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The Comparation of Anthropometric and Metabolic Indices in the Regulation and Prediction of Fatty Liver: a population-based crosssectional study in China

Fangfei Xie

the Affilicated Suzhou Hospital of Nanjing Medical University

Yuyu Pei

the Affilicated Suzhou Hospital of Nanjing Medical University

Yun Wang

the Affilicated Suzhou Hospital of Nanjing Medical University

Jiongyan Li

the Affilicated Suzhou Hospital of Nanjing Medical University

Xuehua Xu

the Affilicated Suzhou Hospital of Nanjing Medical University

Hong Zhou

the Affilicated Suzhou Hospital of Nanjing Medical University

Kangyun Sun (714388761@qq.com)

Research

Keywords: Fatty liver, Anthropometric and metabolic indices, obesity

Posted Date: July 30th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-45312/v1

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Abstract

Background: The association between anthropometric and metabolic indices and fatty liver (FL) remain not fully elucidated. We aimed to determine the role of these anthropometric and metabolic indices on FL prediction and regulation via cross-sectional study, thus providing clues for further research in FL field.

Methods: A total of 658 participants aged over 18 years were included in this study. Anthropometric and metabolic indices (including WC, WHR, BMI, BFM, VFA, TG/HDL, AST/ALT, SBP, DBP and FBG) were measured. Difference analyses, logistic and predictive analyses were used to evaluate the association and discrimination ability between these indices and FL.

Results: Compared with non-FL, anthropometric and metabolic indices in FL and mild FL people showed a significant increase after adjustment. In the multivariate ranked logistic regression analysis, WC, TG/HDL, AST/ALT and FBG have a strong association with FL (β = 0.03, 0.19, 0.41, -1.89 and 0.28, P<0.05). And AST/ALT showed the lowest predicted power with an AUC of 0.22 among all indices. WC showed to be the best predictors with an AUC of 0.86 in participants.

Conclusions: This is a comprehensive profile for FL related indices. These can enhance our understanding of the mechanisms for hepatic on inflammation and fat and is also important for the prevention and treatment of FL.

Background

Epidemiological studies indicated that Fatty Liver (FL) had became a global problem of public health over the past few decades with the incidences around 30% and 25% in Western and Asia countries, which also caused huge medical burden in both developed and developing countries [1–5]. FL is also characterized by complex pathogenesis and difficulty in diagnosis[6, 7]. Thus, it is of great necessity to further explore the pathogenesis or the prediction for the diagnosis of FL. FL is commonly associated obesity, type II diabetes, dyslipidemia, and metabolic disorders[8–12]. The relationship between FL and type II diabetes is complex and bidirectional and occurs in the context of a wider association between FL and metabolic syndrome[13, 14]. In the last decades, an alarming increase in the prevalence of FL has been observed, along with increasing rates of obesity[15]. Some studies found more advanced fatty liver related fibrosis[7, 11]. In recent years, several anthropometric or metabolic indices had been reported to be associated with FL in both cross-sectional and cohort studies[16–23]. However, most existing studies mainly focused on common indices (such as waist, body mass index, triglyceride and blood glucose). The association of other indices (such as waist-hip ratio, visceral fat area and transamination) with FL, which might be even more important than common indices, remain unclear. Exploring correlation profile between these indices and FL would facilitate the understanding of the complex regulatory mechanisms and provide clues for further research. Herein, we explored the comprehensive relationship between multiple indices and FL and we hypothesized that anthropometric and metabolic indices have regulatory and predictive effects on FL with a very complex pattern.

Materials And Methods

Study population

The study subjects were recruited in physical examination Center of Suzhou in southeast of China, during January 2018 to December 2019. Participants in this study were Chinese Han ethnicity ageing over 18 years. After excluding subjects for lacking data, a total of 658 subjects were finally included in the analysis. The study was approved by the ethical committee of the Affiliated Suzhou Hospital of Nanjing Medical University and all subjects agreed to participate into the present study.

Data collection

Health examination was performed in the morning by trained medical staff. Anthropometric indices, including Waist Circumference (WC), Waist-hip Ratio (WHR), Body Mass Index (BMI), Body Fat Mass (BFM) and Visceral Fat Area (VFA), were measured by the InBody770 analyzer which can estimate body composition with small individual error[24]. The participants were instructed to stand upright and to grasp the handles of the analyzer, thereby providing contact with a total of eight electrodes. Metabolic markers, including Triglyceride(TG), High Density Lipoprotein(HDL), Glutamic oxaloacetylase(AST), Alanine aminotransferase(ALT), and Fasting Blood Glucose (FBG), were measured biochemically within 3 hours after peripheral blood drawn. TG/HDL and AST/ALT was calculated as the ratio of TG to HDL and AST to ALT, respectively. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by sphygmomanometer following standard procedure. Diagnoses of FL was based on the four abdominal ultrasonography standard (parenchymal brightness, hepatorenal echo contrast, deep beam attenuation, and bright vessel walls) by experienced radiologists with expertise in liver imaging[25, 26].

