WHtR may be a Better and Stronger Indictor for Fatty Liver: A Population-Based Cross-sectional Comparison Study of Anthropometric and Metabolic Indices for Identification Fatty Liver in China

Fangfei Xie
the Affilicated Suzhou Hospital of Nanjing Medical University
Yuyu Pei
Nanjing Medical University Affiliated Suzhou Hospital: Suzhou Municipal Hospital
Quan Zhou
Nanjing Medical University Affiliated Suzhou Hospital: Suzhou Municipal Hospital
Yun Wang
Nanjing Medical University Affiliated Suzhou Hospital: Suzhou Municipal Hospital
Renfang Han
Nanjing Medical University Affiliated Suzhou Hospital: Suzhou Municipal Hospital
Nimei Zeng
Nanjing Medical University Affiliated Suzhou Hospital: Suzhou Municipal Hospital
Kangyun Sun (714388761@qq.com)
the Affilicated Suzhou Hospital of Nanjing Medical University

Research

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Abstract

Background: This study aimed to comprehensively evaluate the predictive performance anthropometric and metabolic indices in identifying fatty liver (FL) diseases in Chinese adults. Indices including Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Total Cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein (LDL), Fasting Blood Glucose (FBG), Alanine aminotransferase (ALT and AST), Waist Circumference (WC), Waist–hip Ratio (WHR), Waist-to-Height Ratio (WHtR), Body Mass Index (BMI), Abdominal Volume Index (AVI), Atherogenic Index of Plasma (AIP), Triglyceride Glucose (TyG), and ALT/AST were selected.

Methods: A total of 1748 participants aged over 18 years were included in this study. Univariate analyses were performed to determine the associations between these indices and FL with odds ratio (ORs). The predictive performance of these indices to identify FL was compared using receiver operating characteristic (ROC) curves and areas under curves (AUCs).

Results: WHtR had the greatest AUC in males (AUC = 0.81) and females (AUC = 0.85). Furthermore, WC and AVI had the greatest AUC in 20-40 years (AUC = 0.96), while TyG had the greatest AUC in 40- years (AUC = 0.80) of females. And WHtR had the second diagnostic ability in both two decades of age (20-40 and 40- years) of females.

Conclusions: WHtR might be the best for predicting FL in males and females, while WC and AVI might be best for identifying FL for males aged 20-40 years, while TyG for those aged over 40 years.

Introduction

Epidemiological studies indicated that FL had become a global public health issue over the past few decades with the incidences around 30% and 25% in Western and Asia countries, respectively, and FL have also caused huge medical and economic 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 effective predictive indicators for the diagnosis of FL, which is critical for the prevention and treatment of FL.

Although the pathogenesis of FL is still not fully understood, visceral adiposity has been demonstrated to play a major role in most of the pathogenic pathways involved in FL. FL is commonly associated with obesity, type □ diabetes, dyslipidemia, and metabolic disorders[8–12]. The relationship between FL and type □ 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 that regional distribution of lean and fat mass may influence the development of FL and suggested that abdominal fat are risk factors for fatty liver and more advanced fatty liver related fibrosis[7, 11]. Therefore, obesity, type II diabetes and metabolic syndrome associated factors might be utilized for predicting FL.

As expected, several anthropometric or metabolic indices such as skeletal muscle mass[16], atherogenic index[17, 18], Body Mass Index (BMI)[19], the ratio of Triglyceride (TG) to High-Density Lipoprotein cholesterol[20], visceral adipose tissue[21], Total cholesterol (TC) to High-Density Lipoprotein cholesterol ratio[22] and Triglyceride Glucose (TyG)[23, 24], as well as blood pressure[25] had been reported to be associated with FL in both cross-sectional and cohort studies. However, most existing studies mainly focused on only one or two indices, which might have limitations for predicting FL considering the high complexity of the pathogenesis of FL. Meanwhile, it remains unclear which indices might be even more advantageous for predicting FL. This study aimed to evaluate the performance of FL-related indices, including Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), TC, TG, Low Density Lipoprotein (LDL), Fasting Blood Glucose (FBG), Alanine aminotransferase (ALT and AST), Waist Circumference (WC), Waist–hip Ratio (WHR), Waist-to-Height Ratio (WHtR), BMI, Abdominal Volume Index (AVI), Atherogenic Index of Plasma (AIP), TyG, and ALT/AST, in identifying FL in Chinese adults, hopefully we will provide theoretical basis for utilizing anthropometric and metabolic indices to predict FL .

