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ORIGINAL RESEARCH

Association of Lipid and Blood Glucose Profiles with MASLD Among Young Adults

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Background: Comparative analyses of metabolic biomarkers for Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) in young adults remain limited. While previous studies have examined metabolic predictors of MASLD, few have specifically focused on young adult populations in China, where rising obesity rates and lifestyle changes are creating new patterns of metabolic risk.

Methods: In this retrospective study, young adults underwent abdominal ultrasounds and metabolic profiling were included in the analysis. Eleven blood lipid and glucose profiles were analyzed. MASLD is defined according to the liver ultrasound findings and self-reported alcohol consumption. Multivariable logistic regression and ROC curves were employed to analyze the association between each indicator and the outcome. Based on the five indicators most strongly indicators, the number of major risk factors for patients was defined, and a logistic regression model with adjusted covariates was used to investigate the impact of the coexistence of risk factors on MASLD.

Results: A total of 24.55% (n=10,332) of participants aged 35 years and under had MASLD. All indicators were significantly associated with MASLD separately after adjusting for covariates. Elevated TG/HDL-C ratio≥ 1.44 (OR: 3.87, 95% CI:3.62, 4.15), TyG ≥ 8.8 (OR: 3.78, 95% CI: 3.51, 4.07), and TG≥ 1.61mmol/L (OR: 3.62, 95% CI: 3.38, 3.88) exhibited the strongest associations with MASLD. ROC analysis indicated comparable predictive performance for TG/HDL ratio (AUC: 0.85, 95% CI:0.84, 0.85) and TyG (AUC: 0.83, 95% CI:0.83, 0.84). Cumulative risk factor analysis indicated that individuals with more risk factors suffered increasing risk compared to those with no risk factors. The associations were stable among participants with different amount of metabolic risk factors.

Conclusion: Our study establishes that lipid ratios and insulin resistance indices maintain strong predictive value for MASLD in young Chinese adults, even when traditional metabolic risk factors are absent. These findings highlight the importance of incorporating TG/HDL-C ratio and TyG index into routine health screenings for early MASLD detection in young populations.

Keywords: lipid, glucose, MASLD, physical examination

Introduction

Metabolic Dysfunction–Associated Steatotic Liver Disease (MASLD) has emerged as a pressing global health challenge, increasingly affecting young people due to its association with metabolic syndrome, insulin resistance (IR), and cardiovascular risk.[1,2] MASLD involves excess fat accumulation in the liver, which can progress to more severe stages such as metabolic dysfunction-associated steatohepatitis (MASH), fibrosis, or cirrhosis.[3] Its global prevalence is increasing, with recent evidence suggesting that it affects a quarter of the world's population.[4] In China, lifestyle change along with rising obesity and metabolic dysfunction, have led to higher MASLD rates, notably among younger groups.[5]

The pathogenesis of MASLD is closely linked to metabolic dysregulation, particularly insulin resistance, which plays a central role in the development and progression of the disease.[6] Traditional lipid profiles, such as low-density lipoprotein

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cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) have been widely studied in relation to MASLD.[7–9] Recent findings indicate that composite indices, such as the triglyceride-glucose index (TyG), may provide a more thorough evaluation of metabolic health and insulin resistance. The TyG index has demonstrated reliability as a marker for insulin resistance and has been linked to several metabolic disorders, including MASLD.[10–12] While prior studies have examined metabolic biomarkers in MASLD, most have focused on older or mixed-age populations, with limited data on young adults, particularly in China.[13,14] Young adults represent a unique population, as they are often overlooked in metabolic studies despite being at risk for early-onset metabolic disorders. By leveraging a robust sample size and focusing on this unique population, novel insights into the distinct metabolic drivers of MASLD in young adults are warranted, enabling earlier detection and tailored interventions.

This study examines the connection between different lipid and glucose markers and MASLD in young adults. By determining the most predictive biomarkers, this work aims to improve early identification and preventive measures for MASLD in this at-risk population.

Methods

Study Population

The investigation was carried out utilizing data obtained from a health check-up network affiliated with the Healthcare Management Center of Peking University International Hospital, which offers annual comprehensive health evaluations to the community. The specifics regarding the study population and data sources for this research are elaborated upon in a preceding publication.[15] In summary, the study population comprised individuals who underwent an abdominal ultrasound examination between January 2019 to December 2023. Participants were aged 18 to 35 years at the time of their first examination. From 101,416 individuals undergoing physical examinations, we excluded 15,832 without baseline abdominal ultrasound or missing data of drinking alcohol, 558 with alcoholic fatty liver disease, and 42,935 aged greater than 35 years, resulting in 42,091 eligible participants (Supplementary Figure 1).

The study complies with the Declaration of Helsinki. The proposal was approved by the Ethics Committee of Peking University International Hospital (ethics number: 2023-KY-0045-01). Given that the analyses employed only de-identified data, the requirement for individual consent was waived by the Ethics Committee.

Data Collection and Definition of Risk Factors

All requisite data were collected through the electronic medical records. This study primarily concentrated on indicators of blood lipid and glucose profiles, which were categorized into three distinct groups: (1) Individual parameters: including blood glucose indicated by fasting plasma glucose (FPG), blood lipid indicated by total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and remnant cholesterol (RC, RC=TC minus LDL-C minus HDL-C). (2) Lipid ratios: including LDL-C/HDL-C, TC/HDL-C, TG/HDL-C, and FPG/HDL-C. (3) Composite index: Triglyceride-glucose index (TyG, TyG =ln[TG× FPG/2]. TG and FPG using unit of mg/dL).

