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ORIGINAL ARTICLE

Predictive Power of Visceral Adiposity Index and Model of Adipose Distribution in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD)

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ABSTRACT

Background: Nowadays, non-alcoholic fatty liver disease (NAFLD) is considered as the hepatic manifestation of metabolic syndrome. Visceral adiposity index (VAI) and model of adipose distribution (MOAD) are novel indicators of abdominal fat dysfunction shown to have a strong correlation with cardiovascular diseases, even there is controversy for patients with NAFLD. This study aimed to compare VAI and MOAD in patients with NAFLD and healthy individuals.

Methods: In a case-control study, 44 patients with NAFLD aged 20-60 years and 44 healthy individuals of the same age and sex were enrolled. Liver enzymes and lipid profile were measured after fasting for 10-12 hours. Anthropometric data, blood pressure, MOAD and VAI were determined for each subject separately.

Results: Although the mean of body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), VAI, and MOAD indices were significantly different between case and control groups, all indices could only predict NAFLD in females except for BMI.

Conclusion: This study showed that BMI is not a predictor for the development of NAFLD in males and females. VAI, MOAD indices can be used to estimate the relationship for NAFLD regarding two indices of WC and WHtR as the most powerful indices for estimation of the proportion of the risk for developing NAFLD.

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Introduction

Non-alcoholic fatty liver disease (NAFLD) is a liver dysfunction which can lead to progressive and the irreversible disease of cirrhosis, if it is not detected early and treated properly (1). New reports suggested that NAFLD prevalence was more than what was estimated and many patients with non-specific symptoms were identified by periodic check-ups. Since assessment of the outbreak is correlated with the diagnostic methods used, different studies presented various results (2).

The prevalence of NAFLD was reported 68% based on findings of the liver sonography, but the prevalence of the disease was approximately estimated 40% when MRI was used for the diagnosis. It is noteworthy that the level of serum liver enzymes is normal for 80% of individuals with fatty liver disease based on MRI findings. It represents the weakness of laboratory methods in the diagnosis of NAFLD. If laboratory methods are used for diagnosis of NAFLD, only 5-8% of patients will be detected; so laboratory methods are not only suitable tests for diagnosis of the disease (3).

It was shown that the prevalence of disease in Western countries is 20-30% (4). Although hepatitis A and B virus infections have a decreasing trend in Iran (5, 6), but unfortunately due to the obesity epidemic in developing countries, it seems that adverse effects such as an increase in serum lipids, cardiovascular diseases and fatty liver disease may be observed (7). A recent study undertaken on the prevalence of fatty liver in northern Iran, suggested a prevalence of 43.8%. In this study, waist circumference (WC) was reported as the strongest predictor of developing NAFLD among the criteria for metabolic syndrome (8).

Overweight and obesity are closely related to NAFLD and the degree of obesity increases the probability of disease progression. According to the data gathered in recent years, many individuals with NAFLD were shown to have abdominal obesity classified in non-obese groups based on body mass index (BMI). So in these subjects, WC was considered as a factor to be correlated to NAFLD and independence of BMI (9), and was demonstrated that body fat distribution is more important than the total body fat. Visceral obesity measured by WC benchmark had a stronger association with type 2 diabetes and NAFLD than the total body obesity measured by BMI (10, 11).

Since WC is a poor index to differentiate between visceral and subcutaneous fats (12, 13); computerized tomography scanning (CT scan) and magnetic resonance imaging (MRI) were the suggested methods for the assessment of abdominal fat, even they cannot be used because of their cost, radiation exposure, lack of easy access and being time-consuming (14). Lipid profile disorders as part of the metabolic syndrome along with abdominal obesity are effective in the pathogenesis of NAFLD. Free fatty acids would increase the concentrations of triglycerides (TG) and cholesterol ester in the liver due to insulin resistance. High concentrations of TG in VLDL would induce cholesterol ester transfer protein (CETP) activity, resulting into an increase in TG transmission from Very low-density lipoprotein (VLDL) to high-density lipoprotein (HDL) cholesterol and ultimately reduces the concentration of HDL (10).