Materials And Methods

Study population

The study subjects were recruited in physical examination Center of Suzhou in southeast of China, during January 2020 to December 2020. Participants in this study were Chinese Han ethnicity ageing over 18 years. After excluding subjects for lacking of data, a total of 1748 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. Height, weight, Hip Circumference (HC) and WC were measured by the InBody770 analyzer which can estimate body composition with small individual error[26]. The participants were instructed to stand upright and to grasp the handles of the analyzer, thereby providing contact with a total of eight electrodes. SBP and DBP were measured by sphygmomanometer

following standard procedure. Metabolic markers, including TC, TG, LDL, FBG, ALT and AST were measured biochemically within 3 hours after peripheral blood drawn.

The fatty liver-related indices, including WHtR, WHR, BMI, AVI, AIP, TyG and ALT/AST were calculated using the following equations[18, 19, 23, 27].

$BMI = weight\ (kg) / height^2\ (m)$

$WHtR = WC\ (cm) / height\ (cm)$

$WHR = WC\ (cm) / HC\ (cm)$

$AVI = [2 \times WC^2(cm) + 0.7 \times (WC - HC)^2(cm)]/1000$

$AIP = Ln\ [TG\ (mmol/L)) / HDL\ (mmol/L)]$

$TyG = Ln\ [TG\ (mg/dL) \times FBG\ (mg/dL)/2]$

$ALT/AST = ALT(U/L) / AST\ (U/L)$

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[28, 29].

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data. Categorical variables were expressed as number (percentage). All participants were divided into 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. Univariate analyses were performed to determine the associations between FL and these anthropometric and metabolic indices with odds ratio (ORs) and 95% Confidence Intervals (CI). The first quartile was used as a reference to calculate the OR for FL of the 2nd, 3rd, and 4th quartiles of each index. Receiver Operating Characteristic (ROC) curves were generated to assess the performance of the different indices in identifying FL. Areas Under Curves (AUCs) were calculated to compare the predictive ability of the various indices to identify 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

Characteristics of the Study Population

A total of 1748 subjects were included in our study, including 526 (30.09%) patients and 1222 (69.91%) control. The mean age of patients and controls were 48.55 ± 14.21 and 46.18 ± 14.74 years ($p < 0.01$). In these subjects, 464 (26.54%) males and 62 (3.55%) females had FL. Table 1 compared the demographic characteristics, anthropometric and metabolic indices of individuals in groups. The percentage of FL in males is higher than that in females, while females is influenced by age. Subjects with FL had higher SBP, DBP, TC, TG, LDL, FBG, ALT, AST, WC, WHR, WHtR, BMI, AVI, AIP, TyG and ALT/AST both in males and females' groups, with significant differences were observed among the groups ($p < 0.01$).

Table 1
Demographic, anthropometric, and metabolic characteristics of the study participants.

characteristics	All (n = 1748)			Male (n = 1153)			Female (n = 595)		
	FL (+)	FL (-)	p-Value	FL (+)	FL (-)	p-Value	FL (+)	FL (-)	p-Value
n (%)	526(30.09%)	1222(69.91%)	< 0.01	464(26.54%)	689(39.42%)	< 0.01	62(3.55%)	533(30.49%)	< 0.01
Age (year)	48.55 ± 14.21	46.18 ± 14.74	< 0.01	47.74 ± 13.96	48.54 ± 15.53	> 0.05	54.60 ± 14.77	43.13 ± 13.05	< 0.01
Clinical parameters									
SBP (mmHg)	132.62 ± 18.88	122.46 ± 18.81	< 0.01	132.20 ± 18.16	126.56 ± 18.27	< 0.01	135.74 ± 23.47	117.09 ± 18.14	< 0.01
DBP (mmHg)	80.00 ± 11.43	73.48 ± 11.37	< 0.01	80.32 ± 11.50	76.22 ± 11.36	< 0.01	77.63 ± 10.69	69.93 ± 10.36	< 0.01
FBG (mg/dL)	6.00 ± 1.62	5.27 ± 0.95	< 0.01	6.03 ± 1.68	5.39 ± 1.11	< 0.01	5.80 ± 1.00	5.11 ± 0.65	< 0.01
TC (mg/dL)	5.23 ± 1.02	4.96 ± 0.97	< 0.01	5.20 ± 0.99	4.98 ± 0.93	< 0.01	5.50 ± 1.16	4.94 ± 1.01	< 0.01
TG (mg/dL)	2.37 ± 1.63	1.35 ± 0.90	< 0.01	2.41 ± 1.70	1.50 ± 0.97	< 0.01	2.00 ± 0.95	1.16 ± 0.74	< 0.01
LDL (mg/dL)	3.31 ± 0.72	3.04 ± 0.73	< 0.01	3.28 ± 0.70	3.10 ± 0.71	< 0.01	3.49 ± 0.82	2.97 ± 0.75	< 0.01
ALT (U/L)	39.75 ± 30.02	21.00 ± 36.91	< 0.01	41.73 ± 31.02	24.33 ± 47.70	< 0.01	24.93 ± 14.07	16.68 ± 12.32	< 0.01
AST (U/L)	28.76 ± 13.93	23.26 ± 25.29	< 0.01	29.28 ± 14.14	25.01 ± 32.54	< 0.01	24.82 ± 11.07	20.99 ± 9.42	< 0.01
FL-related indice									
WC (cm)	94.21 ± 9.29	82.41 ± 8.39	< 0.01	94.92 ± 9.33	84.59 ± 8.45	< 0.01	88.90 ± 7.04	79.60 ± 7.42	< 0.01
WHR	0.93 ± 0.05	0.88 ± 0.05	< 0.01	0.93 ± 0.05	0.89 ± 0.05	< 0.01	0.92 ± 0.04	0.87 ± 0.05	< 0.01
WHtR	0.55 ± 0.05	0.50 ± 0.05	< 0.01	0.55 ± 0.05	0.50 ± 0.05	< 0.01	0.56 ± 0.04	0.50 ± 0.05	< 0.01
BMI (kg/m^2)	26.76 ± 3.08	22.66 ± 2.93	< 0.01	26.91 ± 3.11	23.29 ± 2.85	< 0.01	25.60 ± 2.60	21.86 ± 2.83	< 0.01
AVI	17.97 ± 3.65	13.82 ± 2.78	< 0.01	18.24 ± 3.70	14.55 ± 2.84	< 0.01	15.95 ± 2.47	12.88 ± 2.40	< 0.01
AIP	0.59 ± 0.60	-0.13 ± 0.61	< 0.01	0.61 ± 0.60	0.03 ± 0.60	< 0.01	0.37 ± 0.52	-0.35 ± 0.56	< 0.01
TyG	4.92 ± 0.29	4.59 ± 0.28	< 0.01	4.93 ± 0.30	4.65 ± 0.27	< 0.01	4.86 ± 0.26	4.51 ± 0.26	< 0.01
ALT/AST	1.31 ± 0.47	0.86 ± 0.31	< 0.01	1.35 ± 0.47	0.93 ± 0.33	< 0.01	0.98 ± 0.26	0.77 ± 0.26	< 0.01

