cm/s)	1384.09 ± 228.86	1297.38 ± 237.58	< 0.001

NAFLD: Non-alcoholic fatty liver disease; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting blood glucose; WC: Waist circumference; TG: Triglycerides; HDL: High-density lipoprotein; TC: Total cholesterol; LDL: Low-density lipoprotein; baPWV: Brachial-ankle pulse wave velocity; UA: Uric acid.

Table 2 Relationship between brachial-ankle pulse wave velocity and non-alcoholic fatty liver disease n (%)

	High baPWV	Non-high baPWV	OR	95%CI	P value
Males with NAFLD					
No	1436 (46.4)	1219 (34.2)	-	-	-
Yes	1659 (53.6)	2348 (65.8)	1.667	1.510-1.841	< 0.001
Females with NAFLD					
No	1004 (79.9)	372 (54.4)		-	-
Yes	253 (20.1)	312 (45.6)	3.328	2.714-4.082	< 0.001
Entire population					
No	2440 (56.1)	1591 (37.4)	-	-	-
Yes	1912 (43.9)	2660 (62.6)	2.134	1.957-2.326	< 0.001

NAFLD: Non-alcoholic fatty liver disease; baPWV: Brachial-ankle pulse wave velocity (high baPWV was defined as a value equal to or higher than the median).

showed that NAFLD had an impact on high baPWV in males (OR = 1.667), females (OR = 3.328), and the entire population (OR = 2.134) (Table 2).

Relationship between severity of NAFLD and baPWV

We analyzed the proportions of high baPWV in four NAFLD groups (groups 0, 1, 2, and 3) and found that the incidence of high baPWV gradually increased in the entire population (39.5%, 53.6%, 58.1%, and 70.5%, respectively; χ^2 = 320.3, P < 0.001), in males (45.9%, 54.5%, 60.2%, and 71.4%, respectively; χ^2 = 118.0, P < 0.001), and in females (27.0%, 49.1%, 55.60%, and 60.0%, respectively; χ^2 = 145.8, P < 0.001) with an increase in the degree of NAFLD (Figure 1). The value of baPWV increased gradually in females (from group 1 to group 4, P < 0.001), and males (from group 1 to group 3, P < 0.01; Figure 2).

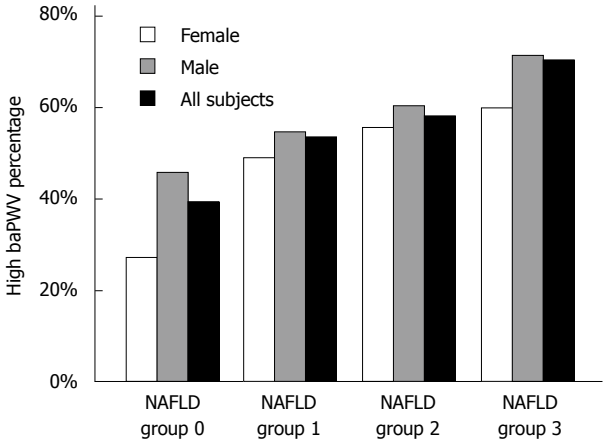

Figure 1 Relationship between the severity of non-alcoholic fatty liver disease and brachial-ankle pulse wave velocity. The subjects were divided into four groups (0, 1, 2, and 3) based on the degree of fatty liver (0: none; 1: mild; 2: moderate; and 3: severe). baPWV: Brachial-ankle pulse wave velocity; NAFLD: Non-alcoholic fatty liver disease.

Relationship between NAFLD and baPWV after stratification of metabolic risk factors

The metabolic risk factors were stratified into two groups according to the diagnostic criteria of MS and metabolic factors. With the presence of fatty liver as the independent variable and high baPWV as the dependent variable (high baPWV was defined as a value equal to or higher than the median), logistic regression analysis was performed to determine the relationship between fatty liver and high baPWV. The results showed that, in all groups of non-high metabolic risk factors and high metabolic risk factors, NAFLD has an effect on baPWV, particularly in females - except for females with MS (P < 0.01) (Table 3).

