Association between Insulin Resistance, Metabolic Syndrome and Nonalcoholic Fatty Liver Disease in Chinese Adults

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Abstract

Background: The aim of this study was to assess the association between insulin resistance, metabolic syndrome and nonalcoholic fatty liver disease (NAFLD) in Chinese adults.

Methods: Fifty five subjects with NAFLD and 55 controls were enrolled for the study. Waist circumference, blood pressure, plasma triglyceride, high density lipoprotein cholesterol and fasting plasma glucose concentrations and homeostasis model assessment of insulin resistance (HOMA-IR) values as an index used to quantify insulin resistance were measured and analyzed. Logistic regression was analyzed to predict independent risk factors of NAFLD.

Results: The prevalence of metabolic syndrome in NAFLD group was obviously higher than in controls group (47.3% VS 3.6%, $P<0.001$). There were all significant differences of each component of metabolic syndrome and HOMA-IR values in comparison of nonalcoholic fatty liver disease (NAFLD) and controls group. In a logistic regression analysis, age, diastolic blood pressure, waist circumference and HOMA-IR were the covariates independently associated with the presence of NAFLD (Odds Ratio=1.107, 1.083, 1.218 and 16.836; 95% CI: 1.011 ~ 1.211, 1.001~1.173, 1.083 ~ 1.370 and 3.626~78.168, respectively; $P<0.05$)

Conclusion: NAFLD was closely associated with metabolic syndrome and insulin resistance was a very strong predictor of NAFLD.

Keywords: Insulin Resistance, Metabolic syndrome, Nonalcoholic Fatty Liver Disease, China

Introduction

Both nonalcoholic fatty liver disease (NAFLD) and metabolic syndrome (MetS) are common clinical conditions in the world. NAFLD includes a spectrum of liver diseases ranging from simple steatosis to nonalcoholic steatohepatitis, and can progress to fibrosis and cirrhosis (1). NAFLD is a common liver disease strongly associated with obesity, type 2 diabetes mellitus and hyperlipidemia (2). The pathogenic mechanism of NAFLD has been based on a 'a 2-hit hypothesis'. Additionally, a'third-hit'has been added to reflect inadequate hepato-cyte proliferation(1). Of all factors, insulin resistance (IR) plays a key role in NAFLD progression. Some reports have also identified with this viewpoint (3, 4).

MetS consists of a cluster of cardiometablic risk factors (5, 6). Insulin resistance is also a central feature of MetS, having a strong association with components of the syndrome (7). Even NAFLD is now considered the hepatic manifestation of MetS (8). Thereby relationship between IR, MetS and NAFLD is close. Recent studies also showed their strong

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association (3, 9, 10); however, related articles are still insufficient. The aim of this study was to assess the association between IR, MetS and NAFLD in Chinese adults and it may be useful to prevent and treat NAFLD.

Materials and Methods

Subjects

Subjects were selected from those visited our center for a related health checkup during the period April 2008 to November 2008. Subjects whose related personal data were inadequate or alcoholic consumption was more than 20g/day were excluded. Subjects with known diabetes, cardiovascular disease (CVD) and any chronic diseases including liver diseases and renal failure were also excluded from the study. Ultimately, a total of 110 subjects were enrolled. Among these, 55 subjects (age: 45.1±8.9, 9 women) who were diagnosed to have NAFLD by using abdominal ultrasound imaging classified as NAFLD group, while 55 subjects(age:43.6±8.6, 17 women) who had normal liver ultrasound imaging and whose alamine trans-aminase (ALT) value was less than 1.5 times of the upper normal value were taken as controls group.

Definition of MetS and ultrasound imaging

We used the definition to MetS in international diabetes federation (IDF) (11). The results of abdominal ultrasound imaging were reported by immovable ultrasound doctors (medical apparatus equipped with a 3.5-MHZ probe, LOGIQ7 (GE health care, US), or SIEMENS VF-105(Siemens, Germany)). Steatosis was diagnosed on the basis of high level, abnormal intense echoes (12). Waist circumference (WC) and blood pressure (BP) were measured by qualified technicians. Waist circumference was measured on standing subjects with a soft tape midway between the lowest rib and the iliac crest. BP was taken after at least 5 minutes of rest.

Biochemical tests

Venous blood samples were obtained after a minimum 8-h fast for the measurement of plasma indexes. Triglyceride(TG) and high density lipoprotein cholesterol(HDL-C) concentrations were measured by the terminal method, using OLYMPUS AU machine. Fasting plasma glucose(FPG) concentration was measured by the hexokinase method, using OLYMPUS AU machine. Fasting insulin (FINS) concentration was measured by the antibody sandwich ELISA method, using DPL IMMULITE automatic immunoanalyzer. In the study, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was used to quantify IR. The HOMA-IR(13) was calculated according to the following formula: HOMA-IR=[FINS(uIU/ml)×FPG(mmol/L)] / 22.5. ALT was measured by velocity method, using OLMPUS 5400 machine.

Statistical Analysis

The SPSS statistical package, version 13.0 was used for the statistical analysis. P< 0.05 was considered statistically significant. A normal-distribution data were expressed as the mean ± SD. Skewed distribution data were expressed as the Median $(P_{25}\sim P_{75})$. Difference of MetS prevalence was tested using Chi-square test between cases and controls. Independent sample t test was used to detect the differences between cases and controls for the HOMA-IR, HDL-C, WC, Systolic blood pressure(SBP) and diastolic blood pressure(DBP) values. Moreover, FPG and TG values in cases were skewed distribution. The FPG and TG values in cases became a normal distribution by taking a Log of it; the independent sample t test was used to compare the transformed data.