Abbreviations: SBP, Systolic Blood Pressure, DBP, Diastolic Blood Pressure, TC, Total Cholesterol, TG, Triglyceride, LDL, Low Density Lipoprotein, FBG, Fasting Blood Glucose, ALT and AST, Alanine aminotransferase, WC, Waist Circumference, WHR, Waist–hip Ratio, WHtR, Waist-to-height Ratio, BMI, Body Mass Index, AVI, Abdominal Volume Index, AIP, Atherogenic index of plasma, TyG, Triglyceride Glucose.

ORs for FL Risk Across Quartiles of Each Index

We divided each parameter into quartiles and used univariate analyses to assess the associations with FL across quartiles of these parameters. Table 2 showed that all analyzed parameters were significantly associated with FL in both males and females ($p < 0.01$). The ORs for FL increased across the quartiles of each indices all in males and females, with females increased more per quartiles than that in males. Among the whole subjects, WC and BMI showed the highest correlation with FL among all the indices (r = 0.527, $p < 0.01$). However, WHtR had the strongest association with FL after considering the influence of gender (r = 0.507 in males and r = 0.371 in females, $p < 0.01$).

Table 2
ORs for FL stratified by quartiles of each index.

	All	Men	Women
SBP			
Q1	1	1	1
Q2	2.69 (1.91, 3.79) **	1.81 (1.28, 2.54) **	3.95 (1.08, 14.45) *
Q3	3.79 (2.71, 5.29) **	1.82 (1.29, 2.57) **	5.26 (1.47, 18.88) **
Q4	5.38 (3.86, 7.50) **	2.43 (1.72, 3.44) **	15.94 (4.78, 53.13) **
r for correlation	0.251 **	0.142 **	0.250 **
DBP			
Q1	1	1	1
Q2	2.21 (1.59, 3.06) **	2.00 (1.41, 2.83) **	1.55 (0.49, 4.84)
Q3	2.90 (2.09, 4.01) **	1.97 (1.40, 2.77) **	4.69 (1.72, 12.79) **
Q4	4.97 (3.61, 6.85) **	2.93 (2.08, 4.13) **	7.27 (2.72, 19.42) **
r for correlation	0.245 **	0.175 **	0.214 **
FBG			
Q1	1	1	1
Q2	1.34 (0.96, 1.86)	1.32 (0.92, 1.87)	2.01 (0.59, 6.84)
Q3	1.92 (1.40, 2.66) **	1.74 (1.23, 2.46) **	3.87 (1.24, 12.05) *
Q4	5.12 (3.77, 6.98) **	4.03 (2.84, 5.72) **	11.95 (4.13, 34.56) **
r for correlation	0.270 **	0.239 **	0.256 **
TC			
Q1	1	1	1
Q2	1.32 (0.97, 1.79)	1.29 (0.92, 1.82)	0.91 (0.36, 2.32)
Q3	1.71 (1.27, 2.31) **	1.79 (1.28, 2.52) **	1.71 (0.75, 3.90)
Q4	2.01 (1.50, 2.71) **	1.72 (1.23, 1.42) **	3.15 (1.46, 6.76) **
r for correlation	0.119 **	0.105 **	0.145 **
TG			
Q1	1	1	1
Q2	3.15 (2.01, 4.94) **	1.99 (1.33, 2.98) **	0.70 (0.12, 4.25)
Q3	7.68 (5.02, 11.74) **	4.96 (3.37, 7.29) **	6.87 (1.98, 23.85) **
Q4	22.94 (15.02, 35.02) **	11.19 (7.52, 16.62) **	17.89 (5.39, 59.39) **
r for correlation	0.444 **	0.407 **	0.306 **
LDL			
Q1	1	1	1
Q2	1.84 (1.34, 2.52) **	1.52 (1.08, 2.14) *	1.59 (0.60, 4.23)
Q3	2.22 (1.62, 3.03) **	1.87 (1.33, 2.62) **	1.95 (0.76, 5.04)
Q4	2.92 (2.15, 3.98) **	1.89 (1.34, 2.66) **	5.42 (2.30, 12.76) **