Blood samples obtained following a fasting period of at least eight hours. All above lipid and glucose profiles, along with standard biochemical markers (Alanine aminotransferase[ALT], aspartate aminotransferase [AST], estimated glomerular filtration rate [eGFR]) were tested using automated platforms. Trained staff gathered demographic and clinical data per standardized protocols. Missing values were handled using regression imputation, which incorporated demographic data, as well as information regarding smoking and alcohol consumption habits, and medication history.

In addition, considering close association between MASH and metabolic syndrome (MetS), this study also defined five metabolic risk factors according to the Chinese guideline,[16] and calculated the number of metabolic risk factors each individual had: (1) Abdominal obesity is defined as a BMI of 24 kg/m² or greater, accompanied by a waist circumference exceeding 90 cm for males or 85 cm for females. (2) High blood pressure is characterized by a measurement of 130/85 mmHg or higher, or the use of antihypertensive medications. (3) Hyperlipidemia is indicated by a triglyceride level of 1.7 mmol/L or greater, or the use of antilipidemic agents. (4) Low levels of HDL-C are defined as less than 1.0 mmol/L for males and less than 1.3 mmol/L for females. (5) Hyperglycemia is identified by a fasting blood glucose level of 5.6 mmol/L or higher, or a documented history of type 2 diabetes mellitus.

Assessment of MASLD

Trained sonographers conducted abdominal ultrasonography with a 3- to 5-MHz high-resolution linear array transducer. After fasted for eight hours, participants were instructed to lie supine on the bed with their legs bent and abdominal muscles relaxed. After taking deep breaths, they were to hold their breath for 3 to 5 seconds before exploring the liver in a specific sequence. This sequence began with a sweep from the left lobe of the liver, followed by an oblique sweep from the left subcostal margin; then a longitudinal sweep from the left median paracentral area to right median paracentral area, an oblique sweep from the right subcostal margin; and finally, an exploration of the right intercostal oblique segment.

The diagnosis of MASLD is based on liver imaging findings that fulfill the diagnostic criteria for diffuse fatty liver. Additionally, it requires the absence of a self-reported history of alcohol consumption exceeding 140 grams per week for men and 70 grams per week for women. Furthermore, it is essential to exclude other specific conditions that may contribute to MASH as outlined in the clinical guidelines for MASLD in China. The image manifestations of fatty liver include any one of following criteria: (1) Near-field echoes exhibit a diffuse enhancement within the liver, which is stronger than that observed in the kidneys and spleen, accompanied by a gradual attenuation of far-field echoes. (2) The visualization of intrahepatic ductal structures is suboptimal. (3) The liver demonstrates mild to moderate enlargement characterized by rounded margins. (4) Color Doppler flow imaging indicates a reduction in the visibility of colored intrahepatic flow signals; however, the intrahepatic vascular architecture appears to be normal. (5) The echogenicity of the right lobe of the liver and the transverse septum is unclear and incomplete.

Statistical Analysis

The characteristics of the participants were presented using percentages for categorical variables, while continuous variables were summarized using either the mean ± standard deviation or the median (Q1, Q3). To evaluate the differences between participants with and without MASLD, *t*-test, Wilcoxon–Mann–Whitney, chi-square test and Fisher's exact test were utilized for continuous and categorical variables, separately.

To examine the relationship between each index and MASLD, a multivariable logistic regression analysis was conducted. Each index was firstly treated as a continuous variable and subsequently categorized into quartiles, with quartile 1 serving as the reference group. The analysis comprised an unadjusted model as well as three adjusted models: (1) Model 1 adjusted for age and sex; (2) Model 2 incorporated additional adjustments for lifestyle (smoking history, alcohol consumption) and disease history (hypertension, dyslipidemia, diabetes, and chronic kidney disease); and (3) Model 3 further included adjustments for physical examination and laboratory test indicators, such as blood pressure, body mass index, waist circumference, pulse rate, eGFR, AST and ALT. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated and reported, while the efficacy of these metrics in relation to MASLD was evaluated through receiver operating characteristic (ROC) curves generated from a fully adjusted logistic regression model.

We conducted an analysis of the cumulative impacts of the five major risk factors associated with MASLD, as indicated by the highest odds ratios. The concurrence of these risk factors was assessed by counting their presence in individuals. Those with any two of the five were classified as having two concurrent risk factors. A fully adjusted logistic regression model examined the impact of this concurrence on MASLD, using the absence of risk factors as the reference category.

A sensitivity analysis was conducted among participants with different amount of metabolic risk factors. Statistical analyses were conducted utilizing SAS version 9.4 (SAS Institute Inc., Cary, North Carolina). A significance level of $p < 0.05$ was employed to determine statistical significance.

Results

Characteristics of Subjects

The study included 42,091 participants, with a mean age of 29.3 ± 3.6 years; 56.37% were male. Common metabolic risk factors included low HDL-C (23.88%), high triglycerides (16.33%), and abdominal obesity (15.62%). Of these, 10,332 participants (24.55%) had MASLD. Those with MASLD were older in age, predominantly male, had larger waist circumferences and BMI, and were more likely to smoke and consume alcohol, with poorer blood pressure and lab results ($p<0.01$; Table 1).