Mortality in patients with NAFLD is frequently reported as the leading cause of cardiovascular diseases, since NAFLD has often a slow processing speed. In other words, it seems that majority of patients with fatty liver die from the metabolic syndrome of cardiovascular diseases before the development of cirrhosis (15). Visceral adiposity index (VAI) and model of adipose distribution (MOAD) as equation models provide a comprehensive figure of individual's cardio-metabolic status for each sex separately. Simple anthropometric indices, such as WC, BMI, TG and HDL are considered as indirect markers for chronic inflammatory status that matches with imaging techniques of visceral fat (16).

Although the accuracy of this relationship is not certainly determined (17, 18), and the association of NAFLD with these indices have been reported inconsistently (19-21), the application of VAI was shown to be beneficial in Iran as a country of the Middle East with a high prevalence of risk factors for chronic diseases. Therefore, this study was conducted to compare VAI and MOAD in patients with NAFLD and healthy individuals.

Materials and Methods

This case-control study carried out in Hajar Hospital in Shahrekord, Iran for 44 patients with NAFLD (Case group) and 44 healthy individuals (Control group) aged between 20 and 60 years. Blood samples and sonography were performed after obtaining the individual's consent to participate in the project. Healthy people were matched regarding gender, age (±5) and BMI (±3). Specialists confirmed the risk of NAFLD by liver function tests of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and by ultrasonography (22).

Individuals with the following conditions were excluded from the study including (i) Patients with acute and chronic liver diseases, such as viral hepatitis, (ii) Patients with malignant tumors, (iii) Patients who consumed drugs that affect the liver, such as oral contraceptives, significant weight losses during the last 3 months, alcohol consumption, smoking, pregnancy and breastfeeding. Demographic information were provided in an interview, after the completion of an informed consent form and recorded in a questionnaire.

Weight was measured with the minimum possible clothes and an accuracy of 1.0 Kg. Height and waist circumferences were measured with an accuracy of 5.0 cm by a tape measure and BMI was calculated as a weight in kilograms divided by the square of the height in meters. WC was measured at the end of natural exhalation with an inelastic tape at the level of the narrowest part of the waist between the last rib and the upper part of the pelvis. Blood pressure was measured from right arm after 5 min of resting in sitting position. Waist-to-height ratio (WHtR) was calculated by dividing WC by height (23).

A fasting blood sample was collected from each participant in the morning after at least 10 h of fasting. Values for fasting plasma glucose (FPG), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) were obtained using an autoanalyzer. Visceral adiposity index (VAI) and model of adipose distribution (MODE) were detrermined using the following equation while TG expressed in mg/dL and HDL-C in mg/dL (16):

Males: VAI=[WC/39.68+(1.88×BMI)]×(TG/1.03)×(1.31/HDL); Females: VAI=[WC/36.58+(1.89 × BMI)]×(TG/0.81)×(1.52/HDL); Males: MOAD=WC/39.68+(1.88×BMI); Females: MOAD=WC/36.58+(1.89×BMI)

Descriptive statistics calculated continuous variables (Mean±SD) and categorical variables (No. and %). The differences between groups were evaluated by T-test for continuous and Chi-square test for categorical data. Since anthropometric indices were correlated with sex, BMI, WC, VAI, MOAD and WHtR, OR and 5% confidence intervals (CIs) for NAFLD were separately assessed for males and females. All the statistical analyses were performed using SPSS software (Version 19.0, Chicago, IL, USA) and *p*-values less than 0.05 were considered statistically significant. The Kolmogorov-Smirnov test was used to assess if the variables followed a normal distribution. Variables showing a normal distribution were analyzed with a Student's *t*-test while the ones that did not follow a normal distribution were analyzed through nonparametric Mann-Whitney test.

Results

Eighty-eight subjects participated in this case-control study who were matched for gender, age (in age groups of 20-30 and 31-40 and 41-50 and 51-60) and BMI (±3). Distribution of qualitative variables in both groups were shown in Table 1. The highest percentage of individuals was in the age groups of 51-60 years old. There was no significant difference for age distribution between the two groups (p=0.91) that represents the similarity between two groups in terms of age category.