Abbreviations: SBP, Systolic Blood Pressure, DBP, Diastolic Blood Pressure, TC, Total Cholesterol, TG, Triglyceride, LDL, Low Density Lipoprotein, FBG, Fasting Blood Glucose, ALT and AST, Alanine aminotransferase, WC, Waist Circumference, WHR, Waist–hip Ratio, WHtR, Waist-to-height Ratio, BMI, Body Mass Index, AVI, Abdominal Volume Index, AIP, Atherogenic index of plasma, TyG, Triglyceride Glucose.

* p-value < 0.05. ** p-value < 0.01. Values expressed as OR and 95% CI.

	All	Men	Women
r for correlation	0.166 **	0.113 **	0.185 **
ALT			
Q1	1	1	1
Q2	4.10 (2.55, 6.60) **	2.60 (1.72, 3.95) **	1.46 (0.32, 6.63)
Q3	8.97 (5.68, 14.16) **	5.94 (3.97, 8.88) **	9.18 (2.69, 31.27) **
Q4	29.31 (18.60, 46.19) **	13.69 (9.04, 20.73) **	14.10 (4.21, 47.18) **
r for correlation	0.456 **	0.420 **	0.264 **
AST			
Q1		1	1
Q2	1.82 (1.30, 2.56) **	1.54 (1.08, 2.19) *	5.52 (1.84, 16.57) **
Q3	2.84 (2.04, 2.23) **	2.17 (1.53, 3.09) **	3.39 (1.07, 10.77) *
Q4	5.41 (3.91, 7.47) **	3.60 (2.53, 5.11) **	8.02 (2.72, 23.60) **
r for correlation	0.268 **	0.223 **	0.150 **
WC			
Q1	1	1	1
Q2	5.71 (2.95, 11.08) **	4.97 (3.03, 8.15) **	4.03 (0.45, 36.46)
Q3	25.92 (13.83, 18.58) **	11.69 (7.20, 18.97) **	11.80 (1.50, 92.58) **
Q4	74.21 (39.52, 139.35) **	31.92 (19.36, 52.65) **	68.08 (9.24, 501.71) **
r for correlation	0.527 **	0.493 **	0.353 **
WHR			
Q1	1	1	1
Q2	3.31 (2.23, 4.95) **	3.00 (1.98, 4.54) **	3.50 (0.86, 14.25)
Q3	10.66 (7.17, 15.86) **	7.65 (5.19, 11.27) **	8.21 (2.35, 28.76) **
Q4	16.55 (11.29, 24.24) **	13.26 (8.86, 19,83) **	23.46 (7.06, 77.94) **
r for correlation	0.429 **	0.429 **	0.300 **
WHtR			
Q1	1	1	1
Q2	6.10 (3.53, 10.53) **	5.47 (3.45, 8.66) **	3.33 (0.60, 18.47)
Q3	18.17 (10.64, 31.02) **	12.57 (7.78, 20.32) **	10.29 (2.30, 46.02) **
Q4	51.95 (30.14, 89.54) **	33.72 (20.74, 54.82) **	54.55 (12.89, 230.84) **
r for correlation	0.490 **	0.507 **	0.371 **
BMI			
Q1	1	1	1
Q2	12.79 (5.82, 28.09) **	3.96 (2.46, 6.38) **	4.08 (0.45, 36.97)
Q3	31.50 (14.55, 68.20) **	9.12 (5.73, 14.51) **	14.15 (1.83, 109.59) **
Q4	132.37 (61.07, 286.93) **	33.22 (20.41, 54.05) **	62.62 (8.49, 461.70) **

Abbreviations: SBP, Systolic Blood Pressure, DBP, Diastolic Blood Pressure, TC, Total Cholesterol, TG, Triglyceride, LDL, Low Density Lipoprotein, FBG, Fasting Blood Glucose, ALT and AST, Alanine aminotransferase, WC, Waist Circumference, WHR, Waist–hip Ratio, WHtR, Waist-to-height Ratio, BMI, Body Mass Index, AVI, Abdominal Volume Index, AIP, Atherogenic index of plasma, TyG, Triglyceride Glucose.