Logistic regression analysis after adjustment for age and metabolic components

The metabolism risk factors were divided into 7 groups (0, 1, 2, 3, 4, 5, 6 and above groups) according to metabolic component number. Logistic regression analysis was also performed to determine the relationship between fatty liver and baPWV after adjusting for metabolic components (the number of metabolism risk factors to be assumed dummy variable). OR value for baPWV was still higher than 1.2 (in males and females) (P < 0.05) (Table 4).

DISCUSSION

NAFLD is associated with atherosclerosis and coronary heart disease. Research has shown that liver histopathology is closely correlated with early atherosclerosis in NAFLD patients[12]. Although it has been proposed that carotid-femoral pulse wave velocity may be the gold standard during the non-invasive examination of arteriosclerosis, arterial pulse wave velocity remains a well-recognized

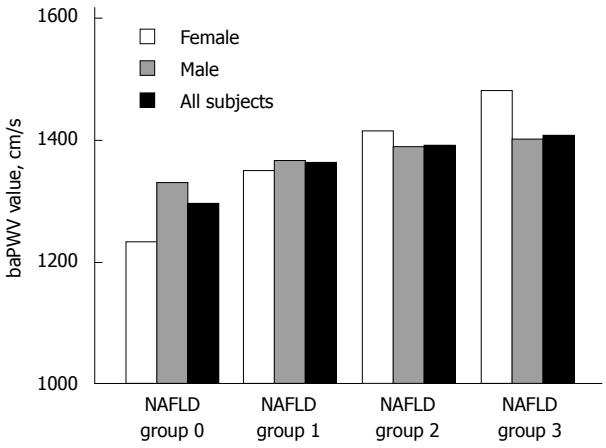

Figure 2 Relationship between the severity of non-alcoholic fatty liver disease and the value of brachial-ankle pulse wave velocity. The subjects were divided into four groups (0, 1, 2, and 3) based on the degree of fatty liver (0: none; 1: mild; 2: moderate; and 3: severe). baPWV: Brachial-ankle pulse wave velocity; NAFLD: Non-alcoholic fatty liver disease.

parameter for assessing vascular elasticity in the early phases of atherosclerosis; it is also a method for assessing arterial stiffness and reflecting the risk of cardiovascular lesions. Together with advances in the non-invasive detection of arteriosclerosis, monitoring of arterial pulse wave velocity has been widely used to screen individuals with early atherosclerotic vascular disease and for assessing cardiovascular risks[13].

In the current study, we determined the relationship between baPWV and NAFLD, and found that baPWV was significantly increased in the NAFLD group compared with the control group, suggesting a close relationship between baPWV and NAFLD. Logistic regression analysis showed that NAFLD affected baPWV in both males and females in the entire population. In addition, the incidence of high baPWV gradually increased with exacerbation of NAFLD, further indicating the clear relationship between NAFLD and baPWV. Many studies have shown that NAFLD is a marker of subclinical CVD, and the pathogenesis of NAFLD may involve early atherosclerotic cardiovascular disease[14], while the role of NAFLD in promoting the development of atherosclerosis remains unclear**.** The following mechanisms may be involved: (1) patients with NAFLD also have other metabolic risk factors, and the number and degree of these factors are associated with early atherosclerosis; (2) NAFLD promotes systemic inflammation and oxidative stress, intensifies insulin resistance, and triggers the occurrence of atherosclerosis and coronary heart disease. Notably, NAFLD can cause changes in vascular structure and function. By affecting vascular endothelial function and the hypercoagulation/hypofibrinolysis status, NAFLD can cause endothelium-dependent flow-mediated vasodilation as well as oxidative stress-lipid peroxidation, thus leading to arteriosclerosis[15]; and (3) NAFLD may lead to an increase in free fatty acids, mainly from visceral adipose tissues with increased flow and may cause a significant increase in the prevalence of cardiocerebrovascular diseases. Therefore, NAFLD may be a marker of subclinical cardiovascular disease at the early stages of atherosclerosis[16].

