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The triglyceride glucose related index is an indicator of Sarcopenia

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The triglyceride glucose (TyG) related index, a metric used to evaluate assessing insulin resistance (IR), has received limited attention in its association with sarcopenia. Our study aims to explore the predictive potential of the TyG index for sarcopenia. This study utilized data from the China Health and Retirement Longitudinal Study, a nationally representative, community-based cohort study, including a sample size of 10,537 participants aged 45 years and older. Associations between TyG related index and sacopenia was explored using multivariate logistic regression. Analysis of the predictive value of TyG related index for sarcopenia using receiver-operating characteristic curve (ROC). We evaluated the correlation between the TyG related index and the risk of sarcopenia using Cox proportional hazards models. Additionally, we utilized restricted cubic spline (RCS) regression analyses to explore the connections between the TyG-related index and sarcopenia. Logistic regression analysis showed an association between TyG (OR 0.961[0.955,0.968], P < 0.001), TyG-body mass index (TyG-BMI) (OR 0.872[0.867,0.878], P < 0.001), TyG- waist circumference (TyG-WC) (OR 0.896[0.890,0.902], P < 0.001) and sarcopenia. The results of the ROC analysis indicated that the area under the curve values for TyG, TyG-BMI, and TyG-WC were 0.659, 0.903, and 0.819, respectively. Compared to those without sarcopenia, patients with sarcopenia had a 37.7% (HR 0.623[0.502,0.774], P < 0.001), 4.8% (HR 0.952[0.947,0.958], P < 0.001), and 0.4% (HR 0.996[0.995,0.996], P < 0.001) lower risk with increasing TyG, TyG-BMI, and TyG-WC, respectively. RCS results show nonlinear relationship between TyG-BMI (P < 0.001) and TyG-WC (P < 0.001) and risk of sarcopenia. We observed a correlation between the TyG-related index and sarcopenia, with the TyG-BMI index demonstrating strong predictive capability for sarcopenia.

Keywords Sarcopenia, Triglyceride glucose index, Body mass index, Insulin resistance

Sarcopenia, a prevalent geriatric ailment, manifests as the gradual decline in muscle mass, strength, and functionality[1]. With the aging population, the incidence of sarcopenia is on the ascent, imposing a substantial strain on both societal health and healthcare infrastructure[2]. Sarcopenia is closely associated not only with the frail state of the elderly[3], but also with the development and prognosis of a variety of metabolic diseases[4]. Therefore, early recognition of sarcopenia and effective interventions are important.

Insulin resistance (IR) is a common metabolic abnormality and there is a strong association between it and sarcopenia[5]. IR leads to a blockage of insulin signaling within muscle cells, which reduces the utilization of glucose by muscle tissues, making the energy supply within the muscle cells insufficient and affecting the synthesis and maintenance of muscle proteins, thus leading to a reduction in muscle mass[6,7]. IR also affects on protein synthesis and catabolism as well as energy metabolism in muscle cells[8]. In addition, IR may cause an inflammatory response and oxidative stress, affecting on muscle strength[9,10].

The triglyceride glucose (TyG) index was regarded as a reliable proxy for IR, as it considers both fasting blood glucose (FBG) and triglyceride (TG)[11,12]. Compared to the gold standard high insulin-normal glucose clamp for assessing IR, the TyG related index has the advantage of simplicity and cost-effectiveness for large-scale use[13]. Recent studies have also identified the TyG index as a potential marker for sarcopenic obesity in older adults, highlighting its broader applicability in identifying individuals at risk for both sarcopenia and obesity[14].

The diagnosis of sarcopenia is complex involving muscle strength, muscle mass, and physical performance. Recently, there has been a proposal suggesting that the sarcopenia index (SI), specifically the creatinine/cystatin C ratio, is related to muscle mass and can be used as a predictor of sarcopenia in intensive care unit (ICU) patients[15]. Therefore, our primary objective was to explore the correlation between the TyG related index and

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sarcopenia, and to determine its potential as a predictor of sarcopenia; the secondary objective was to assess the efficacy of the SI in predicting sarcopenia within the general population.

Methods

Participants

For the baseline analysis we used the China Health and Retirement Longitudinal Study (CHARLS) 2015, 10,537 participants were included in the analyses, participants included in the analyses had available physical examination data, blood data, demographic data, and other required data, see **Supplementary Fig. 1** for specific inclusion and exclusion criteria.

To further understand the relationship between IR indicators and the risk of developing sarcopenia, we additionally used CHARLS 2011 and CHARLS 2013 data, with the same inclusion and exclusion criteria as in the 2015 version; we excluded participants diagnosed with sarcopenia in 2011, and a total of 3,022 participants took part in the 5-year follow up.