* p-value < 0.05. ** p-value < 0.01. Values expressed as OR and 95% CI.

	All	Men	Women
r for correlation	0.527 **	0.506 **	0.340 **
AVI			
Q1	1		1
Q2	5.82 (3.00, 11.27) **	4.89 (2.98, 8.02) **	4.14 (0.46, 37.48)
Q3	25.68 (13.70, 48.14) **	11.68 (7.19, 18.98) **	11.88 (1.51, 93.20) **
Q4	72.53 (38.63, 136.19) **	31.42 (19.06, 51.79) **	67.20 (9.12, 495.08) **
r for correlation	0.523 **	0.492 **	0.350 **
AIP			
Q1	1	1	1
Q2	5.00 (2.97, 8.41) **	2.51 (1.66, 3.80) **	4.08 (0.45, 36.97)
Q3	12.87 (7.81, 21.21) **	5.69 (3.81, 8.48) **	19.06 (2.50, 145.19) **
Q4	38.23 (23.21, 62.96) **	14.09 (9.31, 21.31) **	54.82 (7.42, 404.93) **
r for correlation	0.474 **	0.425 **	0.321 **
TyG			
Q1	1	1	1
Q2	3.72 (2.34, 6.00) **	2.51 (1.64, 3.84) **	4.11 (0.45, 37.21)
Q3	9.97 (6.37, 15.62) **	6.75 (4.49, 10.14) **	19.77 (2.60, 150.58) **
Q4	29.45 (18.81, 46.14) **	15.37 (10.08, 23.43) **	55.56 (7.52, 410.37) **
r for correlation	0.466 **	0.442 **	0.323 **
ALT/AST			
Q1	1	1	1
Q2	2.19 (1.55, 3.08) **	3.48 (2.24, 5.39) **	4.75 (0.99, 22.73)
Q3	3.35 (2.40, 4.67) **	7.39 (4.80, 11.36) **	9.86 (2.23, 43.67) **
Q4	5.62 (4.06, 7.79) **	18.56 (11.92, 28.91) **	25.78 (6.08, 109.30) **
r for correlation	0.456 **	0.444 **	0.277 **

Abbreviations: SBP, Systolic Blood Pressure, DBP, Diastolic Blood Pressure, TC, Total Cholesterol, TG, Triglyceride, LDL, Low Density Lipoprotein, FBG, Fasting Blood Glucose, ALT and AST, Alanine aminotransferase, WC, Waist Circumference, WHR, Waist–hip Ratio, WHtR, Waist-to-height Ratio, BMI, Body Mass Index, AVI, Abdominal Volume Index, AIP, Atherogenic index of plasma, TyG, Triglyceride Glucose.

* p-value < 0.05. ** p-value < 0.01. Values expressed as OR and 95% CI.

ROC Curves and AUC for Indices in Identifying FL

To assess the accuracy of anthropometric and metabolic indices for predicting FL, AUC were conducted and shown in Table 3. Among all the indices, WHtR had the greatest AUC in males (AUC = 0.81) and women (AUC = 0.85). In men, BMI had the same diagnostic ability for FL (AUC = 0.81), followed by WC (AUC = 0.80) and AVI (AUC = 0.80). In women, BMI (AUC = 0.84) had the second greatest predict ability, while WC, AVI, AIP and TyG showed the same ability for predicting FL (AUC = 0.83) in third. Moreover, BMI and AVI had the highest Youden index values in males and females, respectively.

Table 3
AUC, Youden index, sensitivity, specificity and cut-off point of clinilcal parameters and FL-related indices for predicting FL.

