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Does Adding Anthropometry Improve the Triglyceride-Glucose Index?

Comparing TyG-Based Indices for Probable MASLD Prediction

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Running title: Triglyceride-Glucose Index and TyG-Based Indices for Probable MASLD Prediction

Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a major cause of chronic liver disease. Simple and affordable surrogates of insulin resistance may aid in identifying at-risk individuals. In this study, we examined the association between the triglyceride-glucose (TyG) index and TyG-based anthropometric composites (TyG-BMI, TyG-WC, and TyG-WHtR) and development of probable MASLD after 10 years. We set up the main outcome based on the Hepatic Steatosis Index (HSI>36) and sensitivity outcome based on the Fatty Liver Index (FLI≥60). During the follow-up of 10 years, probable MASLD developed in 53.9% of participants based on HSI and 37.5% based on FLI. Each 1-SD increment of TyG independently raised the risk of developing probable MASLD. Moreover, the third tertile of TyG was also associated with elevated odds of probable MASLD compared to the first tertile (OR=1.60 for HSI and OR=2.20 for FLI). Discrimination capacity of TyG alone was modest (AUC=0.59 for HSI and AUC=0.68 for FLI), while composite indices showed larger AUC (0.73 to 0.84 for HSI and 0.79 to 0.85 for FLI), the highest for TyG-BMI. However, since BMI and WC are included in HSI and FLI, adjusting for the related anthropometric variable substantially reduced the associations of the composite indices.

Keywords: TyG index; MASLD; HIS; FLI; TyG-BMI; MASHAD cohort

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously termed Non-alcoholic fatty liver disease (NAFLD), is one of the most common chronic liver diseases worldwide and affects more than 25% of adults (1). MASLD is characterized by excessive fat accumulation in hepatocytes without significant alcohol consumption or other secondary causes of hepatic steatosis. MASLD ranges from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH) and can progress to hepatic fibrosis, cirrhosis, and hepatocellular carcinoma (2, 3). The growing prevalence of MASLD commonly parallels the global burden of obesity, dyslipidemia, type 2 diabetes mellitus, hypertension, and metabolic syndrome and is associated with an increased burden of cardiovascular and other metabolic diseases (4, 5).

Insulin resistance plays a central role in the pathogenesis of hepatic steatosis. Impaired insulin signaling increases adipose tissue lipolysis and free fatty acid delivery to the liver while disrupting glucose and lipid metabolism (6). These metabolic abnormalities promote hepatic triglyceride accumulation and may contribute to hepatic inflammation and disease progression (4). Therefore, simple surrogate markers of insulin resistance may help identify individuals with an adverse metabolic profile and a higher likelihood of hepatic steatosis, particularly in large population-based studies.

Triglyceride glucose index (TyG index), which can be easily measured by triglycerides and glucose levels, is a practical surrogate indicator for insulin resistance (7). Both previous studies and systematic reviews have shown that high TyG index value is positively correlated with MASLD (8, 9). Nevertheless, heterogeneity in the results still exists, and there are many studies concentrated on cross-sectional data.

Assessment of MASLD in large cohort studies is challenging because liver biopsy and advanced imaging are not always feasible. The Hepatic Steatosis Index (HSI) and Fatty Liver Index (FLI) provide non-invasive approaches based on routinely collected anthropometric and biochemical variables and have been widely used for epidemiological assessment of hepatic steatosis (10, 11). Both are surrogate definitions rather than direct diagnostic tests, and their performance may vary across populations.

In addition to TyG alone, the combination of TyG with other measurements of adiposity might provide additional information on insulin resistance and body fat distribution. The TyG-BMI, TyG-WC, and TyG-WHtR indices consist of the TyG index and body mass index, waist circumference, and waist-to-height ratio, respectively, which were investigated as combined metabolic parameters previously (12-14).

In this study, we first evaluated the association between baseline TyG and subsequent probable MASLD in the MASHAD cohort. We then examined three TyG-based composite anthropometric indices (TyG-BMI, TyG-WC, and TyG-WHtR) using the same outcome definitions and assessed whether their associations persisted after adjustment for the corresponding anthropometric component.

Result

Baseline characteristics across TyG tertiles

The study population was divided into tertiles of baseline TyG: T1 (TyG ≤8.25, n=2,512), T2 (TyG >8.25 to ≤8.77, n=2,505), and T3 (TyG >8.77, n=2,508) (Table 1). Participants in higher TyG

tertiles were older and had higher BMI, WC, hip circumference, fasting glucose, triglycerides, and total cholesterol, together with lower HDL-C (all $p<0.001$). The prevalence of diabetes, hypertension, and metabolic syndrome also increased across TyG tertiles (all $p<0.001$), confirming that TyG tertile grouping captured a coherent gradient of metabolic risk. Physical activity scores decreased across increasing TyG tertiles ($p<0.001$), while education level did not differ significantly across groups ($p=0.19$).

ROC analysis

Baseline TyG Index distinguished probable MASLD with fair discrimination for the HSI definition (AUC=0.592, n=7,251) and good discrimination for the FLI definition (AUC=0.679, n=7,172) (Table 2, Figure 2). The Youden optimal TyG threshold value for HSI-defined probable MASLD was 8.34 with 68.0% sensitivity and 46.6% specificity, and for FLI-defined probable MASLD was 8.50 with 67.8% sensitivity and 59.4% specificity.

Multivariable logistic regression (continuous and tertile TyG)

The baseline TyG index was independently associated with probable MASLD using both criteria in the three regression models (Table 3). Using the primary criterion (HSI>36), each SD increment in the TyG index predicted 38% higher odds of probable MASLD before adjusting for other variables (OR=1.38, 95%CI 1.32-1.45, P<0.001), 55% higher odds in the second model (OR=1.55, 95%CI 1.47-1.63, P<0.001), and 33% higher odds in the fully adjusted third model (OR=1.33, 95%CI 1.23-1.43, P<0.001). In the tertile analysis, there was a linear dose-response relationship between the TyG index and probable MASLD (P for trend, Model 3: OR=1.27 per tertile, 95%CI 1.16-1.38, P<0.001), where individuals in the third tertile had 60% higher odds of probable MASLD compared to those in the first tertile (T3 vs. T1, Model 3: OR=1.60, 95%CI 1.35-1.89,

P<0.001), while the second tertile was also statistically different from the reference group (T2 vs. T1: OR=1.32, 95%CI 1.16-1.52, P<0.001).