A logistic regression was carried out to identify the independent predictors of NAFLD considering age, gender, HOMA-IR, FPG, HDL-C, TG, WC, SBP and DBP as covariates and to estimate odds ratio(OR) and 95% confidence interval (95%CI).

Results

The prevalence of MetS was 3.6 % (2/55) in controls group and 47.3% (26/55) in NAFLD group. The prevalence of MetS in NAFLD group was obviously higher than in controls group (*P*=0.000) (Table 1).

Comparison of age and gender between NAFLD and controls groups wasn't statistically significant. Significantly higher values of HOMA-IR, FPG, TG, WC, SBP and DBP were recorded in NAFLD than in controls group (All *P*≤0.001). The values of HDL-C were signifi-

cantly lower in NAFLD than in controls group (*P*=0.002) (Table 2).

In a logistic regression analysis including nine covariates(age, gender, HOMA-IR, FPG, HDL-C, TG, WC, SBP and DBP) performed in the 110 subjects, age, DBP , WC and HOMA-IR were the covariates independently associated with the presence of NAFLD(OR=1.107, 1.083, 1.218 and 16.836; 95% CI: 1.011 ˜ 1.211, 1.001~1.173, 1.083 ˜ 1.370 and 3.626~78.168, respectively; All *P*<0.05) (Table 3).

Table 1: Prevalence of MetS in NAFLD and controls group respectively

		MetS	Without MetS
Control	(55)	2 (3.6%)	53 (6.4%)
NAFLD	(55)	26 (47.3%)	29 (52.7%)

Chi-Square test: *P*=0.000 in the comparison with the prevalence of MetS between cases and controls

Table 2: Comparison of HOMA-IR, FPG, HDL-C, TG, WC, SBP and DBP between NAFLD and controls group

	NAFLD	Control	*P* value
Age (year)	45.1±8.9	43.6±8.6	0.350
Gender(F/M)	9/46	17/38	0.115*
HOMA-IR	2.73±1.42	1.06±0.53	<0.001
FPG (mg/dl)	91.0(84.0~100.0)	85.8±7.1	0.001
HDL-C (mg/dl)	49.9±10.1	56.2±10.3	0.002
TG (mg/dl)	205.2±89.6	107.0(73.0~146.0)	<0.001
WC (cm)	90.8±6.4	77.9±7.3	<0.001
SBP (mmHg)	129.4±12.4	116.2±14.3	<0.001
DBP (mmHg)	80.0±8.9	69.2±10.1	<0.001

* Chi-square test

Table 3: Logistic regression model for analysis of predictors of NAFLD

	B	S.E.	Wald	*P*	OR	95.0%C.I.for OR	
						Lower	Upper
Age	0.101	0.046	4.871	0.027	1.107	1.011	1.211
DBP	0.080	0.041	3.910	0.048	1.083	1.001	1.173
WC	0.197	0.060	10.822	0.001	1.218	1.083	1.370
HOMA-IR	2.824	0.783	12.992	0.000	16.836	3.626	78.168

Discussion

In this study, the diagnosis of the MetS was based on the criteria in the IDF report. NAFLD

was assessed by liver ultrasound imaging. The prevalence of MetS in NAFLD group was ob-

viously higher than in controls group. The results showed that NAFLD was closely associated with the MetS. Angelic et al. (3) reported that patients with MetS were more IR had a higher prevalence of severe steatosis. It is well known that the MetS was related with subsequent increases in the incidence of cardiovascular disease and diabetes mellitus morbidity (5, 14) and therefore NAFLD is also strong association with cardiovascular disease and diabetes mellitus. Several previous studies also showed that NAFLD was a strong predictor of subsequent cardiovascular events and diabetes mellitus (15-17). The possible molecular mediators linking NAFLD and CVD include the release of proatherogenic mediators from the liver including C-reactive protein, interleukin-6, and plasminogen activator inhibitor-1(16).

Association between components of MetS, HOMA-IR and NAFLD was assessed in further study. The results showed that significantly higher values of HOMA-IR, FPG, TG, WC, SBP and DBP (significantly lower values of HDL-C) were recorded in NAFLD than in controls group. It illustrated that NAFLD was closely related with each component of MetS and IR. It can be considered that NAFLD is a manifestation of MetS. Some articles have the similar consideration (8, 18, 19).

On the other hand, IR has been as not only a key role of MetS (7), but a major feature of NAFLD. IR may enhance hepatic fat accumulation by increasing free fatty acid delivery by the effect of hyperinsulinemia to stimulate anabolic processes (20). In our further study, four independent risk factors for NAFLD were indicated, including age, DBP, WC and HOMA-IR. Among four independent risk factors, HOMA-IR was the strongest independent risk factors, which indicated the importance of IR in the process of occurrence and development of NAFLD. Bajaj et al. (10) reported the similar result. A recent study (21) also showed that NAFLD patients had higher insulin, glycemia, and HOMA-IR values than control group.

Therefore, using agents that improve insulin sensitivity are significant to prevent and treat NAFLD.

This study has its limitations. The subjects did not represent the general population, who were only a small group to visit our center. On the other hand, we all know, liver biopsy is as gold standard to diagnose NAFLD, therefore, it is another limitation that ultrasound imaging was used to diagnose NAFLD in our study. However, the ultrasound imaging may be more suitable to be performed than other methods in a checkup population.

In conclusion, our findings showed that NAFLD was closely associated with MetS and IR was a very strong predictor of NAFLD.

Ethical Considerations

Ethical issue principles including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc. have been completely observed by the authors. The study was approved by the Ethical Committee of the Second Affiliated Hospital, school of Medicine, Zhejiang University, Hangzhou, China.

Acknowledgements

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