Table 1 Characteristics of All Participants with and Without MASLD

Characteristics	Overall N=42091	MASLD N=10332	No MASLD N=31759	p value
Age, years	29.3±3.6	30.1±3.4	29.0±3.6	<0.001*
Sex				
Male	23728(56.37)	8980(86.91)	14,748(46.44)	<0.001*
Female	18363(43.63)	1352(13.09)	17,011(53.56)	
Smoking history	4473(10.63)	2032(19.67)	2441(7.69)	<0.001*
Alcohol consumption	5821(13.83)	1294(12.52)	4527(14.25)	<0.001*
Disease History				
Hypertension	401(0.95)	273(2.64)	128(0.4)	<0.001*
Diabetes	131(0.31)	74(0.72)	57(0.18)	<0.001*
Dyslipidemia	133(0.32)	99(0.96)	34(0.11)	<0.001*
Coronary heart disease	9(0.02)	6(0.06)	3(0.01)	<0.001*
Chronic kidney disease	40(0.1)	11(0.11)	29(0.09)	0.66
Stroke	3(0.01)	1(0.01)	2(0.01)	0.72
Cancer or malignant tumors	106(0.25)	31(0.3)	75(0.24)	0.26
Physical and lab examination				
BMI, kg/m^2	23.4±3.4	26.6±3.6	22.4±2.6	<0.001*
SBP, mmHg	115.4±12.0	122.3±12.0	113.2±11.2	<0.001*
DBP, mmHg	68.9±8.7	73.8±9.3	67.3±7.9	<0.001*
Waist circumference, cm	80.6±10.0	90.1±9.2	77.5±8.1	<0.001*
AST, U/L	21.73±14.87	27.32±15.03	19.91±14.35	<0.001*
ALT, U/L	17(11, 27)	33(22, 50)	14(10, 20)	<0.001*
eGRF, $mL/min/1.73m^2$	107.43±15.78	106.68±15.87	107.68±15.74	<0.001*
eGRF<60	19(0.05)	6(0.06)	13(0.04)	0.48
Metabolic risk factors				
Abdominal obesity	6114(14.53)	4274(41.37)	1840(5.79)	<0.001*
High blood pressure	5320(12.64)	2593(25.1)	2727(8.59)	<0.001*
Hypertriglyceridemia	6872(16.33)	4625(44.76)	2247(7.08)	<0.001*
Low HDL-C	10053(23.88)	4262(41.25)	5791(18.23)	<0.001*
Hyperglycemia	1727(4.1)	1096(10.61)	631(1.99)	<0.001*
Amount of metabolic risk factors				<0.001*
0	23,582(56.03)	2070(20.03)	21,512(67.74)	
1	10,777(25.6)	2986(28.9)	7791(24.53)	
2	4902(11.65)	2904(28.11)	1998(6.29)	
3	1950(4.63)	1565(15.15)	385(1.21)	
4	745(1.77)	674(6.52)	71(0.22)	
5	135(0.32)	133(1.29)	2(0.01)	

Note: *p value<0.01.

Abbreviations: BMI, Body Mass Index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, High-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; eGFR, estimated glomerular filtration rate.

All lipid and glucose indicators significantly differed between the two groups ((p<0.01). Participants with MASLD had higher levels of FPG, TC, TG, LDL-C, RC, and the ratios of TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, FPG/HDL-C, and TyG, except for HDL-C (Table 2).

Associations Between Lipid and Blood Glucose Indicators and MASLD

All indicators demonstrated a significant association with MASLD when analyzed as continuous variables, following the adjustment for covariates (Table 3). The odds ratios were: FPG (OR=1.69), TC (OR=1.24), TG (OR=2.37), LDL-c (OR=1.37), HDL-c (OR=0.06), RC (OR=3.74), TyG (OR=4.4), FPG/HDL-c (OR=1.97), TC/HDL-c (OR=2), TG/HDL-c