	Men					Women				
	AUC (95% CI)	Sensitivity(%)	Specificity(%)	Youden Index	Cut-off point	AUC (95% CI)	Sensitivity(%)	Specificity(%)	Youden Index	Cut-off point
Clinical parameters										
SBP (mmHg)	0.59 (0.56, 0.62)**	67.9	53.4	0.145	122.5	0.75 (0.69, 0.81)**	71.0	30.8	0.402	122.5
DBP (mmHg)	0.60 (0.57, 0.64)**	81.7	66.3	0.154	70.5	0.70 (0.64, 0.77)**	79.0	45.0	0.340	70.5
FBG (mg/dL)	0.64 (0.61, 0.68)**	42.0	20.0	0.220	5.68	0.77 (0.71, 0.83)**	67.7	27.0	0.407	5.30
TC (mg/dL)	0.57 (0.53, 0.60)**	67.7	55.4	0.122	4.76	0.64 (0.57, 0.72)**	71.0	47.7	0.233	4.95
TG (mg/dL)	0.75 (0.72, 0.78)**	75.0	35.8	0.392	1.47	0.81 (0.76, 0.86)**	77.4	24.8	0.527	1.34
LDL (mg/dL)	0.58 (0.54, 0.61)**	75.9	62.1	0.137	2.86	0.70 (0.63, 0.76)**	53.2	22.1	0.331	3.41
ALT (U/L)	0.77 (0.74, 0.79)**	67.5	27.4	0.400	25.8	0.76 (0.71, 0.82)**	87.1	40.3	0.468	14.9
AST (U/L)	0.64 (0.61, 0.68)**	61.2	39.0	0.222	24.2	0.65 (0.59, 0.72)**	90.3	66.0	0.243	17.5
FL-related indices										
WC (cm)	0.80 (0.78, 0.83)**	81.3	35.7	0.455	87.2	0.83 (0.78, 0.88)**	77.4	19.9	0.575	85.4
WHR	0.75 (0.73, 0.83)**	73.9	33.1	0.408	0.905	0.79 (0.74, 0.84)**	80.6	31.7	0.489	0.895
WHtR	0.81 (0.79, 0.84)**	87.1	40.8	0.463	0.505	0.85 (0.80, 0.89)**	82.3	25.3	0.569	0.525
BMI (kg/m^2)	0.81 (0.79, 0.84)**	70.3	22.1	0.482	25.1	0.84 (0.80, 0.89)**	85.5	29.1	0.564	23.2
AVI	0.80 (0.78, 0.83)**	81.5	35.7	0.458	15.3	0.83 (0.78, 0.88)**	77.4	20.1	0.573	14.6
AIP	0.76 (0.73, 0.79)**	69.0	28.7	0.402	0.295	0.83 (0.78, 0.87)**	83.9	28.9	0.550	-0.0850
TyG	0.77 (0.74, 0.80)**	73.7	31.6	0.421	4.75	0.83 (0.79, 0.88)**	87.1	32.1	0.550	4.61

Abbreviations: SBP, Systolic Blood Pressure, DBP, Diastolic Blood Pressure, TC, Total Cholesterol, TG, Triglyceride, LDL, Low Density Lipoprotein, FBG, Fasting Blood Glucose, ALT and AST, Alanine aminotransferase, WC, Waist Circumference, WHR, Waist–hip Ratio, WHtR, Waist-to-height Ratio, BMI, Body Mass Index, AVI, Abdominal Volume Index, AIP, Atherogenic index of plasma, TyG, Triglyceride Glucose.

* p-value < 0.05. ** p-value < 0.01.

	Men					Women				
ALT/AST	0.78 (0.75, 0.80)**	72.0	31.8	0.402	1.04	0.76 (0.70, 0.81)**	74.2	32.3	0.419	0.815

Abbreviations: SBP, Systolic Blood Pressure, DBP, Diastolic Blood Pressure, TC, Total Cholesterol, TG, Triglyceride, LDL, Low Density Lipoprotein, FBG, Fasting Blood Glucose, ALT and AST, Alanine aminotransferase, WC, Waist Circumference, WHR, Waist–hip Ratio, WHtR, Waist-to-height Ratio, BMI, Body Mass Index, AVI, Abdominal Volume Index, AIP, Atherogenic index of plasma, TyG, Triglyceride Glucose.

* p-value < 0.05. ** p-value < 0.01.

Figure 1 showed the ROC curves and AUCs of indices for FL in males (A) and females (B), respectively. The ROC curves and AUCs of indices for FL in females stratified by two decades of age (20–40 (B-a) and 40- years (B-b)) were shown in Fig. 2. WC and AVI had the greatest AUC in 20–40 years (AUC = 0.96) of females, while TyG had the greatest AUC in 40- years (AUC = 0.80) of females. Besides, DBP in 20–40 years and TC in 40- years had no significant predictive ability for female subjects ($p > 0.05$).

Discussion

Although the relationship between these FL related indexes (SBP, DBP, TC, TG, LDL, FBG, ALT, AST, WC, WHR, WHtR, BMI, AVI, AIP, TyG and ALT/AST) and FL were analyzed separately in many articles, few articles put them together to evaluate. In this cross-sectional survey, we comprehensively evaluated the predictive ability and cutoff value of anthropometric and metabolic indices, including SBP, DBP, FBG, TC, TG, LDL, ALT, AST, WC, WHR, WHtR, BMI, AVI, AIP, TyG and ALT/AST, in identifying FL among adults and found that the ORs in females increased more per quartiles than that in males. WHtR had the greatest AUC regardless of gender. Furthermore, WC and AVI had the greatest AUC in 20–40 years (AUC = 0.96) of females, while TyG had the greatest AUC in 40- years (AUC = 0.80) of females.