TyG-related index

The collection of blood samples and the methods of analysis have been described in previous articles[16]. The TyG index, regarded as an effective surrogate for IR, is computed using the formula: ln [FBG (mg/dL) × TG (mg/dL)/2][17]. Two other indicators related to the TyG index: TyG-body mass index (TyG-BMI) as well as TyG-waist circumference (TyG-WC) combine BMI and WC and are thought to reflect levels of IR as well. The TyG-BMI calculation formula: TyG × BMI, and TyG-WC calculation formula: TyG × WC[17,18].

Muscle strength

The Asian Working Group for Sarcopenia (AWGS) 2019 recommends the use of grip strength as an indication of skeletal muscle strength, with the threshold for low grip strength being < 18 kg for women and < 28 kg for men[19]. We used the average of four grip strengths as the grip strength data, and in order to keep the sample size as small as possible, participants with two or more valid grip strength data were also included in the analysis.

Muscle mass

Muscle mass was assessed through the calculation of appendicular skeletal muscle mass (ASM) utilizing anthropometric equations previously validated for the Chinese population:

ASM = 0.193×weight (Kg) + 0.107 × height (m) − 4.157×sex (males are represented by 1, females by 2) − 0.037×age (years) − 2.631[20].

The lowest 20% of the ASM/Ht^2 (use ASM divided by the square of the height) in study population was defined as low muscle mass[21]. In our study, ASM/Ht^2 < 7.08 kg/m^2 in men and ASM/Ht^2 < 5.43 kg/m^2 in women were considered low muscle mass.

Physical performance

Participants walked 2.5 m at a normal pace, using a stopwatch to time their journey. Participants usually walked twice and we calculated the average time of the two walks, participants with only one walking time were included in the study. The chair stand text measures the time it takes for participants to stand five times in a row[22]. The 6-m walk < 1.0 m/s, or 5-time chair stand test ≥ 12 s were considered low physical performance.

Assessment of Sarcopenia

We employed the diagnostic algorithm recommended by AWGS 2019[1]. Participants who did not exhibit low muscle strength, low muscle mass, or low physical performance were classified as having no sarcopenia. Those without reduced muscle mass with or without reduced physical performance or reduced muscle strength were considered to have possible sarcopenia. Both of the above were considered as not having sarcopenia. The diagnosis of sarcopenia was established when reduced muscle mass was accompanied by diminished muscle strength or impaired physical performance. Severe sarcopenia is considered to be present when there is a decrease in muscle mass, muscle strength, and physical performance. These two states are considered to have sarcopenia.

Covariates

Demographic characteristics include age, sex (male, female) and place of residence (village, other areas) and education (illiteracy, < 6 years, ≥ 6 years). Have hyperlipidemia, hypertension, hyperglycemia, heart disease and stroke from a doctor's diagnosis. Systolic, diastolic, high density lipoprotein (HDL) and low density lipoprotein were also considered. In addition, sensitivity analyses were conducted by including anti-diabetic medications, lipid-lowering drugs, and healthy physical activity as additional covariates to assess their potential confounding effects on the results. Healthy physical activity was defined as engaging in vigorous exerciseor moderate activities for at least 30 min, three times a week.

Statistical analyses

Analysis of Variance (ANOVA) or the Kruskal–Wallis test was employed for continuous variables. Categorical variables were employed for chi-square tests. To further understand the differences between TyG related index and SI across sarcopenia diagnoses, we used ANOVA and Bonferroni post-hoc tests to assess differences between groups. Additionally, multiple linear regression models were utilized to investigate the relationship between the TyG related index and grip strength, ASM/Ht^2, 5-time chair stand test measures, and SI. Multivariate logistic regression was used to investigate the association between the TyG related index and sarcopenia, muscle strength,

muscle mass, and physical performance. We assessed the diagnostic value of the TyG related index, as well as the SI, through receiver-operating characteristic curve (ROC) analysis, and TyG related index and SI were grouped according to the cutoff value of the ROC curve. To validate the predictive performance of the TyG related index, we performed a 5-fold cross-validation procedure. This approach ensured that the model's predictive ability was consistent and reliable across different subsets of the data, reducing the risk of overfitting.

Exploring the connection between the TyG related index and the likelihood of sarcopenia development, we calculated the cumulative incidence rate through the Kaplan-Meier method. Estimating the hazard ratio (HR) with a 95% confidence interval (CI) for sarcopenia, we employed the Cox proportional risk model. Subgroups were analyzed according to age, gender, cutoff value, and the presence of hyperglycemia, hyperlipidemia, hypertension, and heart disease. Cox proportional risk regression model with four-knots restricted cubic spline (RCS) and a trend test were used to explore the association between the TyG related index and sarcopenia.

Given that all outcome variables were standardized to z-scores in the model, the coefficient represents the standardized effect. Statistical analyses were performed using R version 4.2.0, with statistical significance set at $P < 0.05$ for all analyses.