Table 2 Profile of Blood Lipid or Glucose Indices with and Without MASLD

Indicators (min-max)	Overall N=42091	MASLD N=10332	No MASLD N=31759	p value
FPG, mmol/L	4.78±0.67	5.05±1.09	4.7±0.43	<0.001*
Q1(<4.60)	13,103(31.13)	2022(19.57)	11,081(34.89)	<0.001*
Q2(4.60–4.89)	13,359(31.74)	2809(27.19)	10,550(33.22)	
Q3(4.90–5.20)	11,067(26.29)	3262(31.57)	7805(24.58)	
Q4(>5.20)	4562(10.84)	2239(21.67)	2323(7.31)	
TC, mmol/L	4.52±0.79	4.78±0.84	4.43±0.75	<0.001*
Q1(<4.10)	12,623(29.99)	2036(19.71)	10,587(33.34)	<0.001*
Q2(4.10–4.60)	12,295(29.21)	2564(24.82)	9731(30.64)	
Q3(4.60–5.18)	9714(23.08)	2808(27.18)	6906(21.75)	
Q4(>5.18)	7459(17.72)	2924(28.3)	4535(14.28)	
TG, mmol/L	0.92(0.65, 1.38)	1.58(1.11, 2.27)	0.8(0.59, 1.12)	<0.001*
Q1(<0.73)	13,655(32.44)	647(6.26)	13,008(40.96)	<0.001*
Q2(0.73–1.07)	11,394(27.07)	1607(15.55)	9787(30.82)	
Q3(1.07–1.61)	9432(22.41)	3111(30.11)	6321(19.9)	
Q4(>1.61)	7610(18.08)	4967(48.07)	2643(8.32)	
HDL-C, mmol/L	1.31±0.3	1.09±0.2	1.38±0.3	<0.001*
Q1(<0.73)	9539(22.66)	5220(50.52)	4319(13.6)	<0.001*
Q2(0.73–1.07)	10,633(25.26)	3332(32.25)	7301(22.99)	
Q3(1.07–1.61)	10,896(25.89)	1390(13.45)	9506(29.93)	
Q4(>1.61)	11,023(26.19)	390(3.77)	10,633(33.48)	
LDL-C, mmol/L	2.7±0.7	3.02±0.72	2.6±0.66	<0.001*
Q1(<2.3)	12,095(28.74)	1481(14.33)	10,614(33.42)	<0.001*
Q2(2.30–2.74)	11,791(28.01)	2339(22.64)	9452(29.76)	
Q3(2.74–3.26)	10,093(23.98)	2967(28.72)	7126(22.44)	
Q4(>3.26)	8112(19.27)	3545(34.31)	4567(14.38)	
RC, mmol/L	0.45(0.34, 0.59)	0.58(0.42, 0.8)	0.42(0.32, 0.54)	<0.001*
Q1(<0.37)	13,545(32.18)	1850(17.91)	11,695(36.82)	<0.001*
Q2(0.37–0.50)	11,616(27.6)	1963(19)	9653(30.39)	
Q3(0.50–0.68)	9976(23.7)	2717(26.3)	7259(22.86)	
Q4(>0.68)	6789(16.13)	3778(36.57)	3011(9.48)	
TC/HDL-C	3.61±1.03	4.52±1.07	3.32±0.82	<0.001*
Q1(<3)	13,092(31.1)	489(4.73)	12,603(39.68)	<0.001*
Q2(3–3.64)	11,206(26.62)	1491(14.43)	9715(30.59)	
Q3(3.64–4.41)	9516(22.61)	3217(31.14)	6299(19.83)	
Q4(>4.41)	8277(19.66)	5135(49.7)	3142(9.89)	
TG/HDL-C	0.71(0.45, 1.2)	1.47(0.97, 2.27)	0.58(0.4, 0.91)	<0.001*
Q1(<0.51)	13,328(31.66)	430(4.16)	12,898(40.61)	<0.001*
Q2(0.51–0.85)	11,276(26.79)	1437(13.91)	9839(30.98)	
Q3(0.85–1.44)	9554(22.7)	3165(30.63)	6389(20.12)	
Q4(>1.44)	7933(18.85)	5300(51.3)	2633(8.29)	
LDL-C /HDL-C	2.19±0.82	2.85±0.81	1.98±0.7	<0.001*
Q1(<1.70)	12,614(29.97)	513(4.97)	12,101(38.1)	<0.001*
Q2(1.70–2.22)	10,964(26.05)	1554(15.04)	9410(29.63)	
Q3(2.22–2.80)	9645(22.91)	3164(30.62)	6481(20.41)	
Q4(>2.80)	8868(21.07)	5101(49.37)	3767(11.86)	
FPG/HDL-C	3.87±1.19	4.81±1.5	3.56±0.87	<0.001*
Q1(<3.22)	12,714(30.21)	465(4.5)	12,249(38.57)	<0.001*
Q2(3.22–3.91)	11,523(27.38)	1734(16.78)	9789(30.82)	
Q3(3.91–4.73)	10,395(24.7)	3621(35.05)	6774(21.33)	
Q4(>4.73)	7459(17.72)	4512(43.67)	2947(9.28)	

(*Continued*)

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Table 2 (Continued).

Indicators (min-max)	Overall N=42091	MASLD N=10332	No MASLD N=31759	p value
TyG	8.21±0.61	8.76±0.6	8.03±0.5	<0.001*
Q1(<7.92)	14,322(34.03)	642(6.21)	13,680(43.07)	<0.001*
Q2(7.92–8.34)	11,763(27.95)	1749(16.93)	10,014(31.53)	
Q3(8.34–8.80)	9231(21.93)	3301(31.95)	5930(18.67)	
Q4(>8.80)	6775(16.1)	4640(44.91)	2135(6.72)	

Note: *p value<0.01.

Abbreviations: HDL-C, High-density lipoprotein cholesterol; TG, Triglycerides; TC, Total cholesterol; LDL-C, Low-density lipoprotein cholesterol; FPG, fasting plasma glucose; RC, remnant cholesterol; TyG, triglyceride-glucose index.