Statistical analysis

All participants were divided into FL, Mild-FL and non-FL groups. The baseline variables (gender, age, anthropometric and metabolic indices) were compared using the Chi-square test and Rank tests appropriately. All measurement data are expressed as mean ± standard deviation. Univariate and multivariate ranked logistic regression analyses were conducted to evaluate the association between anthropometric, metabolic indices and FL. Odd

Ratios (OR) were obtained from logistic regression analysis, and the results were presented as OR with 95% Confidence Interval (CI). Area Under the Curve (AUC) of Receiver Operating Characteristic (ROC) was calculated to compare the predictive value between these indices for predicting FL. All statistical analyses were performed with the Statistical Package for the Sciences (SPSS, version 17.0). A value of P < 0.05 in two-tailed test was considered significant.

Results

A total of 658 subjects were included in our study, including 98 (14.89%) FL patients, 88 (13.37%) Mild-FL patients, and 472 (71.73%) controls. Among FL and Mild-FL patients, 87.75% and 85.22% individuals were males, which was significantly higher than those in females (12.25% and 14.78%, P < 0.01). The mean age of three groups were 45.20 ± 11.35, 45.78 ± 10.70 and 43.42 ± 11.50, respectively. Table 1 compared the demographic characteristics, anthropometric and metabolic indices of individuals in three groups. Significant differences were observed among the groups. After adjustment for gender, the differences remained to be significant (P < 0.01). (Table 1)

	All				Male				Female			
	FL	Mild-FL	Non-FL	P value	FL	Mild- FL	Non-FL	P value	FL	Mild- FL	Non-FL	P value
Number(%)	98 (14.89)	88 (13.37)	472(71.73)		86 (87.76)	75 (85.23)	269 (56.99)		12 (12.24)	13 (14.77)	203 (43.01)	
Age, years	45.20 ± 11.35	45.78 ± 10.70	43.42 ± 11.50	0.11	43.26 ± 10.25	43.12 ± 10.66	43.81 ± 11.36	> 0.01	59.17 ± 8.96	49.62 ± 10.52	42.89 ± 11.69	< 0.01
Anthropometric indices												
WC, cm	99.00 ± 9.90	93.93 ± 8.76	83.69 ± 7.81	< 0.01	99.57 ± 9.58	95.09 ± 8.44	86.84 ± 6.88	< 0.01	94.97 ± 11.55	87.24 ± 7.26	79.52 ± 6.97	< 0.01
WHR	0.96 ± 0.06	0.94 ± 0.05	0.89 ± 0.05	< 0.01	0.96 ± 0.06	0.95± 0.05	0.90 ± 0.04	< 0.01	0.97 ± 0.05	0.92 ± 0.05	0.88 ± 0.05	< 0.01
BMI, kg/m ²	27.94 ± 3.40	26.07 ± 2.69	23.02 ± 2.78	< 0.01	28.06 ± 3.22	26.32 ± 2.63	23.86 ± 2.56	< 0.01	27.14 ± 4.64	24.65 ± 2.73	21.92 ± 2.68	< 0.01
BFM, kg	25.26 ± 7.04	21.76 ± 5.49	17.05 ± 4.61	< 0.01	25.21 ± 6.86	21.76 ± 5.64	17.03 ± 4.67	< 0.01	25.64 ± 8.54	21.75 ± 4.76	17.06 ± 4.59	< 0.01
VFA, cm ²	115.68 ± 37.37	97.90 ± 29.24	75.83 ± 24.71	< 0.01	113.42 ± 35.77	96.24 ± 29.18	73.10 ± 21.87	< 0.01	131.88 ± 45.86	107.48 ± 28.80	79.45 ± 27.67	< 0.01
Metabolic indices												
TG/HDL	5.17 ± 1.47	4.66 ± 0.99	3.94 ± 1.00	< 0.01	5.25 ± 1.52	4.72 ± 0.89	4.26 ± 1.01	< 0.01	4.54 ± 0.76	4.29 ± 1.41	3.50 ± 0.80	< 0.01
AST/ALT	0.79 ± 0.27	0.86 ± 0.29	1.20 ± 0.45	< 0.01	0.76 ± 0.27	0.85± 0.30	1.07 ± 0.39	< 0.01	0.97 ± 0.22	0.93 ± 0.21	1.39 ± 0.45	< 0.01
SBP, mmHg	129.02 ± 17.13	128.65 ± 15.65	120.07 ± 16.85	< 0.01	128.67 ±12.38	128.47 ±13.02	123.04 ±15.54	< 0.01	131.50 ± 20.74	129.69 ± 26.98	116.13 ± 17.72	< 0.01
DBP, mmHg	79.92± 11.76	79.95± 11.33	72.63 ± 10.88	< 0.01	80.12 ± 12.05	80.83 ± 11.00	75.68 ± 10.33	< 0.01	78.50 ± 9.73	74.92 ± 12.39	68.57 ± 10.27	< 0.01
FBG, mmol/l	98 (14.89%)	88 (13.37%)	472(71.73%)	< 0.01	6.58 ± 2.92	5.57 ± 1.13	5.27 ± 0.84	< 0.01	5.80 ± 0.85	5.41 ± 0.40	5.09 ± 0.56	< 0.01