NAFLD has been documented to be a sign of MS in the liver, and most NAFLD patients have cardiovascular disease or cancer. Arteriosclerosis is the pathogenic basis for most cardiocerebrovascular diseases[17]. The change in vascular elasticity is often earlier than the change in vascular morphology. Among the currently available non-invasive methods for detecting arterial stiffness, baPWV can adequately reflect the degree of change in systemic arterial elasticity. Thus, by detecting vascular indicators such as baPWV, assessments and interventions in populations at different levels of risk can be carried out to lower the incidence of early atherosclerosis and its associated cardiocerebrovascular diseases, thus decreasing the NAFLD mortality[18].

Several recent studies reported that NAFLD is probably an independent risk factor for the occurrence of cardiovascular disease[19]. In the current study, we found that no matter whether the metabolic index increased, NAFLD affected baPWV. After adjustment for metabolic components (the number of metabolism risk factors assumed as dummy variable), NAFLD still affected baPWV in males and females. These findings suggest that NAFLD not only affects baPWV independently, but also has a close relationship with arteriosclerosis during an increase in the non-cardiovascular metabolic risk factors. In addition, our study further suggested that NAFLD does not affect baPWV by relying solely on increased metabolic risk factors. NAFLD may be a marker of increased baPWV in early atherosclerosis. A possible mechanism for this may involve hepatocytes, which are rich in mitochondria, the major sites for synthesizing ATP and reactive oxygen species (ROS) in cells. In patients with fatty liver, mitochondria have significantly increased respiratory activities and elevated ROS production, causing oxidative stress and lipid peroxidation. The presence of massive numbers of ROS and lipid peroxides can result in an imbalance between oxidation and antioxidation in the body, leading to angiogenesis and endothelial dysfunction[20], and affect the formation of arterial plaques[21]. Another possible mechanism is that NAFLD is related to oxidative stress and procoagulation and can increase the circulating levels of oxidized low-density lipoprotein, nitrotyrosine, and plasminogen activator inhibitor-1[22], thus leading to early atherosclerosis. The increase in adipose tissue and chronic inflammation cause an imbalance in adipokine secretion, in particular a reduction of adiponectin improving vascular damage[23].

We also found that the correlation between NAFLD and baPWV was closer in females than in males, particularly in individuals with normal metabolic risk

Table 3 Relationship between non-alcoholic fatty liver disease and high brachial-ankle pulse wave velocity after stratification of metabolic risk factors *n* (%)