Similar results were obtained from the sensitivity analysis conducted with the FLI definition (FLI≥60). Every SD rise in TyG index was significantly linked to increased odds ratio of 88% in unadjusted models (OR=1.88, 95% CI 1.78-1.99, p<0.001), 94% in age/sex adjusted models (OR=1.94, 95% CI 1.83-2.05, p<0.001), and 42% in fully adjusted models (Model 3: OR=1.42, 95% CI 1.31-1.53, p<0.001). The tertile analysis also revealed a highly statistically significant relationship (Model 3: OR=1.47 per tertile, 95% CI 1.35-1.60, p<0.001), with the highest tertile being at least two times more likely than the reference category (T3 vs. T1: OR=2.20, 95% CI 1.85-2.62, p=p<0.001).

Restricted cubic spline (linearity test)

The dose response curve between TyG and probability of MASLD, based on HSI, was approximately linear on logit scale (P-value for non-linearity=0.054), whereas sensitivity analysis (FLI) gave statistically significant evidence against linearity (P-value for non-linearity<0.001) and indicated an increase in the probability curve till middle TyG values followed by flattening thereafter (Table 3 and Figure 4).

Composite TyG-anthropometric indices

Next, we assessed the discriminatory performance of TyG-BMI, TyG-WC, and TyG-WHtR as combined measures of probable MASLD (Table 4, Figure 5). TyG-BMI, TyG-WC, and TyG-WHtR all had better discrimination than TyG in predicting the two outcomes studied. In terms of HSI-defined probable MASLD, the AUCs were 0.837 for TyG-BMI, 0.734 for TyG-WC, and

0.764 for TyG-WHtR, whereas that of TyG was 0.591. For probable MASLD defined by the FLI, the AUCs were 0.849, 0.801, and 0.787, compared with 0.679 for TyG.

The greater appearance of discrimination of the composite indices must be considered with caution since the anthropometric indicators used are included in the definitions of the outcomes themselves. Specifically, BMI is a component of HSI, and BMI and WC are components of FLI. Therefore, we conducted regression and decomposition analyses controlling for the relevant anthropometric indicators.

In the multivariable analysis, the indices had a greater association with probable MASLD compared to TyG index alone. For probable MASLD by HSI, the ORs were 6.64 for TyG-BMI, 3.30 for TyG-WC, and 3.59 for TyG-WHtR, versus 1.55 for TyG. In FLI-based probable MASLD, the ORs were 6.92 for TyG-BMI, 4.21 for TyG-WC, and 4.39 for TyG-WHtR, versus 1.93 for TyG. These OR values were computed per 1-SD change and should not be compared directly due to their differences in units of measure (Table 5).

In all three models, the relationships between the composite scores remained statistically significant. For HSI-defined probable MASLD in Model 3, the ORs for TyG-BMI, TyG-WC, and TyG-WHtR were 8.73, 3.05, and 3.41, respectively; for the FLI-defined endpoint, the ORs for these scores were 6.51, 3.44, and 3.58, respectively (all $p<0.001$). Nevertheless, despite the statistical significance of these relationships in the presence of confounders, one cannot claim their biological independence since there is a lot of overlap between the composite scores and the surrogate endpoints (Table 6).

In the supplementary RCS analysis, the composite indices generally showed non-linear relationships with probable MASLD, particularly for the FLI-based definition, where all four

predictors showed evidence of non-linearity (P<0.001 to P=0.022). For the HSI-based outcome, the composite indices showed weaker evidence of non-linearity (TyG-BMI P=0.082; TyG-WHtR P=0.149; TyG-WC P=0.871). Because the supplementary RCS result reported for TyG with the HSI outcome differs from the primary RCS result in Table 3, the corresponding model output should be reconciled before submission (Figure 6).

Given the substantial formula-level overlap between the composite indices and the MASLD outcome definitions, a decomposition analysis was conducted to determine whether TyG-BMI, TyG-WC, and TyG-WHtR provided predictive information beyond their embedded anthropometric components (BMI, waist circumference, and WHtR, respectively) alone. Each composite index was modeled together with its corresponding raw anthropometric measure in the same adjusted (age, sex, smoking, follow-up duration) logistic regression model.

In cases of HSI-probable MASLD, adjusting for BMI reduced the OR for TyG-BMI from 6.64 to 1.40 (95% CI 1.18–1.67) and maintained a strong relationship between BMI and the outcome (OR=6.34; p<0.001). In cases of FLI-probable MASLD, adjustment for BMI reduced the OR for TyG-BMI from 6.92 to 3.82 (95% CI 3.22-4.53) and kept a strong relationship between BMI and the outcome (OR=1.97; p<0.001). The same pattern was obtained for TyG-WC adjusted for WC (OR=1.58 for HSI and 2.85 for FLI) and TyG-WHtR adjusted for WHtR (OR=1.65 for HSI and 3.09 for FLI) (Table 7).

Therefore, the composite indices remained significantly associated even after adjusting for their respective anthropometric measures; however, the high degree of attenuation suggests that the relatively high unadjusted odds ratios of the composite indices contain information that is also present in the anthropometric variables themselves. This suggests that one must be very careful when interpreting any additional effect of the composite indices.

Discussion

In this large prospective cohort, we found that a higher baseline TyG index was associated with increased risk of MASLD during follow-up. This association remained significant after adjustment for several demographic, lifestyle, clinical, and lipid-related factors. We also found a nonlinear association between TyG and MASLD, with a more rapid increase in risk over part of the TyG range and a tendency toward plateau at higher values. These findings suggest that TyG could be a simple marker for identifying individuals at higher risk of developing MASLD, particularly because it can be calculated from routinely available fasting glucose and triglyceride measurements.

There is a growing body of evidence supporting the association between TyG and MASLD (15). Insulin resistance, being appropriately reflected by TyG, has an important role in the development of hepatic steatosis through increased adipose tissue lipolysis, increased delivery of free fatty acids to the liver, increased hepatic de novo lipogenesis, and impaired lipid metabolism (16-18). Previous studies have reported a positive association between higher TyG and MASLD. In a meta-analysis including 17 observational studies and 121,975 participants, higher TyG was associated with increased risk of MASLD, with a pooled HR of 1.70 and an OR of 6.00 when TyG was analyzed as a categorical variable, and a pooled OR of 2.25 when analyzed as a continuous variable (9). Another dose-response meta-analysis including 12 studies and 105,365 participants also demonstrated a positive association between TyG and MASLD (19). In a prospective cohort of 2,056 Chinese participants, higher baseline TyG was independently associated with incident MASLD during a mean follow-up of 2.5 years, with an adjusted HR of 1.78 for each unit increase in TyG (20). These findings are consistent with our results (association of TyG with probable

MASLD with OR of 1.33 and 1.42 for HIS and FLI assessments, respectively) and support the prospective association between higher TyG and development of MASLD.