Univariate analyses showed the significant associations between anthropometric indices, metabolic indices and FL. When including these indices into the multivariate ranked logistic regression analysis, AGE, WC, TG/HDL, AST/ALT and FBG showed a significant relationship with FL (β = 0.03, 0.19, 0.41, -1.89 and 0.28, OR = 1.03, 1.21, 1.51, 0.15, and 1.32, P < 0.05, Table 2).

Variables	Beta	Р	OR (95% Cl)	
Gender	0.57	> 0.05	1.77 (0.74, 4.18)	
Female	-			
Male				
Age	0.03	0.01	1.03 (1.01, 1.05)	
Anthropometric indices				
WC, cm	0.19	0.01	1.21 (1.05, 1.40)	
WHR	-9.61	> 0.05	0	
BMI, kg/m ²	1.07	> 0.05	1.07 (0.84, 1.35)	
BFM, kg	-0.10	> 0.05	0.90 (0.71, 1.74)	
VFA, cm ²	0.01	> 0.05	1.01 (0.97, 1.49)	
Metabolic indices				
TG/HDL	0.41	< 0.01	1.51 (1.22, 1.86)	
AST/ALT	-1.89	< 0.01	0.15 (0.07, 0.34)	
SBP, mmHg	0	> 0.05	0 (0.98, 1.02)	
DBP, mmHg	0.01	> 0.05	1.01 (0.98, 1.04)	
FBG, mmol/l	0.28	< 0.01	1.32 (1.12, 1.57)	

Table 2

Note: FL: Fatty Liver; BMI: Body Mass Index; BFM: Body Fat Mass; VFA: Visceral Fat Area; TC: Triglyceride; TG: Triglyceride; HDL: High D lipoprotein; FBG: Fasting Blood Glucose; OR: Odds Ratio; CI: Confidence Interval

To assess the accuracy of anthropometric and metabolic indices for predicting FL (including FL and Mild-FL), AUC were conducted and showed in Table 3. Among all the indices, WC showed to be the best predictors with an AUC of 0.86 in participants. All indices showed AUCs over 0.6 except AST/ALT with an AUC of 0.22.

Variables	AUC (95% CI)	P
Anthropometric indices		
WC, cm	0.86 (0.83, 0.89)	< 0.01
WHR	0.81 (0.77, 0.84)	< 0.01
BMI, kg/m ²	0.83 (0.80, 0.87)	< 0.01
BFM, kg	0.80 (0.76, 0.84)	< 0.01
VFA, cm ²	0.78 (0.74, 0.82)	< 0.01
Metabolic indices		
TG/HDL	0.75 (0.71, 0.79)	< 0.01
AST/ALT	0.22 (0.18, 0.26)	< 0.01
SBP, mmHg	0.66 (0.62, 0.71)	< 0.01
DBP, mmHg	0.68 (0.64, 0.73)	< 0.01
FBG, mmol/l	0.68 (0.63, 0.73)	< 0.01

Note: FL: Fatty Liver; BMI: Body Mass Index; BFM: Body Fat Mass; VFA: Visceral Fat Area; TC: Triglyceride; TG: Triglyceride; HDL: High Density lipoprotein; FBG: Fasting Blood Glucose; AUC: Area Under the Curve; ROC: Receiver Operating Characteristic

Discussion

In this cross-sectional survey, we explored the comprehensive relationship between anthropometric indices, metabolic indices and FL and found that these indices have regulation and prediction effect on FL with a very complex pattern. To be specific, we demonstrated that 1) AST/ALT had strongest negative association with FL prevalence, while had the lowest predictive value for FL; and that 2) WC possessed the highest ability on predicting FL among all these indices.