Variable	NAFLD	Males (*n* = 6662)			Females (*n* = 1941)		
		Subjects with high baPWV	OR (95%CI)	*P* value	Subjects with high baPWV	OR (95%CI)	*P* value
MS							
No	No	1033 (39.5)	Ref		296 (23.3)	Ref	-
	Yes	1089 (58.2)	1.280 (1.139-1.439)	< 0.001	139 (43.7)	2.550 (1.972-3.297)	< 0.001
Yes	No	185 (66.5)	Ref	-	76 (70.4)	Ref	-
	Yes	1259 (69.4)	1.142 (0.873-1.494)	0.331	173 (70.0)	0.984 (0.600-1.614)	0.950
High BP							
No	No	698 (35.9)	Ref	-	185 (16.3)	Ref	-
	Yes	990 (43.5)	1.374 (1.214-1.556)	<0.001	139 (39.7)	3.383 (2.593-4.413)	< 0.001
Yes	No	520 (73.6)	Ref	-	187 (77.6)	Ref	-
	Yes	1352 (78.8)	1.339 (1.093-1.641)	0.005	173 (80.5)	1.189 (0.756-1.871)	0.453
High WC							
No	No	947 (43.7)	Ref	-	218 (20.5)	Ref	-
	Yes	886 (54.8)	1.559 (1.369-1.775)	< 0.001	75 (47.5)	3.503 (2.478-4.950)	< 0.001
Yes	No	271 (55.5)	Ref	-	154 (48.2)		
	Yes	1462 (61.2)	1.262 (1.036-1.536)	0.021	237 (58.2)	1.439 (1.070-1.936)	0.016
High FPG							
No	No	1019 (43.2)	Ref	-	326 (25.1)	Ref	-
	Yes	1573 (53.4)	1.508 (1.352-1.681)	< 0.001	210 (48.4)	2.801 (2.234-3.512)	< 0.001
Yes	No	199 (67.9)	Ref	-	46 (60.5)	Ref	_
	Yes	775 (73.0)	1.280 (0.967-1.694)	0.084	102 (77.9)	2.294 (1.237-4.255)	0.008
High TG							
No	No	919 (44.2)	Ref	-	315 (25.2)	Ref	-
	Yes	959 (54.1)	1.486 (1.308-1.688)	< 0.001	199 (52.6)	3.296 (2.596-4.186)	< 0.001
Yes	No	299 (52.0)	Ref	-	57 (49.9)	Ref	-
	Yes	1389 (62.2)	1.517 (1.262-1.825)	< 0.001	113 (60.4)	1.875 (1.188-2.960)	0.007
Low HDL							
No	No	933 (45.5)	Ref	-	210 (25.4)	Ref	-
	Yes	1368 (59.2)	1.709 (1.515-1.927)	< 0.001	108 (50.7)	3.027 (2.218-4.131)	< 0.001
Yes	No	285 (45.9)	Ref	-	162 (29.6)	Ref	-
	Yes	980 (57.8)	1.614 (1.341-1.941)		204 (58.0)	3.284 (2.482-4.346)	< 0.001
High TC							
No	No	868 (45.1)	Ref	-	245 (22.6)	Ref	-
	Yes	1373 (56.6)	1.588 (1.408-1.791)	< 0.001	190 (49.5)	3.350 (2.621-4.282)	< 0.001
Yes	No	350 (48.1)	Ref	-	127 (43.3)	Ref	_
	Yes	975 (61.7)	1.736 (1.454-2.073)	< 0.001	122 (67.4)	2.703 (1.835-3.981)	< 0.001
High LDL							
No	No	867 (44.9)	Ref	-	258 (22.7)	Ref	-
	Yes	1544 (58.9)	1.758 (1.561-1.979)	< 0.001	224 (53.6)	3.925 (3.096-4.975)	< 0.001
Yes	No	351 (48.5)	Ref	-	114 (47.3)	Ref	-
	Yes	804 (58.0)	1.466 (1.223-1.756)	< 0.001	88 (59.9)	1.662 (1.097-2.518)	0.017
High UA							
No	No	797 (45.6)	Ref	-	384 (26.4)	Ref	-
	Yes	1544 (58.9)	1.725 (1.523-1.924)	< 0.001	260 (53.3)	3.202 (2.580-3.973)	< 0.001
Yes	No	239 (45.7)	Ref	-	24 (47.0)	Ref	-
	Yes	857 (59.7)	1.543 (1.260-1.890)	< 0.001	52 (67.5)	2.340 (1.130-4.843)	0.022

SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; WC: Waist circumference; TG: Triglycerides; HDL: High-density lipoprotein; TC: Total cholesterol; LDL: Low-density lipoprotein; UA: Uric acid; baPWV: Brachial-ankle pulse wave velocity (high baPWV was defined as a value equal to or higher than the median).

factors. This may be explained by the decreased estrogen level in some post-menopausal women. Estrogen produced by the ovaries can inhibit the accumulation of visceral fats and increase the formation of subcutaneous fats[24]. Furthermore, the distribution profiles of dietary fatty acids may also differ significantly between males and females. The fatty acids in females are more likely to be transformed into ketone bodies and are involved in energy metabolism, and thus cause fat deposition in the liver[25] .

Our research had some limitations: (1) it was a cross-sectional analysis with subjects enrolled following a health check-up. Although the baPWV was adjusted for age and gender to reflect a natural population, sampling bias may still exist; and (2) while the baPWV used in our study is a good parameter for measuring arterial stiffness, it is not the gold standard for arteriosclerosis.