More recent prospective studies have further supported these findings. Gao et al. evaluated 10,703 rural residents in northwest China and found that higher TyG was associated with increased risk of incident MAFLD during 5.7 years of follow-up (21). They also evaluated TyG-BMI, TyG-WC, and TyG-WHtR and found significant associations between all four indices and MAFLD, with nonlinear relationships for most of the indices (21). Similarly, Song et al. investigated 25,366 participants free of MASLD at baseline and found that higher TyG and anthropometric TyG indices were associated with increased risk of incident MASLD (22). In their study, TyG-BMI showed the strongest predictive performance among the evaluated indices (22). These findings are particularly consistent with our results, as we also found significant associations of TyG and all three anthropometric TyG indices with subsequent MASLD. However, our study adds to these findings by evaluating TyG using both HSI and FLI, examining the association using different surrogate indices, and specifically evaluating the contribution of the anthropometric components to the performance of the composite indices.

The nonlinear association observed in our study is also of interest. In the cohort study by Zhang et al., the association between TyG and MAFLD was linear in men, while a nonlinear association was observed among women (20). In contrast, the dose-response meta-analysis by Ling et al. reported an overall linear association between TyG and MASLD (23). More recently, Gao et al. reported nonlinear relationships between most TyG-related indices and MAFLD, although the pattern differed according to sex and index (21). Our findings provide further prospective evidence that the association between TyG and fatty liver may not be constant across the whole range of TyG values. The observed plateau at higher TyG levels may suggest that after a certain degree of

metabolic dysfunction, further increases in TyG provide less additional information regarding hepatic steatosis. The clinical significance of this pattern, however, requires further investigation in studies using direct assessment of liver tissue or imaging studies.

The clinical importance of these findings is related to the simplicity and availability of the TyG index. Although TyG alone showed only modest discrimination, particularly when HSI was used to define MASLD, it has significant association with future MASLD. This is particularly relevant in primary prevention, where identification of metabolic abnormalities before development of clinically apparent liver disease provides an opportunity for lifestyle modification and management of associated cardiometabolic risk factors.

We also found that adding anthropometric measures to TyG including TyG-BMI, TyG-WC, and TyG-WHtR substantially improved its discrimination for MASLD, although with a caveat. The association of these indices with MASLD is consistent with the important contribution of obesity and particularly central adiposity to insulin resistance and hepatic fat accumulation. This finding agrees with the recent prospective studies by Gao et al. and Song et al., in which anthropometric TyG indices were more strongly associated with fatty liver than TyG alone (21, 22). In our study, however, the higher performance of these composite indices should be interpreted in the context of their components, as BMI is included in HSI, while BMI and waist circumference are included in FLI. The attenuation observed after adjustment for the corresponding anthropometric component indicates that part of the apparent improvement is related to overlap between the predictor and outcome definitions.

The main limitation of this study is that MASLD was not directly assessed by liver imaging or histopathology. Other limitations was the possibility of residual confounding despite adjustment for several established risk factors.

The large number of participants and prospective design are important strengths of the present investigation. In addition, using both HSI and FLI allowed us to examine the consistency of the association using two different non-invasive definitions of hepatic steatosis. The assessment of TyG as a continuous variable, its tertiles, and its nonlinear relationship with MASLD also provided a more comprehensive assessment of the association.

Conclusion

Overall, our findings indicate that higher baseline TyG is associated with increased long-term risk of MASLD. TyG is inexpensive, easily calculated from routinely available laboratory measurements, and may provide a simple approach for identifying individuals with an adverse metabolic profile and increased risk of MASLD. The addition of anthropometric measures further improves discrimination, although part of this improvement is related to overlap between the components of these indices and the outcome definitions. Future prospective studies using imaging-based assessment of hepatic steatosis could determine whether TyG improves risk stratification beyond conventional metabolic risk factors and could further clarify its role in the early identification and prevention of MASLD.

Method

Study design

Participants were drawn from the Mashhad Stroke and Heart Atherosclerotic Disorders (MASHAD) prospective cohort. Detailed information on the MASHAD study design and

recruitment has been reported previously (24). We recruited subjects who had complete fasting triglycerides and glucose data for the determination of TyG index, no suspected MASLD (HSI ≤36 or FLI <60), and complete data for phase 2 to compute HSI and/or FLI. Subjects who had suspected MASLD at baseline (HSI >36 or FLI ≥60), had any other known liver disease, consumed significant amounts of alcohol, used steatogenic drugs, pregnant women, those without laboratory data, or incomplete follow-up data were excluded from the analysis. This study examined the relationship between baseline TyG and anthropometric parameters and suspected MASLD at follow-up (Figure 1).

The study protocol was approved by the Ethics Committee of the Mashhad University of Medical Sciences (MUMS) and the International Review Board of Mashhad University Medical Center. All participants provided written informed consent.

In the base line examination, the interviews, physical examination and laboratory analysis were done by health professionals who were trained for the purpose. The sociodemographic data was taken in form of standardized questionnaire and included age, gender, marital status, occupation and educational level of the patients. The lifestyle data included smoking and physical activity. The medical history was also taken (24).

Measurements and laboratory data

After removal of heavy outer clothing and footwear, height was measured to the nearest 0.1 cm in the standing position using a stadiometer. Body weight was measured to the nearest 0.1 kg using a digital balance. Waist circumference (WC) was measured with a flexible tape at the midpoint between the lowest rib margin and the iliac crest. Hip circumference was measured at the maximum circumference of the buttocks.

Blood samples from the vein of the arm were drawn after fasting overnight in accordance with standard procedures. Triglycerides, total cholesterol and HDL-C were determined by an automatic analyzer. LDL-C levels were determined using the Friedewald formula (25): LDL-C = TC − HDL-C − (TG / 5), where all concentrations are in mg/dL (only applicable when TG concentration is < 400 mg/dL). The level of high-sensitivity C-reactive protein and uric acid was also determined. The TyG index was calculated based on fasting levels of triglycerides and glucose as follows (26):

TyG = ln[fasting TG (mg/dL) × fasting glucose (mg/dL) / 2]

BMI was calculated as weight in kilograms divided by height in meters squared. WHR was calculated as WC divided by hip circumference, and WHtR as WC divided by height. For the composite analyses, TyG-BMI, TyG-WC, and TyG-WHtR were calculated as TyG multiplied by BMI, WC, and WHtR, respectively.