Table 3 Association of Lipid or Glucose Indices with MASLD

Indicators	Unadjusted model OR(95% CI)	Adjusted Model 1 OR(95% CI)	Adjusted Model 2 OR(95% CI)	Adjusted Model 3 OR(95% CI)
FPG, mmol/L	3.29(3.12,3.47)*	2.71(2.56,2.87)*	2.69(2.54,2.85)*	1.69(1.58,1.8)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	1.46(1.37,1.55)*	1.34(1.25,1.43)*	1.35(1.26,1.44)*	1.19(1.1,1.29)*
Q3	2.29(2.15,2.44)*	1.87(1.75,2)*	1.9(1.78,2.03)*	1.49(1.37,1.62)*
Q4	5.28(4.9,5.69)*	4.17(3.84,4.53)*	4.02(3.7,4.37)*	2.17(1.96,2.41)*
TC, mmol/L	1.73(1.68,1.78)*	1.61(1.56,1.66)*	1.59(1.54,1.64)*	1.24(1.2,1.29)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	1.37(1.28,1.46)*	1.35(1.26,1.44)*	1.35(1.26,1.45)*	1.18(1.09,1.28)*
Q3	2.11(1.98,2.26)*	1.91(1.78,2.05)*	1.91(1.78,2.04)*	1.41(1.3,1.54)*
Q4	3.35(3.14,3.58)*	2.84(2.64,3.05)*	2.76(2.57,2.96)*	1.62(1.49,1.77)*
TG, mmol/L	5.27(5.06,5.5)*	3.9(3.74,4.07)*	3.84(3.68,4.01)*	2.37(2.27,2.48)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	3.3(3,3.63)*	2.59(2.35,2.85)*	2.57(2.33,2.83)*	1.94(1.74,2.16)*
Q3	9.89(9.04,10.82)*	6.13(5.59,6.72)*	6.07(5.53,6.66)*	3.6(3.25,4)*
Q4	37.78(34.46,41.42)*	21.29(19.36,23.41)*	20.5(18.63,22.55)*	8.29(7.44,9.23)*
HDL-C, mmol/L	0.01(0.01,0.01)*	0.02(0.01,0.02)*	0.02(0.02,0.02)*	0.06(0.05,0.07)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	0.38(0.36,0.4)*	0.42(0.4,0.45)*	0.43(0.41,0.46)*	0.58(0.54,0.62)*
Q3	0.12(0.11,0.13)*	0.18(0.17,0.2)*	0.19(0.17,0.2)*	0.32(0.29,0.35)*
Q4	0.03(0.03,0.03)*	0.06(0.05,0.07)*	0.06(0.06,0.07)*	0.14(0.12,0.16)*
LDL-C, mmol/L	2.35(2.27,2.43)*	1.9(1.83,1.97)*	1.89(1.82,1.96)*	1.37(1.31,1.43)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	1.77(1.65,1.9)*	1.5(1.39,1.62)*	1.51(1.4,1.63)*	1.26(1.15,1.38)*
Q3	2.98(2.78,3.2)*	2.15(1.99,2.31)*	2.15(2,2.32)*	1.48(1.36,1.62)*
Q4	5.56(5.19,5.97)*	3.69(3.42,3.97)*	3.64(3.38,3.93)*	1.99(1.82,2.18)*
RC, mmol/L	17.31(15.71,19.07)*	8.96(8.12,9.89)*	8.51(7.71,9.4)*	3.74(3.35,4.17)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	1.28(1.2,1.38)*	1.27(1.18,1.36)*	1.26(1.17,1.36)*	1.15(1.05,1.25)*
Q3	2.36(2.21,2.52)*	1.97(1.84,2.11)*	1.96(1.83,2.1)*	1.56(1.44,1.7)*
Q4	7.92(7.4,8.48)*	5.25(4.88,5.65)*	5.06(4.7,5.44)*	2.89(2.65,3.16)*
TC/HDL-C	3.74(3.63,3.85)*	2.96(2.87,3.06)*	2.92(2.83,3.02)*	2(1.93,2.07)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	3.96(3.56,4.4)*	2.98(2.68,3.32)*	2.98(2.68,3.32)*	2.04(1.81,2.3)*
Q3	13.16(11.91,14.54)*	7.71(6.95,8.55)*	7.63(6.88,8.47)*	4.04(3.6,4.53)*
Q4	42.12(38.09,46.58)*	21.78(19.61,24.19)*	21.1(18.99,23.44)*	7.45(6.62,8.38)*

(*Continued*)

Table 3 (Continued).

Indicators	Unadjusted model OR(95% CI)	Adjusted Model 1 OR(95% CI)	Adjusted Model 2 OR(95% CI)	Adjusted Model 3 OR(95% CI)
TG/HDL-C	5(4.81,5.21)*	3.66(3.51,3.81)*	3.6(3.46,3.75)*	2.23(2.14,2.33)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	4.38(3.92,4.89)*	3.24(2.9,3.63)*	3.23(2.89,3.62)*	2.34(2.07,2.65)*
Q3	14.86(13.38,16.51)*	8.84(7.93,9.86)*	8.73(7.83,9.73)*	4.62(4.1,5.2)*
Q4	60.38(54.26,67.19)*	32.13(28.77,35.89)*	31.04(27.78,34.69)*	11.39(10.08,12.88)*
LDL-C /HDL-C	4.35(4.2,4.51)*	3.26(3.14,3.38)*	3.21(3.09,3.33)*	2.06(1.98,2.15)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	3.89(3.51,4.32)*	2.91(2.62,3.24)*	2.91(2.62,3.24)*	2.04(1.81,2.3)*
Q3	11.51(10.44,12.7)*	6.51(5.88,7.21)*	6.44(5.81,7.13)*	3.52(3.14,3.94)*
Q4	31.93(28.95,35.21)*	16.41(14.82,18.17)*	15.97(14.41,17.69)*	6.09(5.43,6.84)*
FPG/HDL-C	3.49(3.38,3.59)*	2.78(2.69,2.87)*	2.75(2.66,2.83)*	1.97(1.9,2.04)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	4.67(4.2,5.19)*	3.28(2.94,3.65)*	3.28(2.95,3.66)*	2.32(2.05,2.61)*
Q3	14.08(12.73,15.58)*	7.78(7.01,8.64)*	7.73(6.96,8.59)*	4.25(3.78,4.77)*
Q4	40.33(36.36,44.73)*	20.32(18.25,22.63)*	19.56(17.56,21.79)*	7.66(6.78,8.65)*
TyG	12.04(11.39,12.73)*	8.57(8.09,9.08)*	8.38(7.91,8.88)*	4.4(4.12,4.69)*
Q1	Ref.	Ref.	Ref.	Ref.
Q2	3.72(3.39,4.09)*	2.84(2.58,3.13)*	2.84(2.58,3.12)*	2.06(1.86,2.3)*
Q3	11.86(10.84,12.97)*	7.33(6.68,8.04)*	7.24(6.6,7.94)*	4.06(3.66,4.5)*
Q4	46.3(42.13,50.87)*	26.14(23.72,28.82)*	25.12(22.78,27.7)*	9.35(8.38,10.44)*