The prevalence of FL might be influenced by gender and age[3, 4, 8]. In our study, we found that 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[30, 31]. A study of Japanese women showed aging is a risk factor for FL in premenopausal women, independently from weight gain or influence of metabolic syndrome[32].

The association of obesity with FL has been established in multiple previous studies[11, 15, 33, 34]. Epidemiological studies propose a causative link between obesity and progressive liver disease in individuals[15, 34]. Obesity has been linked not only to the 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[35]. Obesity can be expressed in clinical practice by several methods, including anthropometric and metabolic ways[26]. 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[36]. WC, WHR, WHtR and BMI have been proved and used in many clinical trials as an indicator for the severity of fatty liver disease[19, 22]. AVI is used to assess general volume, and it has been highly associated with dysfunction of glucose metabolism[37]. Researches found that there were concordances between increased AIP and the incidence of FL[17, 18]. TyG are often used to explore the relationship between insulin resistance and excessive visceral fat accumulation[38, 39]. Additionally, accumulating evidence strongly suggests that advanced blood lipids, blood pressure and blood sugar could also lead to more severe histological changes and poorer clinical outcomes[14, 22, 40]. Once FL is established, insulin resistance can promote the progression to the more severe state of liver endangerment like non-alcoholic steatohepatitis.

In our study, we found differences of these related indexes between FL and non-FL stratified by the gender. We firstly demonstrated that the ORs in females increased more per quartiles than that in males. This may be explained by hormone changes in age. Testosterone has been shown to increase their risk of FL in females with polycystic ovary syndrome, independently from obesity and insulin resistance[41]. The study by Park et al. expands upon existing data by highlighting the association of testosterone and FL even among women without “high” testosterone levels[42]. A research in Development in Young Adults cohort found that increasing levels of free testosterone in premenopausal women were associated with prevalent NAFLD in midlife, including women without androgen excess[43].

Our results further revealed that WHtR had the strongest association and diagnostic ability (cut-off points, 0.505 in men and 0.525 in women) with FL after considering the influence of gender, which is consistent with the research by Nima Motamed et al. who calculated cut-off points for WHtR (0.533 in men and 0.58 in women)[44]. The subtle differences between the two studies may be owing to difference between Chinese and Iranian. Our findings is in contrast with the study by Zheng et al., who reported the ability of WHtR for predicting FL was weaker than WHR, it should be mentioned that their research may be more useful in the prediction of FL for males due to the high proportion of males and low number of study population [45]. Additionally, we found an age-specific effects of these marker for predicting FL. As we all know, diabetes is one of the strongest

risk factors for FL, the increasing prevalence of diabetes along with age especially in female subjects s[12, 46] may explain the result that WC and AVI had the greatest AUC in 20–40 years, while TyG had the greatest AUC in 40- year.

This study evaluated the predictive ability and cutoff value of anthropometric and metabolic indices. 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.

Conclusions

In summary, we comprehensively compared the association of anthropometric and metabolic indices with FL. We found the ORs in females increased more per quartiles than that in males for all the analyzed markers and identified that WHtR had the greatest AUC for both males and females. We further found an age-dependent differences in indices for predicting FL in female subjects, especially, WC and AVI had the greatest diagnostic ability in 20–40 years, while TyG for those aged more than 40 years.

Declarations

Ethics approval and consent to participate

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

Consent for publication

All authors were agreed with publication.

Availability of data and materials

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there is no competing interests.

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Author Contributions

XFF and PYY contributed to the study planning and design, ethics applications, organisational collaborations, data collection, analysis and interpretation, and writing of the manuscript. SKY contributed to the study design, ethics applications, organisational collaborations, data collection, data interpretation and manuscript revision. ZQ, WY, LJY, XXH, ZH contributed to the study design, ethics applications, data interpretation and manuscript revision.