Outcome definitions and follow-up

Participants were reassessed after a follow-up period of 10 years, and the present analysis used Phase 2 measurements to define probable MASLD. The primary outcome was probable MASLD defined by the hepatic steatosis index (HSI) > 36 (10),

HSI = 8 × (ALT/AST) + BMI (+2 if female; +2 if diabetes mellitus).

The sensitivity outcome was probable MASLD defined by the fatty liver index (FLI) ≥ 60 (11),

FLI = [e^y / (1 + e^y)] × 100 and y = 0.953 × ln(TG) + 0.139 × BMI + 0.718 × ln(GGT) + 0.053 × waist circumference − 15.745 (TG in mg/dL, GGT in U/L, waist in cm, BMI in kg/m²).

Because these definitions were based on non-invasive surrogate indices rather than liver imaging or histopathology, the outcome is referred to throughout the manuscript as probable MASLD.

Statistical analysis

The primary exposure was baseline (Phase 1) TyG, analyzed as a continuous variable per 1-SD increase and as cohort-derived tertiles. The three composite indices, TyG-BMI, TyG-WC, and TyG-WHtR, were subsequently evaluated as continuous variables per 1-SD increase.

The primary outcome was probable MASLD at Phase 2, defined as HSI >36.

The sensitivity outcome was probable MASLD at Phase 2, defined as FLI ≥60.

For TyG alone, three logistic regression models were fitted: Model 1 was unadjusted; Model 2 was adjusted for age and sex; and Model 3 was the main multivariable model, adjusted for age, sex, smoking status, physical activity level, education level, hypertension, LDL-C, HDL-C, total cholesterol, and eGFR (CKD-EPI).

BMI and diabetes status were not included in the primary models because BMI is incorporated into HSI and diabetes is closely related to the outcome definition; avoiding these variables was intended to reduce overadjustment and adjustment artifacts. The same covariate framework was applied to the composite-index analyses.

ROC curves were generated for TyG and each composite index, and the Youden J statistic was used to identify the optimal cutoff. Restricted cubic spline models using Harrell's basis with four knots at the 5th, 35th, 65th, and 95th percentiles were used to assess the shape of the association between each index and probable MASLD. For the composite indices, a decomposition analysis additionally modeled each composite index together with its corresponding anthropometric

component (BMI, WC, or WHtR) to assess whether the association persisted beyond the embedded anthropometric measure.

Statements and Declarations

Ethics approval and consent to participate

A written informed consent form was signed by each participant in order to take part in the study. The Mashhad University of Medical Sciences Ethics Committee reviewed the study protocol and approved all methods. All techniques were used in accordance with the applicable regulations and rules.

Consent for publication

Each participant signed a written informed consent form to participate in the study. Additionally, this manuscript does not have consent for image publication. The figures presented in this manuscript were created with the purpose of illustrating the findings of the current study.

Data Availability Statement

The corresponding author can provide the datasets used and/or analyzed in this study upon reasonable request.

Competing interests

The authors declare no conflict of interest.

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Author contributions

Aida Yavari Kondori: Methodology, Supervision, Writing Original Draft, review & editing; Funding Acquisition; Seyed Reza Moallem: Conceptualization, Writing Original Draft, review & editing; Majid Ghayour-Mobarhan: Funding Acquisition, Data Curation; Habibollah Esmaily: Formal Analysis, Data Curation; Mohsen Mouhebati: Investigation, Supervision, Funding Acquisition; Susan Darroudi: Investigation, Formal Analysis, Writing – review & editing;

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Table 1. Baseline Demographic, Anthropometric, and Metabolic Characteristics by TyG Tertile

Characteristic		T1 (<8.25)	T2 (8.25-8.77)	T3 (>8.77)	p-value
N		2512	2505	2508	
— Demographic —					
Age (years)		45.8 ± 7.9	47.6 ± 7.9	49.2 ± 7.8	<0.001
Female sex, n (%)		1581 (62.9%)	1525 (60.9%)	1417 (56.5%)	<0.001
Education level	Low	1289 (51.4%)	1340 (53.5%)	1350 (53.8%)	0.19
	Moderate	925 (36.9%)	891 (35.6%)	855 (34.1%)	
	High	295 (11.8%)	272 (10.9%)	302 (12.0%)	
Smoking status	Never	1807 (71.9%)	1755 (70.1%)	1740 (69.4%)	0.01
	Former	194 (7.7%)	239 (9.5%)	267 (10.6%)	
	Current	511 (20.3%)	511 (20.4%)	501 (20.0%)	
Physical activity level (PAL score)		1.66 ± 0.28	1.59 ± 0.28	1.54 ± 0.28	<0.001
— Anthropometric —					
BMI (kg/m²)		26.3 ± 4.6	28.2 ± 4.5	29.1 ± 4.4	<0.001
Waist circumference (cm)		90.7 ± 11.6	95.9 ± 11.7	98.5 ± 11.0	<0.001
Hip circumference (cm)		101.6 ± 8.9	104.4 ± 9.1	105.0 ± 9.1	<0.001
— Metabolic —					
Fasting glucose (mg/dL)		77.0 ± 11.2	83.6 ± 15.1	112.8 ± 54.5	<0.001
Triglycerides (mg/dL)		73.6 ± 18.6	123.4 ± 24.5	224.8 ± 109.6	<0.001
Total cholesterol (mg/dL)		173.5 ± 31.8	191.7 ± 34.6	207.2 ± 41.0	<0.001
HDL-C (mg/dL)		45.6 ± 10.2	42.7 ± 9.3	40.2 ± 9.2	<0.001
LDL-C (mg/dL)		110.6 ± 29.0	120.1 ± 33.4	118.7 ± 41.0	<0.001
Diabetes, n (%)		67 (2.7%)	159 (6.4%)	726 (29.2%)	<0.001
Hypertension, n (%)		466 (18.6%)	767 (30.7%)	1002 (40.1%)	<0.001
Metabolic syndrome, n (%)		274 (10.9%)	732 (29.2%)	1828 (72.9%)	<0.001

Continuous variables are reported as mean ± SD and compared across tertiles using the one-way ANOVA test; categorical variables are reported as n (%) and compared using the Chi-square test. TyG tertile boundaries: T1 (low) TyG ≤ 8.26; T2 (mid) 8.26 < TyG ≤ 8.78; T3 (high) TyG > 8.78.