Note: *p value<0.01.

Abbreviations: Adjusted model 1, adjusted for age and sex; Model 2, further adjusted for history of smoking, alcohol, hypertension, diabetes, hyperlipidemia, and CKD; Model 3, further adjusted for physical exam or lab test indicators, including SBP, DBP, pulse rate, BMI, waist, eGFR, AST and ALT.

(OR=2.23), and LDL/HDL-c (OR=2.06). ROC curves indicated that TG/HDL had a better area under the curve (AUC) than TyG (Figure 1 and supplementary Table 1).

The association remained significant when analyzed categorically. Participants in the fourth quartile (Q4) showed significantly different risks of MASLD occurrence compared to those in the first quartile (Q1). Subgroup analysis confirmed these findings across varying metabolic risk factors (Table 3 and Supplementary Table 2).

Associations Between the Quantity of Lipid and Blood Glucose Risk Indicators and MASLD

The risk factors for each indicator were determined based on the Q4 group, while the Q1 group was employed for the analysis of HDL-C. Employing a comprehensively adjusted model, the ORs for each risk factor were computed and subsequently prioritized. Among the eleven indicators assessed, the five most significant risk factors identified were TG/HDL-C ≥ 1.44, TyG ≥ 8.8, TG ≥ 1.61, TC/HDL-C ≥ 4.41, and FPG/HDL-C ≥ 4.73, with corresponding ORs (95% confidence intervals) of 3.87(3.62,4.15), 3.78(3.51,4.07), 3.62(3.38,3.88), 2.83(2.65,3.03) and 2.71(2.53,2.91), respectively (see Figure 2).

The enumeration of the top five risk factors was performed. In comparison to participants without any risk factors, those with one, two, three, four, and five risk factors exhibited an increased risk of MASLD, with ORs and 95% CIs of 1.84 (1.67,2.02), 2.93(2.61,3.29), 3.69(3.29,4.13), 5.14(4.57,5.79) and 6.56(5.88,7.32), respectively. A significant positive correlation was identified between the number of risk factors and the level of risk (Figure 2). The results were additionally corroborated by the subgroup analysis detailed in Supplementary Table 3.