Both groups were quite similar for gender and marital status without any significant difference between the two groups (p=0.06). Level of education had the same distribution between the two groups

Table 1: Demographic data of subjects enrolled in the study

Variables	Groups	Control group n=44 Number (%)	Case group n=44 Number (%)	*p*-value†
Age	20-30	2 (4.5)	1 (2.3)	0.91
	31-40	9 (20.5)	8 (18.2)	
	41-50	14 (31.8)	16 (36.4)	
	51-60	19 (43.2)	19 (43.2)	
Sex	Male	10 (22.7)	10 (22.7)	1
	Female	34 (77.3)	34 (77.3)	
Matrial status	Married	41 (93.2)	35 (79.5)	0.06
	Single	3 (6.8)	9 (20.5)	
Education	Secondary school	20 (45.5)	18 (40.9)	0.34
	Diploma	13 (29.5)	19 (43.2)	
	Graduate	11 (25)	7 (15.9)	
Location	Province	14 (31.8)	18 (40.9)	0.21
	Urban	23 (52.3)	15 (34.1)	
	Rural	7 (15.9)	11 (25)	
Occupation	Housewife	31 (70.5)	27 (61.4)	0.33
	Clerk	6 (13.6)	12 (27.3)	
	Self-employed	6 (13.6)	5 (11.4)	
	Labor/Farmer	1 (2.3)	0 (0)	

p value†: test was χ^2

(case and control groups; *p*=0.34). A quarter of control group and 15.9% of case group had university education. Area of residence like other variables showed no significant difference between the two groups (*p*=0.21). The employment status was similar in case and control groups (*p*=0.33). There was no significant difference between case and control groups in terms of demographic variables known as confounding factors that were uniformly distributed and were similar in two groups.

Data obtained from independent T and Mann-Whitney tests were presented in Table 2 to compare mean of anthropometric and cardiometabolic indices between the two groups. As it was shown, the difference was not statistically significant between the mean of TG and diastolic blood pressure (DBP) variables of the two groups (*p*=0.12, *p*=0.16, respectively). There was a significant difference between five anthropometric, systolic blood pressure (SBP) and other serum indices between the two groups. Mann-Whitney statistical test was used for three variables of fasting blood sugar (FBS), ALT and AST due to non-normal distribution Since VAI and MOAD indices had different calculation for each sex, they were reported based on gender in Table 3. Both indices showed a significant difference only in women between the two groups.

The results of multiple logistic regression analysis were shown in Table 4 for each five predictive indices based on gender. ORs of NAFLD in various indices showed different trends after adjustment for age, education, occupation, marital status and SBP and DBP. BMI did not significantly show odds ratio in females. A significant increasing trend of odds ratio for NAFLD with an increasing trend of waist were noticed. Only the highest and the lowest figures considered as the reference were significantly different regarding VAI index (CI: 1.59-19.38, OR=5.5 at *p*=0.007). The same trend was observed for MOAD index, but with more significance (*p*<0.001). WHtR index showed a significant increasing trend of odds ratio for NAFLD (OR=3.7 and OR=9.63, respectively), but none of the indices represented statistically significant association in males.

Discussion

In this study, over 77% of the population were female. There was a significant difference for the mean of each 5 anthropometric indices of WC, BMI, VAI, MOAD and WHtR between case and control groups. Since calculating the indices of VAIO, MODE were different in male and females, these two indices were also assessed separately for the two genders. As it was shown in Table 3, this index had a different mean only among females of

Table 2: Comparing clinical characteristics and other indices in patients with NAFLD and healthy individuals

Variable	Control group (Mean±SD)	Case control (Mean±SD)	*p*-value
BMI (Kg/m^2)	27.93±3.18	29.44±3.60	0.039†
WC (cm)	60.38±9.53	98.89±9.18	<0.001†
WHtR	0.57±0.63	0.62±0.07	<0.001†
VAI	6.23±2.67	8.67±4.50	0.003†
MOAD	1.01±0.07	1.06±0.07	0.002†
Fasting blood sugar	104.25±33.89	121.27±45.39	0.005‡
ALT	21.11±8.75	50.59±32.48	<0.001‡
AST	23.25±8.02	39.68±19.16	<0.001‡
Triglyceride	167.57±55.36	189.66±75.94	0.12†
HDL	49.39±11.06	43.57±8.43	0.007†
Systolic blood pressure	118.52±12.55	125.34±13.48	0.01†
Diastolic blood pressure	80.45±10.55	8.41±9.01	0.16†