Table 2. ROC analysis: baseline TyG index predicting probable MASLD

Outcome	n	AUC	Optimal TyG cutoff (Youden)	Sensitivity	Specificity
HSI>36 (primary)	7251	0.592	8.34	68.0%	46.6%
FLI>=60 (sensitivity)	7172	0.679	8.50	67.8%	59.4%

Table 3. Restricted cubic spline: test of non-linearity (Model 3 adjustment)

Outcome	P-nonlinearity (LR test, Model 3 adjustment)	Interpretation
HSI>36 (primary)	0.05	Approximately linear (borderline)
FLI>=60 (sensitivity)	<0.001	Significant non-linearity

Table 4. ROC analysis: TyG and composite indices predicting probable MASLD

Outcome	Predictor	AUC	95% CI (bootstrap)	Optimal Cutoff (Youden)
Probable MASLD (HSI>36)	TyG	0.591	0.579-0.605	8.34
Probable MASLD (HSI>36)	TyG-BMI	0.837	0.828-0.845	234.16
Probable MASLD (HSI>36)	TyG-WC	0.734	0.723-0.744	806.18
Probable MASLD (HSI>36)	TyG-WHtR	0.764	0.753-0.775	4.97
Probable MASLD (FLI≥60)	TyG	0.679	0.668-0.690	8.50
Probable MASLD (FLI≥60)	TyG-BMI	0.849	0.841-0.859	245.84
Probable MASLD (FLI≥60)	TyG-WC	0.801	0.791-0.812	840.52
Probable MASLD (FLI≥60)	TyG-WHtR	0.787	0.777-0.798	5.05

Table 5. Adjusted logistic regression (continuous, per 1-SD): TyG and composite indices predicting probable MASLD

Predictor	Outcome	n	Events	OR	95% CI	p-value
TyG	Probable MASLD (HSI>36)	7193	3868	1.55	1.47-1.63	<0.001
TyG-BMI	Probable MASLD (HSI>36)	7183	3864	6.64	6.04-7.29	<0.001
TyG-WC	Probable MASLD (HSI>36)	7187	3866	3.30	3.08-3.55	<0.001
TyG-WHtR	Probable MASLD (HSI>36)	7184	3865	3.59	3.34-3.87	<0.001
TyG	Probable MASLD (FLI≥60)	7117	2662	1.93	1.83-2.04	<0.001
TyG-BMI	Probable MASLD (FLI≥60)	7107	2659	6.92	6.29-7.60	<0.001
TyG-WC	Probable MASLD (FLI≥60)	7111	2660	4.21	3.90-4.55	<0.001
TyG-WHtR	Probable MASLD (FLI≥60)	7108	2659	4.39	4.05-4.75	<0.001

Table 6. Three-model adjusted logistic regression: TyG and composite indices predicting probable MASLD

Predictor	Outcome	Model	n	Events	OR	95% CI	p-value
TyG	Probable MASLD (HSI>36)	Model 1 (unadjusted)	7251	3910	1.38	1.32-1.45	<0.001
TyG	Probable MASLD (HSI>36)	Model 2 (+age,sex)	7251	3910	1.55	1.47-1.63	<0.001
TyG	Probable MASLD (HSI>36)	Model 3 (fully adjusted)	7251	3910	1.33	1.23-1.43	<0.001
TyG	Probable MASLD (FLI≥60)	Model 1 (unadjusted)	7172	2688	1.88	1.78-1.99	<0.001
TyG	Probable MASLD (FLI≥60)	Model 2 (+age,sex)	7172	2688	1.94	1.83-2.05	<0.001
TyG	Probable MASLD (FLI≥60)	Model 3 (fully adjusted)	7172	2688	1.42	1.31-1.53	<0.001
TyG-BMI	Probable MASLD (HSI>36)	Model 1 (unadjusted)	7250	3910	5.80	5.32-6.31	<0.001
TyG-BMI	Probable MASLD (HSI>36)	Model 2 (+age,sex)	7250	3910	6.63	6.03-7.28	<0.001
TyG-BMI	Probable MASLD (HSI>36)	Model 3 (fully adjusted)	7250	3910	8.73	7.77-9.82	<0.001
TyG-BMI	Probable MASLD (FLI≥60)	Model 1 (unadjusted)	7171	2688	6.18	5.65-6.76	<0.001
TyG-BMI	Probable MASLD (FLI≥60)	Model 2 (+age,sex)	7171	2688	6.89	6.27-7.57	<0.001
TyG-BMI	Probable MASLD (FLI≥60)	Model 3 (fully adjusted)	7171	2688	6.51	5.86-7.25	<0.001
TyG-WC	Probable MASLD (HSI>36)	Model 1 (unadjusted)	7251	3910	2.69	2.53-2.86	<0.001
TyG-WC	Probable MASLD (HSI>36)	Model 2 (+age,sex)	7251	3910	3.29	3.06-3.52	<0.001
TyG-WC	Probable MASLD (HSI>36)	Model 3 (fully adjusted)	7251	3910	3.05	2.80-3.31	<0.001
TyG-WC	Probable MASLD (FLI≥60)	Model 1 (unadjusted)	7172	2688	3.95	3.67-4.25	<0.001
TyG-WC	Probable MASLD (FLI≥60)	Model 2 (+age,sex)	7172	2688	4.21	3.90-4.55	<0.001
TyG-WC	Probable MASLD (FLI≥60)	Model 3 (fully adjusted)	7172	2688	3.44	3.15-3.75	<0.001
TyG-WHtR	Probable MASLD (HSI>36)	Model 1 (unadjusted)	7250	3910	3.24	3.04-3.47	<0.001
TyG-WHtR	Probable MASLD (HSI>36)	Model 2 (+age,sex)	7250	3910	3.57	3.32-3.85	<0.001
TyG-WHtR	Probable MASLD (HSI>36)	Model 3 (fully adjusted)	7250	3910	3.41	3.13-3.72	<0.001
TyG-WHtR	Probable MASLD (FLI≥60)	Model 1 (unadjusted)	7171	2688	3.54	3.31-3.80	<0.001
TyG-WHtR	Probable MASLD (FLI≥60)	Model 2 (+age,sex)	7171	2688	4.39	4.05-4.75	<0.001
TyG-WHtR	Probable MASLD (FLI≥60)	Model 3 (fully adjusted)	7171	2688	3.58	3.28-3.92	<0.001

Table 7. Decomposition analysis: composite index association before and after adjustment for its embedded anthropometric component