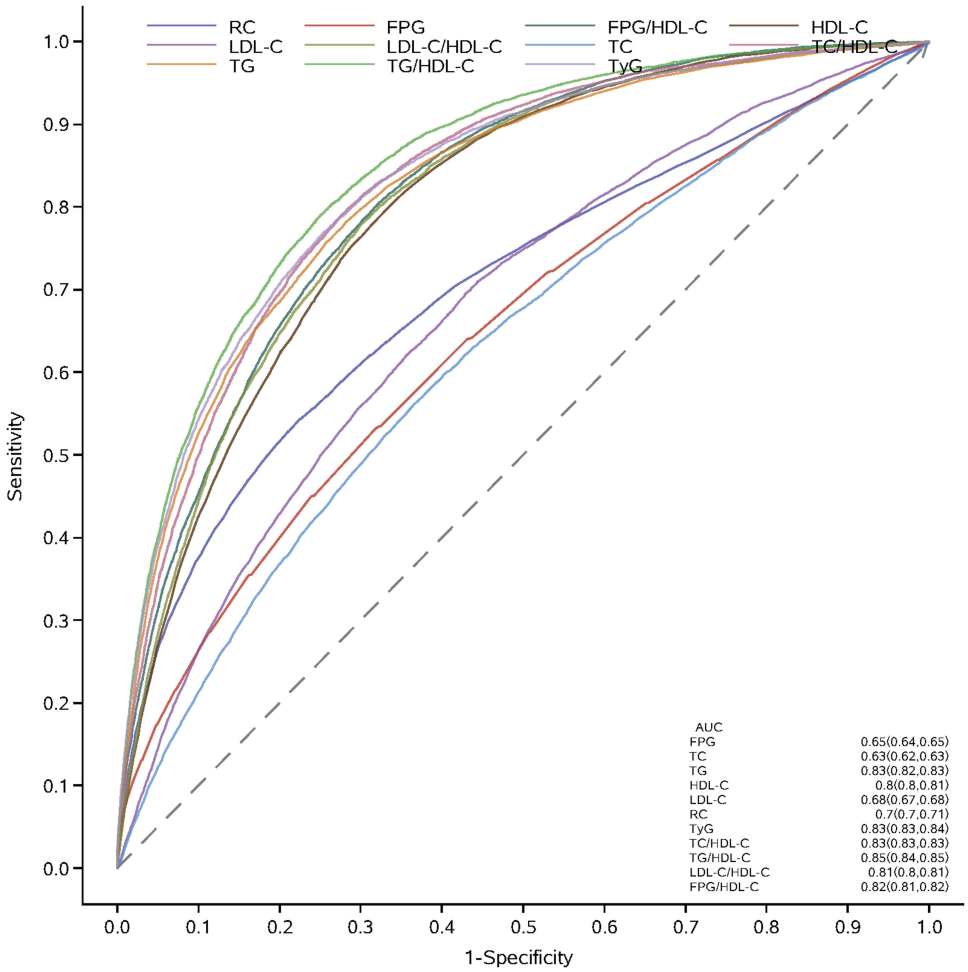

Figure 1 AUCs of blood lipid or glucose indices and MASLD.

Discussion

This investigation reveals important connections between metabolic markers and MASLD in younger individuals. Approximately one-fourth of participants in this age group showed evidence of MASH. Our analysis indicates that higher triglyceride concentrations, along with increased TyG index and TG/HDL-C values, maintain substantial links with MASLD presence after controlling for sex, age, and other metabolic variables. Notably, while the majority of young adults with MASLD had only 0–2 metabolic risk factors - consistent with the expected metabolic profile of this younger population - the strong predictive value of biochemical markers persisted, suggesting their particular relevance for early detection in younger cohorts.

This research has significant insights into the relationship between lipid and glucose profiles and MASLD in young adults. The findings highlight the significant role of insulin resistance, as measured by the TyG index, in the development of MASLD. Elevated TyG levels≥ 8.8 were strongly associated with MASLD, with an odds ratio of 3.78, indicating that individuals with higher TyG values are nearly five times more likely to develop MASLD compared to those with lower values. This finding aligns with previous studies that have demonstrated the TyG index as a reliable marker for insulin resistance and its strong correlation with metabolic disorders, including MASLD.[10,11,14] In a study conducted by Li et al[7] involving 632 participants, it was observed that individuals in the highest tertile of the TyG index (≥ 8.82) exhibited an odds ratio of 4.15 (95% CI: 2.28 to 7.53) when compared to those in the lowest tertile (TyG index < 8.29). It is important to note, however, that this study exclusively focused on patients with atrial fibrillation, and the overall sample size was relatively small. The relationship between the TyG index and MASLD may be attributed to insulin resistance, which can lead to oxidative stress, thereby promoting the proliferation of hepatic stellate cells and the activation of inflammatory

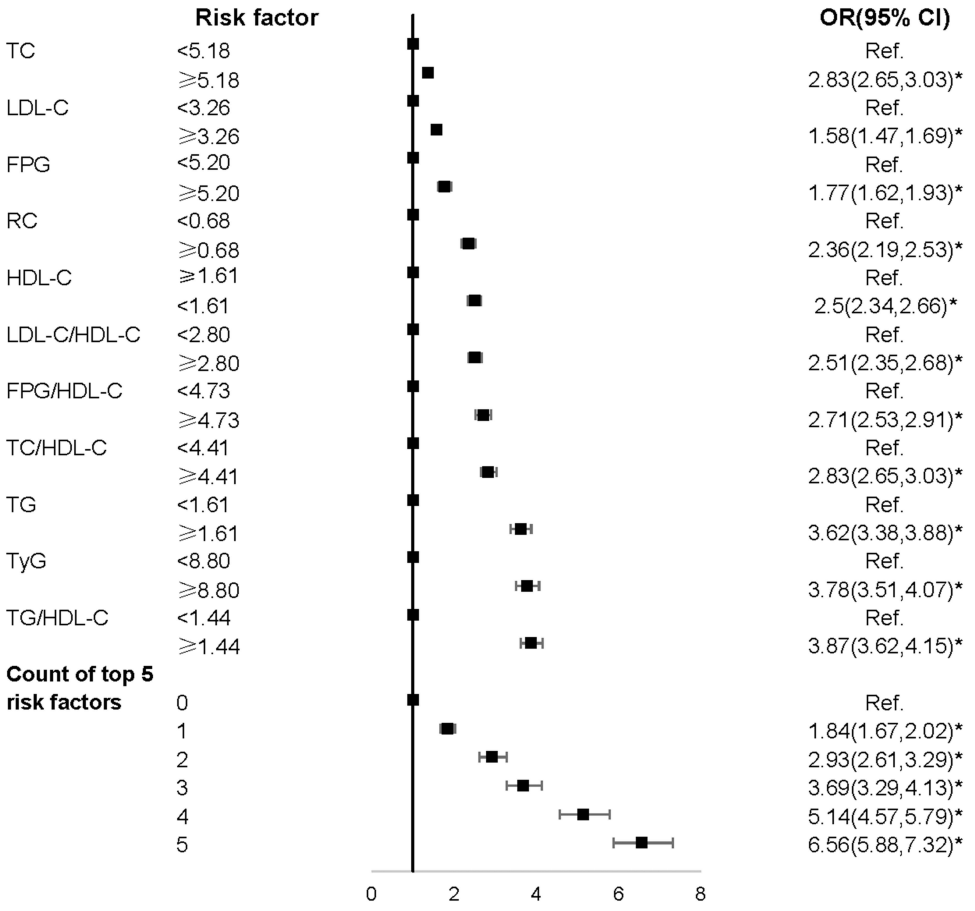

Figure 2 Association of each indicator, count of top 5 risk factors and MASLD.
Note: *p value<0.01.