The association of obesity with FL has been established in multiple previous studies[11, 15, 27, 28]. Epidemiological studies propose a causative link between obesity and progressive liver disease in individuals[15, 28]. Obesity has been linked not only to initial stages of the disease, but also to its severity[11]. The pathophysiology and clinical studies have shown that the progression of FL results from an imbalance between lipid uptake and lipid disposal and eventually causes oxidative stress and hepatocyte injury[29]. Obesity can be expressed in clinical practice by several methods, including anthropometric and metabolic ways[24]. Some studies thought that the visceral adiposity was the main adipose depot responsible for FL and was associated with FL in a dose-dependent manner in a cohort study[30]. WC, WHR and BMI have been proved and used in many clinical trials as an indicator of the severity of fatty liver disease[19, 22]. BFM and VFA are often reported markers in athletes related articles or are used to explore the relationship between insulin resistance and excessive visceral fat accumulation[31, 32]. Additionally, elevated data strongly suggests that advanced blood lipids, blood pressure and blood sugar could also be lead to more severe histological changes and poorer clinical outcomes[14, 22, 33]. Once FL is established, insulin resistance can promote the progression to the more severe state of liver endangerment like non-alcoholic steatohepatitis. Although the relationship between these ten obesity related indexes (WC, WHR, BMI, BFM, VFA, TG/HDL, AST/ALT, SBP, DBP and FBG) and FL were analyzed separately in many articles, few articles put them together to evaluate. Our studies compared all these 10 obesity related indexes with FL and also stratified the data by gender, thus we are capable of determining which factors might be critical for the regulation and prediction of FL.

In our study, we found differences of these ten obesity related indexes in three groups after stratifying the data. Men had a similar prevalence of FL regardless of age, whereas in women the prevalence of FL increased steadily with age. As we all know that sex hormones play a central role in predisposing individuals to metabolic status. Loss of estrogen after menopause leads to extensive changes in the metabolic system, including an increase in visceral adiposity. Although FL is primarily a male disease, the alteration in sex hormone levels, specifically reduced estrogens and increased androgens during and after menopause, is an important factor in the emergence of FL for female subjects[34, 35].

In our studies, we found blood lipids, blood sugar, WC and liver inflammatory indicators showed significant correlation with FL, while AST/ALT had a strongest negative association with increased FL prevalence. As we know, liver inflammation is closely related to metabolic disorders because the liver plays a central role in metabolism of lipids and glucose[7]. Obesity and inflammation exist in the same time in FL almost, successive stages in FL may be reflected by the accumulation of fat in hepatocytes and the onset of steatohepatitis. Although the etiology of FL is multifactorial, it is well accepted that inflammation is a central component of FL pathogenesis[36, 37]. This may explain why the AST/ALT has the maximum increase in our study. And it is also agree with current treatment measures on FL[7]. Besides, we found WC have a strong association with FL compared with VFA. This is in consistent with the study by Church et al. who found that adjustment for VFA attenuated the direct association between waist circumference and FL[38].

We further identified AST/ALT had the lowest predictive value for FL, while WC showed a correspondingly higher ability on prediction in all these indices. Nowadays, the mechanisms of hepatic steatosis and steatohepatitis are being investigated extensively which are regulated by complex pathways[36, 39]. Although inflammation contribute greatly to FL, abdominal obesity remains the main manifestations for FL. Compared with inflammatory changes existed in many diseases, WC have been shown in many studies to be directly related to fatty liver and to be more specific for FL[40–42].

This study characterized and analyzed a comprehensive profile for FL related indices, especially different anthropometric and metabolic indices. These comprehensive correlation analyses can enhance our understanding of the mechanisms for hepatic steatosis and steatohepatitis and is also important for developing strategies for the prevention and treatment of FL. However, there are still some limitations. Firstly, our findings are based on a cross-sectional study, a large-scale cohort study is still necessary to build the definite causal relationship between these indices and FL. Secondly, the data of other confounders, such as, smoking and drinking status and exercise, were not included in this analysis because of the information default.

In summary, this is a comprehensive profile for FL related indices. We identified AST/ALT had a strongest negative association with increased FL prevalence, but had the lowest predictive value for FL. Meantime, WC showed a correspondingly higher ability on predicting FL in all these indices. Findings from our study could provide further theoretical evidence for the understanding of relevant mechanisms for hepatic steatosis and steatohepatitis, as well as for predicting the prevalence of FL.

Abbreviations

FL Fatty Liver BMI Body Mass Index BFM Body Fat Mass VFA Visceral Fat Area тс Triglyceride ΤG Triglyceride HDL High Density lipoprotein FBG Fasting Blood Glucose OR Odds Ratio CI Confidence Interval AUC Area Under the Curve ROC **Receiver Operating Characteristic**

Declarations

Statement of Ethics

The study was approved by the ethical committee of the Affiliated Suzhou Hospital of Nanjing Medical University. Subjects agreeing to participate into the present study provided a written informed consent.

Conflict of Interest Statement

The authors declare that there is no competing interests.

Funding Sources

No funding.

Author Contributions

XFF PYY and SKY designed the study, analyzed the data and wrote the manuscript. WY, LJY, XXH, ZH collected the data. All authors read and approved the final manuscript.

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