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Figures

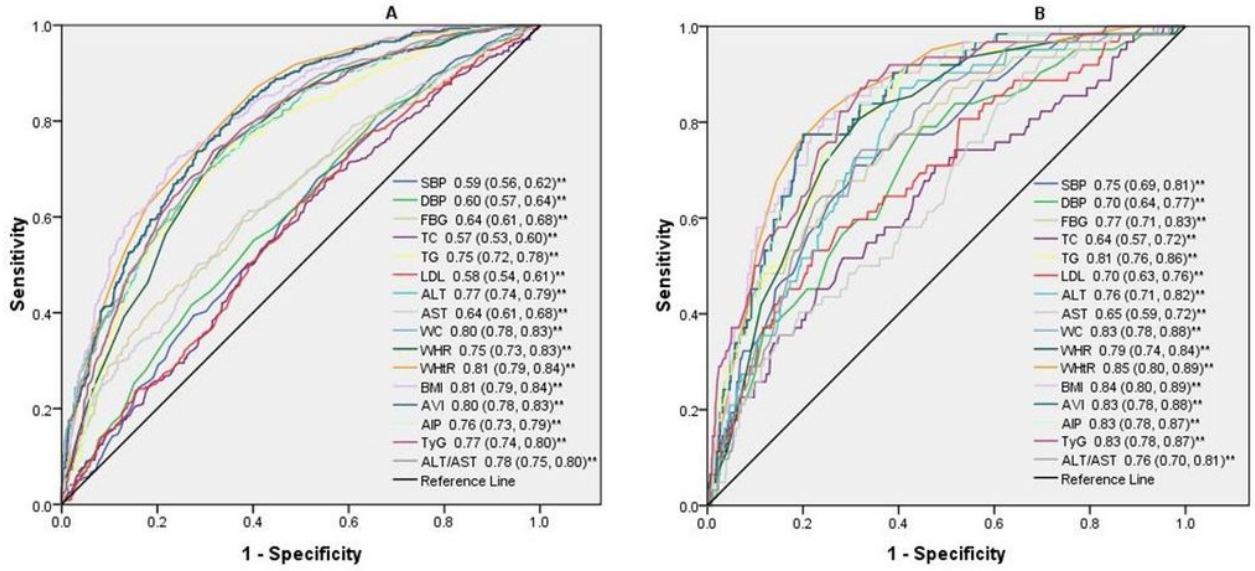

Figure 1. Comparison of the predictive value of FL-related parameters for diagnosis of FL among (A) all males and (B) all females.
* p-value < 0.05 ** p-value < 0.01

Figure 1

Caption found in figure.

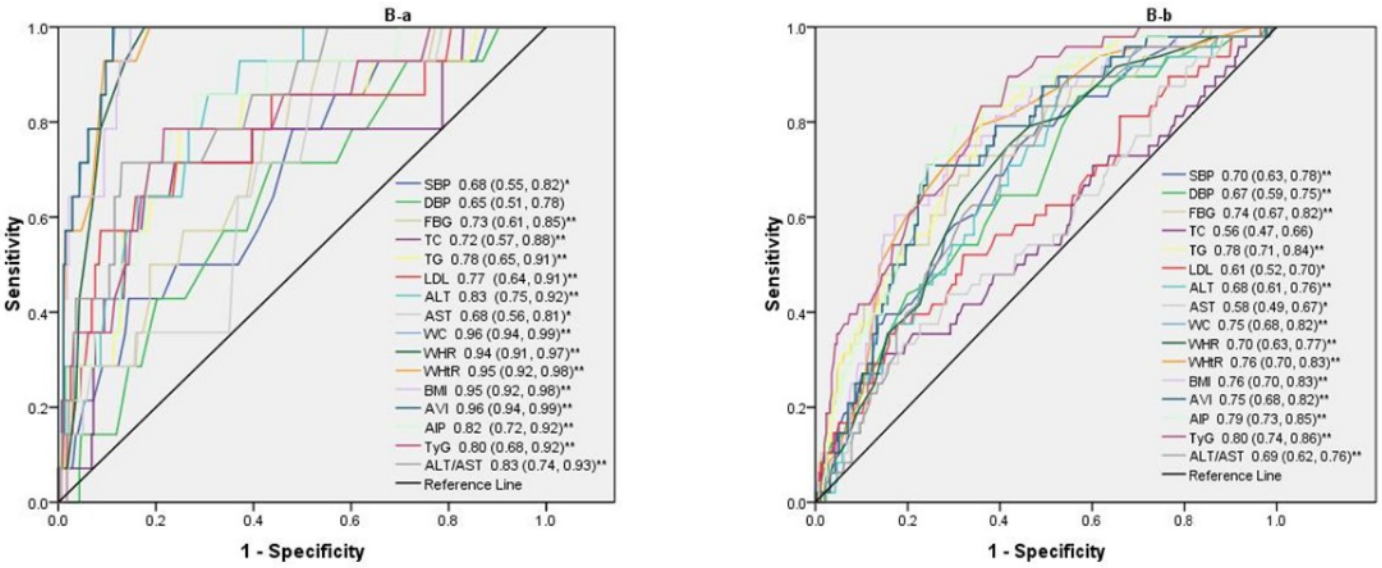

Figure 2. Comparison of the predictive value of FL-related parameters for diagnosis of FL among (B-a) females aged 20−40 years, (B-b) females aged 40-years.
* p-value < 0.05 ** p-value < 0.01

Figure 2

Caption found in figure.