Results

Participants' characteristics

A total of 10,537 people were included, mean age of 59.34 ± 10.09 years, a total female share of 54%, and 73.9% living in village. Compared with individuals with sarcopenia, those without sarcopenia exhibited higher TG, FBG, BMI, WC, grip strength ASM/Ht^2, and TyG-related index and SI, and fewer had hypertension, hyperlipidemia, hyperglycemia, and heart disease (Table 1).

Predictive value of SI in incident Sarcopenia

The SI differed between the sarcopenia and severe sarcopenia groups in patients without sarcopenia; it also differed significantly between the possible sarcopenia and sarcopenia as well as severe sarcopenia groups (Fig. 1A). SI was associated with sarcopenia (OR 0.988[0.982,0.995], $P = 4.03E-4$) and there were between-group differences in the presence or absence of hyperglycaemia, hypertension, hyperlipidaemia, and heart disease (Table 2). Sensitivity analysis indicated that the between-group differences remained significant; however, the association between SI and sarcopenia was not significant after adjusting for anti-diabetic medications, lipid-lowering drugs, and healthy physical activity (**Supplementary Table 1**). There was an association between SI and physical performance, and a non-significant relationship with muscle strength and muscle mass (**Supplementary Table 2**). For the SI, the AUC was 0.609, with a cutoff value of 0.905, sensitivity of 58.90%, and specificity of 57.90% (Fig. 3A). No difference was found between the two groups in the cumulative incidence of sarcopenia according to the cutoff value subgroups (**Supplementary Fig. 3**), and the results of the Cox risk model indicated a HR of 0.812 (0.473,1.394) for SI and sarcopenia (Table 3). The non-linear relationship between SI and sarcopenia was also not significant ($P = 0.625$) (Fig. 4A).

Difference in TyG related index between Sarcopenia categories

To further understand the differences between sarcopenia and the TyG related index, we categorized the participants into four groups: no sarcopenia, possible sarcopenia, sarcopenia, and severe sarcopenia. The TyG related index was significantly different between the four groups. The TyG related index differed between the sarcopenia and severe sarcopenia groups in patients without sarcopenia; it also differed significantly between the possible sarcopenia and sarcopenia as well as severe sarcopenia groups, but not significantly between no sarcopenia and possible sarcopenia groups in patients. Furthermore, there were no significant disparities between the groups with sarcopenia and severe sarcopenia (Fig. 1B-D). We also observed that the mean values of TyG related index were lower in the sarcopenia and severe sarcopenia groups than in the without sarcopenia and possible sarcopenia groups.

Associations of TyG related index with Sarcopenia

TyG related index was associated with sarcopenia, with odds ratio (OR) of 0.961 (0.955,0.968); 0.872 (0.867,0.878); and 0.896 (0.890,0.902) for TyG index, TyG-BMI index, and TyG-WC index, respectively (Table 2). The TyG related index was also significantly associated with muscle strength ($OR_{TyG\ index}$ 0.979[0.971,0.987], $P = 1.31E-7$; $OR_{TyG-BMI\ index}$ 0.974[0.966,0.982], $P = 1.43E-10$; $OR_{TyG-wc\ index}$ 0.978[0.970,0.986], $P = 4.78E-8$) and muscle mass ($OR_{TyG\ index}$ 0.954[0.947,0.962], $P = 2.00E-16$; $OR_{TyG-BMI\ index}$ 0.829[0.823,0.834], $P = 2.00E-16$; $OR_{TyG-wc\ index}$ 0.963[0.857,0.869], $P = 2.00E-16$), but not with physical performance (**Supplementary Table 2**). We found positive correlations between TyG related index and the magnitude of grip strength ($\beta_{TyG\ index} = 0.053$, $P = 2.90E-12$; $\beta_{TyG-BMI\ index} = 0.099$, $P = 2.00E-16$; $\beta_{TyG-wc\ index} = 0.096$, $P = 2.00E-16$) as well as ASM/Ht^2 ($\beta_{TyG\ index} = 0.114$, $P = 2.00E-16$; $\beta_{TyG-BMI\ index} = 0.643$, $P = 2.00E-16$; $\beta_{TyG-wc\ index} = 0.385$, $P = 2.00E-16$), but negative correlations with SI ($\beta_{TyG\ index} = -0.089$, $P = 2.00E-16$; $\beta_{TyG-BMI\ index} = -0.046$, $P = 2.00E-16$; $\beta_{TyG-wc\ index} = -0.038$, $P = 3.00E-14$) (Fig. 2), and only TyG-WC was positively associated with 5-time chair stand test reaction time ($\beta = 0.038$, $P = 3.00E-4$) (**Supplementary Table 3**).