liver macrophages, both of which contribute to the development of MASLD.[17] Furthermore, insulin resistance adversely affects insulin sensitivity and glucose metabolism in tissues, resulting in compromised liver function.[18]

The study also identified traditional lipid ratios, such as TG/HDL-C, as significant predictors of MASLD. The TG/HDL-C ratio exhibited a strong association with MASLD, suggesting that this indicator may be a useful tool for identifying individuals at risk for MASLD. The predictive performance of the TG/HDL-C ratio was comparable to that of the TyG index, with an area under the curve of 0.85, indicating its potential utility in clinical settings for early detection of MASLD. Notably, this association remained robust even in our young adult population where only 7% had ≥3 metabolic risk factors and 78% of MASLD cases presented with 0–2 risk factors - a finding that actually enhances the clinical relevance of lipid ratios. While Chen et al's previous study[19] in older cohorts (mean age 42.5 years) established similar relationships, our results uniquely demonstrate that TG/HDL-C maintains predictive value in younger adults with fewer metabolic abnormalities, suggesting its particular utility for early detection when traditional risk factors are often absent. The comprehensive adjustment for confounders and large sample size strengthen these findings, supporting TG/HDL-C's role in identifying at-risk young adults who would be missed by conventional risk assessment tools. This is clinically important because it provides a practical biomarker for detecting early metabolic dysfunction in populations where standard risk stratification would typically overlook MASLD risk. While traditional lipid profiles remain valuable, composite indices like TG/HDL-C offer more sensitive detection of emerging metabolic dysregulation in younger adults.

An important finding in the present study was the graded relationship between metabolic abnormality clustering and MASLD probability. Participants with multiple risk markers (elevated TyG, TG/HDL-C, and TG) faced substantially greater risk than those with fewer abnormalities. This cumulative effect underscores the importance of comprehensive metabolic profiling in identifying individuals at risk for MASLD.

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Subgroup analyses verified these associations persist across various metabolic groups, supporting biomarker reliability in diverse clinical scenarios. While liver biopsy remains the diagnostic reference, its invasive nature restricts practical use. Imaging alternatives like ultrasound and MRI were also costly and time-consuming.[18] Serum ALT demonstrates poor sensitivity, with four-fifths of imaging-confirmed MASLD cases showing normal levels.[20–22] These limitations underscore the need for better detection methods. Although MASLD research has expanded, biomarker comparisons in younger demographics remain scarce. Our work addresses this gap by evaluating multiple indicators in this vulnerable young group. The results could improve early identification and preventive approaches.

Despite the previous research on the risk factors of MASLD, comparative analyses of metabolic biomarkers, particularly in young adults, remain limited. Young adults represent a unique population, as they are often overlooked in metabolic studies despite being at risk for early-onset metabolic disorders. Understanding the relationship between lipid and glucose profiles and MASLD in this demographic is crucial for early detection and intervention. This study revealed the association between various lipid and glucose indicators, including traditional lipid ratios and composite indices including TG/HDL-C, TyG, and TG with MASLD in young adults. This study results could help to improve early detection and prevention strategies for MASLD in this at-risk population by identifying the most predictive biomarkers.

Several limitations should be acknowledged. First, the cross-sectional study design limits our ability to establish a causal relationship between metabolic markers and MASLD. Longitudinal studies are needed to confirm these associations and assess the predictive value of these biomarkers over time. Second, the reliance on self-reported alcohol consumption may introduce bias, as underreporting of alcohol intake could lead to misclassification of MASLD cases. Finally, the study cohort was sourced from a single health facility in China, which may restrict the applicability of our results to other demographic groups.

In conclusion, our findings emphasize metabolic profiling's value for MASLD detection in young adults. The TyG index and TG/HDL-C ratio show particular promise as clinical tools. The risk gradient observed with accumulating metabolic disturbances reinforces comprehensive screening importance. Future investigations should pursue longitudinal validation and examine whether these markers can guide effective prevention strategies.

Data Sharing Statement

The data are not publicly available yet due to ethical, privacy and security concerns. Please contact the corresponding author to seek approval for data access.

Author Contributions

Wenjing Xiao and Xinghe Sun are co-first authors. All authors made a significant contribution to the work reported. Jihong Zhu and Xiaohui Liu took responsibility in the conceptualization, study methodology and administration. Wenjing Xiao and Xinghe Sun took responsibility in investigation, data curation, formal analysis and validation, visualization and interpretation. Hui Lv took responsibility in investigation and data curation. All authors contributed to writing – original draft and writing – review and editing the article; have agreed on the journal to which the article will be submitted; reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication; and agree to take responsibility and be accountable for the contents of the article.

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Disclosure

The authors declare that they have no competing interests.

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