In summary, NAFLD is independently correlated with baPWV, and NAFLD is closely associated with an increased risk of cardiovascular diseases. Measurement of baPWV in NAFLD populations can facilitate the early

Table 4 Relationship between non-alcoholic fatty liver disease and brachial-ankle pulse wave velocity after adjustment for metabolic components

Group	Males (n = 6662)			Females (n = 1941)		
	n (%)	OR (95%CI)	P value	n (%)	OR (95%CI)	P value
NAFLD0	2653 (39.8)	Ref	-	1376 (70.9)	Ref	-
NAFLD1	4009 (60.2)	1.21 (1.09-1.33)	< 0.001	565 (29.1)	1.40 (1.08-1.82)	< 0.001
MC0	787 (11.8)	Ref	-	451 (23.2)	Ref	-
MC1	955 (14.3)	1.59 (1.29-1.97)	< 0.001	511 (26.3)	3.38 (2.19-5.20)	< 0.001
MC2	1288 (19.3)	2.03 (1.66-2.48)	< 0.001	368 (19.0)	5.04 (3.23-7.87)	< 0.001
MC3	1282 (19.2)	2.66 (2.16-3.27)	< 0.001	272 (14.0)	7.40 (4.67-11.80)	< 0.001
MC4	1117 (16.8)	3.22 (2.60-3.99)	< 0.001	187 (9.60)	9.84 (5.83-16.60)	< 0.001
MC5	763 (11.5)	4.35 (3.42-5.52)	< 0.001	106 (5.50)	11.87 (6.40-22.03)	< 0.001
MC6 and above	470 (7.10)	5.59 (4.23-7.38)	< 0.001	46 (2.40)	20.26 (7.45-55.12)	< 0.001

NAFLD: Non-alcoholic fatty liver disease; MC: Metabolic components (the number of metabolism risk factors assumed as dummy variable).

prediction and assessment of vascular lesions. In patients with NAFLD, clinicians should not only treat the liver disease, but also comprehensively assess the risk of ischemic cardiovascular diseases, which should include the pathogenic effects of different risk factors on the individuals and potential early atherosclerotic disease caused by these risk factors. Such a comprehensive assessment of the various risk factors in NAFLD patients may help to identify the absolute risk of ischemic cardiovascular diseases and thus provide different interventions for populations at different levels of risk to lower the morbidity and mortality associated with NAFLD[26]. Early monitoring of NAFLD may benefit preventive strategies to help decrease the risk of developing arteriosclerosis. In NAFLD patients with a low risk of cardiovascular disease, assessment and management of early arteriosclerosis is still required. In addition, appropriate interventions should be undertaken to lower cardiovascular risks and reduce underlying cardiovascular diseases. However, further prospective studies are needed to clarify the mechanisms governing the change of baPWV in the early stages of arteriosclerosis in NAFLD patients and the subsequent progression of cardiovascular diseases.

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COMMENTS

Background

Non-alcoholic fatty liver disease (NAFLD) is well known as an important risk factor for cardiovascular disease. Brachial ankle pulse wave velocity is closely related to atherosclerosis and cardiovascular disease. However, correlation between non-alcoholic fatty liver disease and arterial stiffness is not completely elucidated.

Research frontiers

The authors determined the relationship between brachial ankle pulse wave velocity (baPWV) and NAFLD, and found that baPWV was significantly increased in the NAFLD group compared with the control group, suggesting a close relationship between baPWV and NAFLD. Logistic regression analysis showed that NAFLD affected baPWV in both males and females in the entire population. In addition, the incidence of high baPWV gradually increased with exacerbation of NAFLD, further indicating the clear relationship between NAFLD and baPWV.

Innovations and breakthroughs

This study found that no matter whether the metabolic index is increased or not, NAFLD is closely related to baPWV, and NAFLD may be a useful indicator for assessing early arteriosclerosis.

Applications

NAFLD can be used to predict early atherosclerosis. This will provide the basis for the prevention and early treatment of atherosclerosis and cardiovascular disease.

Terminology

NAFLD is a clinicopathologic syndrome with pathological changes in liver tissue similar to alcoholic fatty liver disease.

Peer-review

It is important to study the correlation between non-alcoholic fatty liver disease and brachial ankle pulse wave velocity.

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