Composite Index	Outcome	Anthropometric Component	n	OR, composite alone	p	OR, composite (adjusted for component)	p	OR, component (adjusted for composite)	p
TyG-BMI	HSI>36	BMI	7183	6.64	<0.001	1.40 (1.18-1.67)	<0.001	6.34	<0.001
TyG-BMI	FLI≥60	BMI	7107	6.92	<0.001	3.82 (3.22-4.53)	<0.001	1.97	<0.001
TyG-WC	HSI>36	Waist circumference	7187	3.30	<0.001	1.58 (1.39-1.80)	<0.001	2.36	<0.001
TyG-WC	FLI≥60	Waist circumference	7111	4.21	<0.001	2.85 (2.50-3.24)	<0.001	1.59	<0.001
TyG-WHtR	HSI>36	WHtR	7184	3.59	<0.001	1.65 (1.44-1.89)	<0.001	2.55	<0.001
TyG-WHtR	FLI≥60	WHtR	7108	4.39	<0.001	3.09 (2.69-3.54)	<0.001	1.53	<0.001

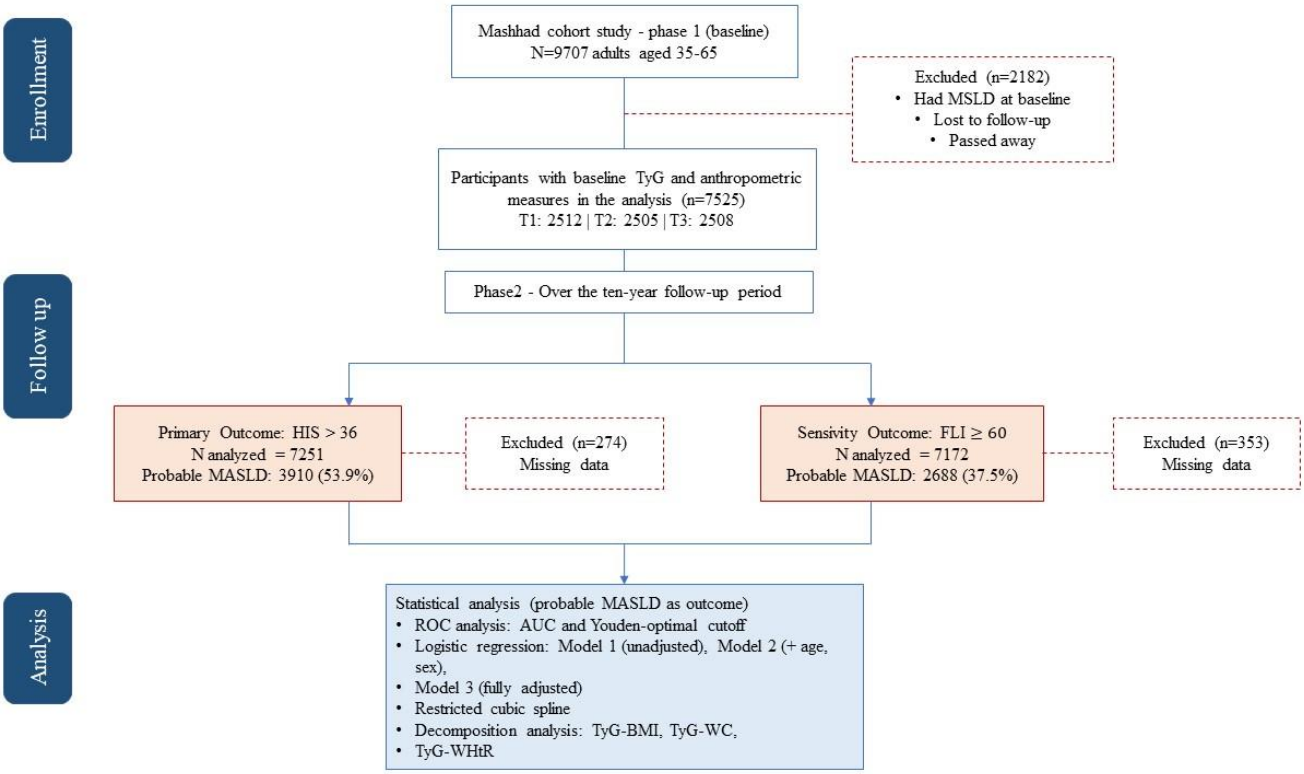


Figure 1. Flowchart

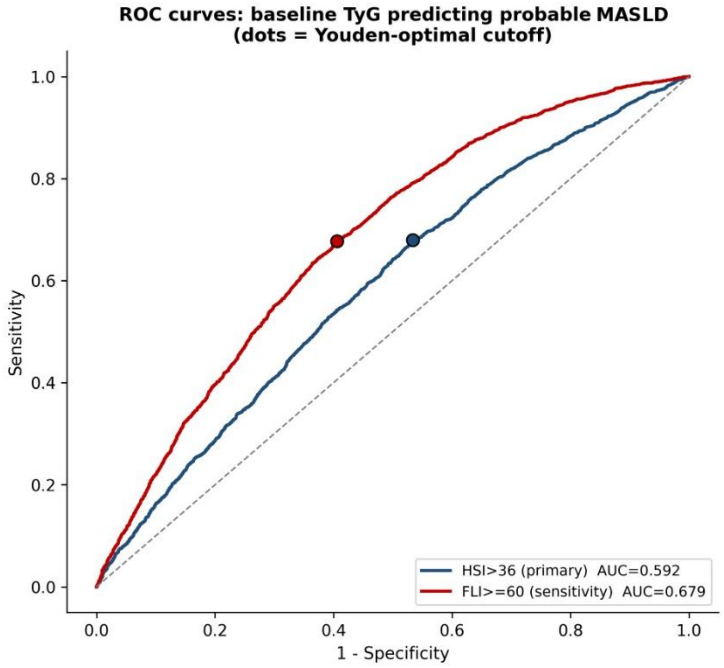


Figure 2. ROC curves for baseline TyG index predicting probable MASLD (HSI>36, primary; FLI>=60, sensitivity); dots indicate the Youden-optimal cutoff.