†*p*-value was calculated by using independent-sample T Test, ‡*p*-value was calculated by using Mann-Whitney Test; BMI: Body mass index; WC: Waist circumference; WHtR: Waist-to-height ratio; VAI: Visceral adiposity index; MOAD: Model of adipose distribution; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HDL: High-density lipoprotein

Table 3: Independent-sample T test in patients with NAFLD and healthy individuals based on sex

Variable	Control group (Mean±SD)	Case Group (Mean±SD)	*p*-value
VAI- male	4.39±1.33	5.23±3.60	0.5†
VAI- female	6.77±2.74	9.69±4.26	0.001†
MOAD- male	1.002±0.08	1.03±0.09	0.4†
MOAD- female	1.007±0.06	1.07±0.06	<0.001†

†*p*-value was calculated by using independent-sample T Test; VAI: Visceral adiposity index; MOAD: Model of adipose distribution

Table 4: Odds ratio (95% CI) of NAFLD for each index#

		Indices				
	Percentile	BMI	WC	VAI	MOAD	WHtR
Female	1	1	1	1	1	1
	2	1.11 [0.34, 3.63]	4.30 [1.17, 15.82]*	2.67 [0.78, 9.12]	1.70 [0.45, 6.39]	3.70 [1.02, 13.47]*
	3	2.70 [0.8, 9.06]	10.20 [2.62, 39.71]**	5.55 [1.59, 19.38]**	22.4 [4.65, 107.9]***	9.63 [2.46, 37.68]**
Male	1	1	1	1	1	1
	2	5 [0.47, 52.96]	0.80 [0.10, 6.30]	0.75 [0.08,6.71]	0.40 [0.04, 3.90]	0.15 [0.01, 2.05]
	3	1.50 [0.15, 14.42]	5.33 [0.30, 75.70]	1.33 [0.14, 11.90]	2.50 [0.25, 24.7]	1.80 [0.20, 17.26]

*p<0.05, **p<0.01, ***p<0.001, #Adjusted for age, education, job, systolic and diastolic blood pressure. BMI: Body mass index; WC: Waist circumference; WHtR: Waist-to-height ratio; VAI: Visceral adiposity index; MOAD: Model of adipose distribution

case and control groups.

In other words, the mean of VAI and MOAD indices in male cases were statistically similar in comparison with healthy control males. This may be partly related to the low population of males in the study; On the other hand, it was shown that high dispersion of items involved in the calculations, particularly TG in males may be effective when using VAI index. As it was shown in table 3, this index had a different mean only among females of case and control groups. In other words, the mean of VAI and MOAD indices in male cases was statistically similar in comparison with healthy control males (24).

This may be partly related to the low population of males in this study, On the other hand, it was demonstrated that high dispersion of items was visible in the calculations, particularly for TG in males that can affect when VAI index is used (24). In a study that evaluated the correlation between anthropometric indices and sonography as gold standard (25), WC was highly associated with the level of fat mass. Theoretically, WHtR is considered as an important index of body fat, because the denominator is a fixed number and is constant while the adult height does not change. So it is reliable to evaluate the situation and track changes (26).

The weak measurement of WC can be partly reduced by considering height, so the genetic differences can be removed. One of these five indices was BMI that was not a suitable index for estimating the risk of metabolic diseases when used alone, as it cannot distinguish the differences between fat and muscular tissues and is not able to describe the method of distribution in the body too (26-28). So VAI, MOAD indices are mathematical models to assess the accumulation of abdominal fat. Two markers of TG and HDL are used in the calculation of VAI that have priority to consider the quantity, but these markers are considered as binary variables in metabolic syndrome (29).

The results of the present study are in line with the study showing that VAI is not the best option for estimating the odds ratio of NAFLD (30). However, females with the highest index were reported with a risk of NAFLD to be 5.5 times more. This study showed that BMI is not a predictor for the development of NAFLD in males and females. VAI, MOAD indices can be used to estimate the relationship for NAFLD regarding two indices of WC and WHtR as the most powerful indices for estimation of the proportion of the risk for developing NAFLD.

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Conflict of Interest

None declared.

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