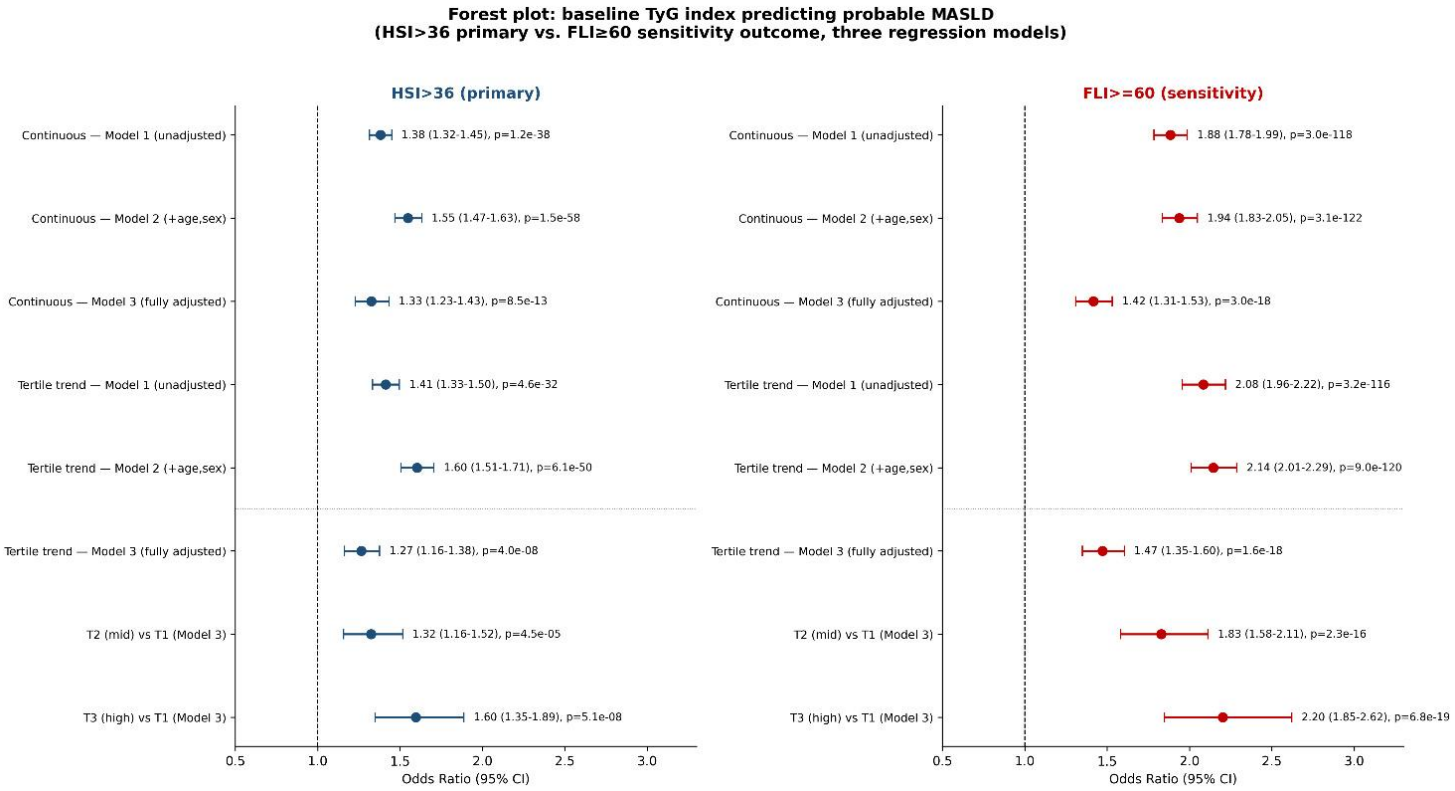


Figure 3: Association between baseline TyG index and probable MASLD across three regression models.

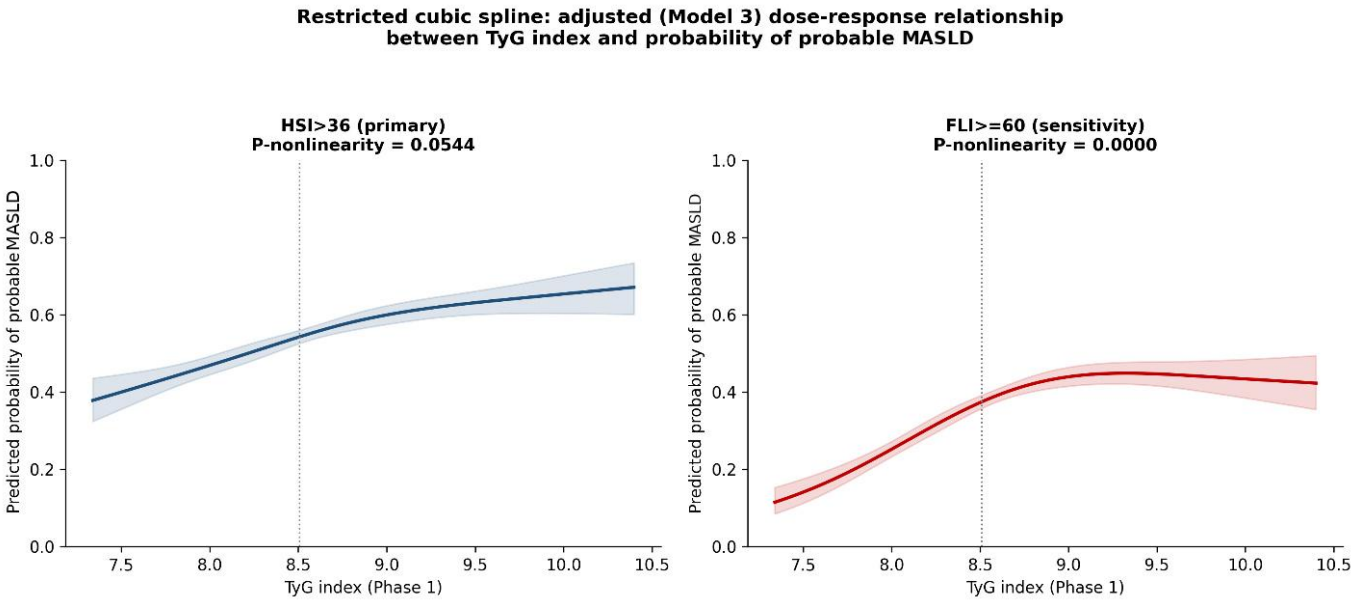


Figure 4. Restricted cubic spline: model-3-adjusted dose-response relationship between TyG index and probability of probable MASLD

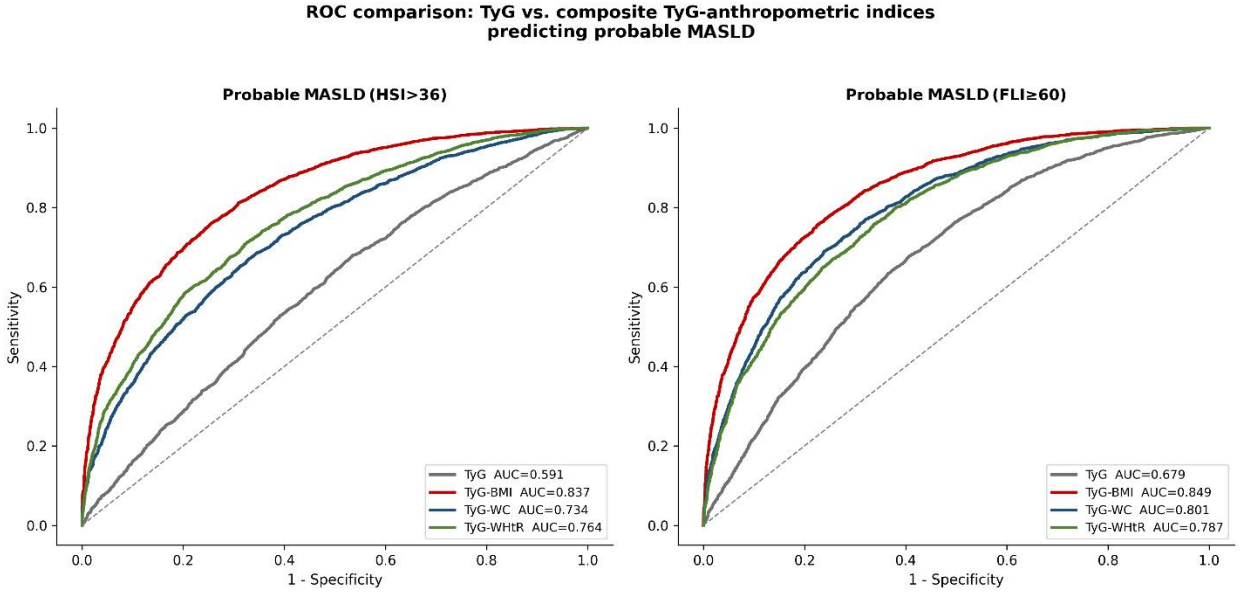


Figure 5. ROC curves comparing TyG and composite TyG-anthropometric indices for predicting probable MASLD (HSI>36, left; FLI≥60, right).

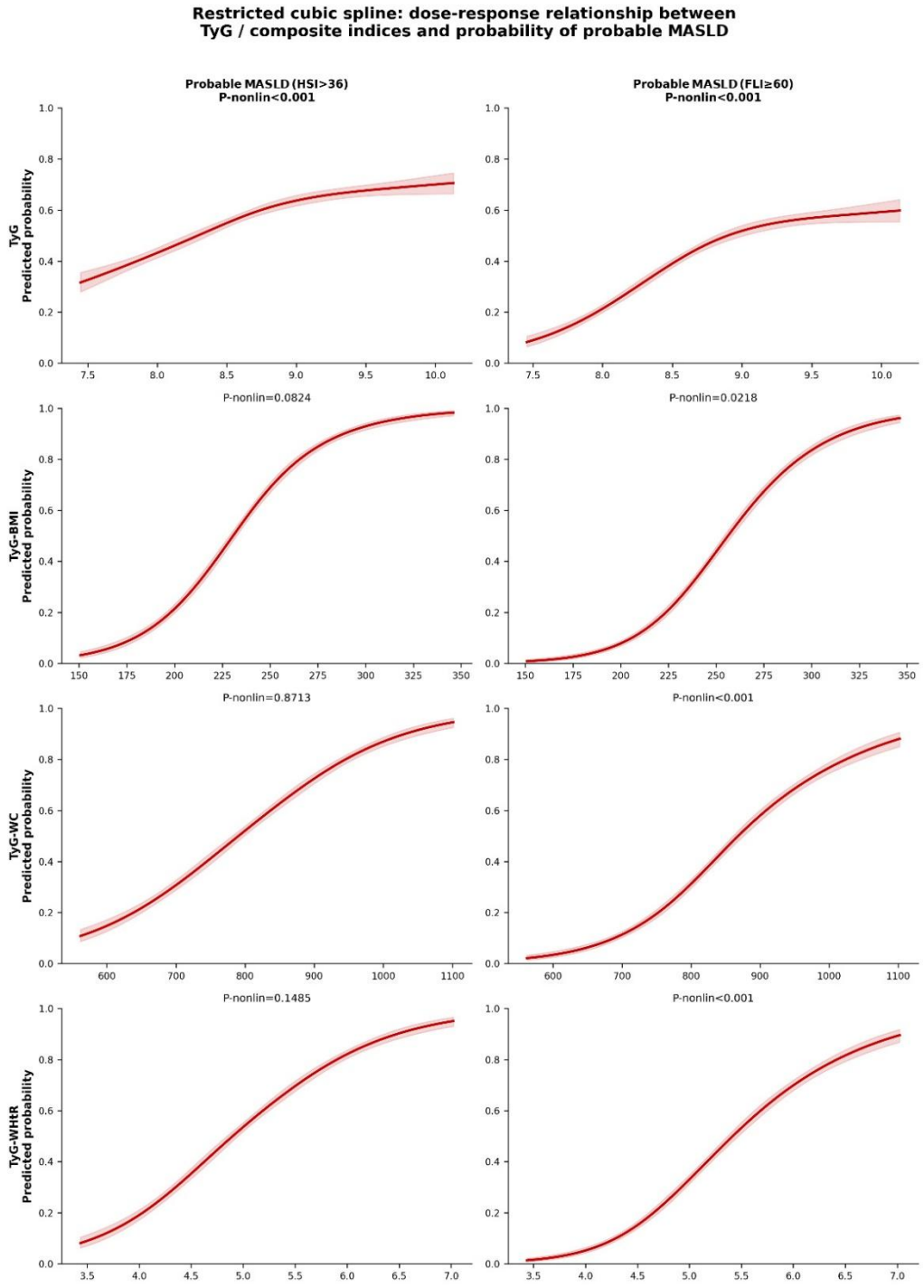


Figure 6. Restricted cubic spline: dose-response relationship between TyG / composite indices and probability of probable MASLD. Rows: TyG, TyG-BMI, TyG-WC, TyG-WHtR. Columns: HSI-based (left) and FLI-based (right) probable MASLD.