We analyzed subgroups according to age, sex, and presence of hypertension, hyperlipidemia, hyperglycemia, cardiac heart disease, and stroke, and in all subgroups, there was an association between the TyG related index and sarcopenia, exhibiting a trend consistent with that of the total population (Table 2). The results remained robust after sensitivity analysis (**Supplementary Table 1**).

Variance	All	No sarcopenia	Sarcopenia	*P*
Number	10,537	8935	1602	
Age	59.34 (10.09)	57.57 (9.31)	69.26 (8.38)	< 0.001
Sex (%)				0.708
Female	5692 (54.0)	4834 (54.1)	858 (53.6)	
Male	4845 (46.0)	4101 (45.9)	744 (46.4)	
Residence (%)				< 0.001
Other	2755 (26.1)	2511 (28.1)	244 (15.2)	
Village	7782 (73.9)	6424 (71.9)	1358 (84.8)	
Education (%)				< 0.001
0 year	724 (6.9)	510 (5.7)	214 (13.4)	
< 6 years	9098 (86.3)	7752 (86.8)	1346 (84.0)	
≥ 6 years	715 (6.8)	673 (7.5)	42 (2.6)	
Systolic pressure (mmHg)	130.83 (22.67)	130.67 (20.67)	131.72 (31.55)	0.088
Diastolic pressure (mmHg)	76.96 (12.32)	77.64 (12.17)	73.12 (12.44)	< 0.001
HDL (mg/dl)	51.40 (11.46)	50.59 (10.95)	55.90 (13.11)	< 0.001
LDL (mg/dl)	102.46 (28.74)	102.84 (28.47)	100.34 (30.13)	0.001
Triglycerides (mg/dl)	137.71 (87.25)	143.67 (90.11)	104.48 (58.99)	< 0.001
Glucose (mg/dl)	100.29 (29.78)	101.05 (30.35)	96.00 (25.97)	< 0.001
Creatinine (mg/dl)	0.80 (0.29)	0.80 (0.29)	0.82 (0.29)	0.004
Cystatin C (mg/l)	0.84 (0.23)	0.83 (0.22)	0.92 (0.27)	< 0.001
BMI (Kg/m2)	24.02 (4.09)	24.82 (3.87)	19.57 (1.75)	< 0.001
Waist circumference (cm)	85.45 (12.82)	87.41 (12.05)	74.57 (11.50)	< 0.001
Handgrip strength (Kg)	28.85 (9.36)	29.93 (9.19)	22.81 (7.90)	<0.001
ASM/Ht2 (kg/m^2)	6.83 (1.15)	7.03 (1.08)	5.75 (0.96)	<0.001
TyG index	8.66 (0.62)	8.71 (0.62)	8.39 (0.52)	< 0.001
TyG-BMI index	208.87 (42.80)	216.86 (40.88)	164.35 (19.80)	< 0.001
Sarcopenia index	0.97 (0.26)	0.98 (0.27)	0.90 (0.23)	< 0.001
Muscle strength (%)				< 0.001
Normal	8557 (81.2)	7723 (86.4)	834 (52.1)	
Abnormality	1980 (18.8)	1212 (13.6)	768 (47.9)	
Muscle mass (%)				< 0.001
Normal	8426 (80.0)	8426 (94.3)	0 (0.0)	
Abnormality	2111 (20.0)	509 (5.7)	1602 (100.0)	
Physical performance (%)				< 0.001
Normal	5483 (52.0)	5360 (60.0)	123 (7.7)	
Abnormality	5054 (48.0)	3575 (40.0)	1479 (92.3)	
Hypertension (%)				< 0.001
No	7569 (71.8)	6333 (70.9)	1236 (77.2)	
Yes	2968 (28.2)	2602 (29.1)	366 (22.8)	
Hyperlipidemia (%)				< 0.001
No	9039 (85.8)	7572 (84.7)	1467 (91.6)	
Yes	1498 (14.2)	1363 (15.3)	135 (8.4)	
Hyperglycemia (%)				0.001
No	9683 (91.9)	8176 (91.5)	1507 (94.1)	
Yes	854 (8.1)	759 (8.5)	95 (5.9)	
Heart disease (%)				0.961
No	8997 (85.4)	7628 (85.4)	1369 (85.5)	
Yes	1540 (14.6)	1307 (14.6)	233 (14.5)	
Stroke (%)				0.578
No	10,272 (97.5)	8714 (97.5)	1558 (97.3)	
Yes	265 (2.5)	221 (2.5)	44 (2.7)	

Table 1. Baseline characteristics of the No Sarcopenia and Sarcopenia groups. Data are mean (SD), n (%), or median (IQR). Abbreviations: LDL, Low-Density Lipoprotein; HDL, High-Density Lipoprotein; ASM/Ht2, appendicular skeletal muscle mass divided by the square of the height; TyG, Triglyceride-Glucose index; BMI, Body mass index.

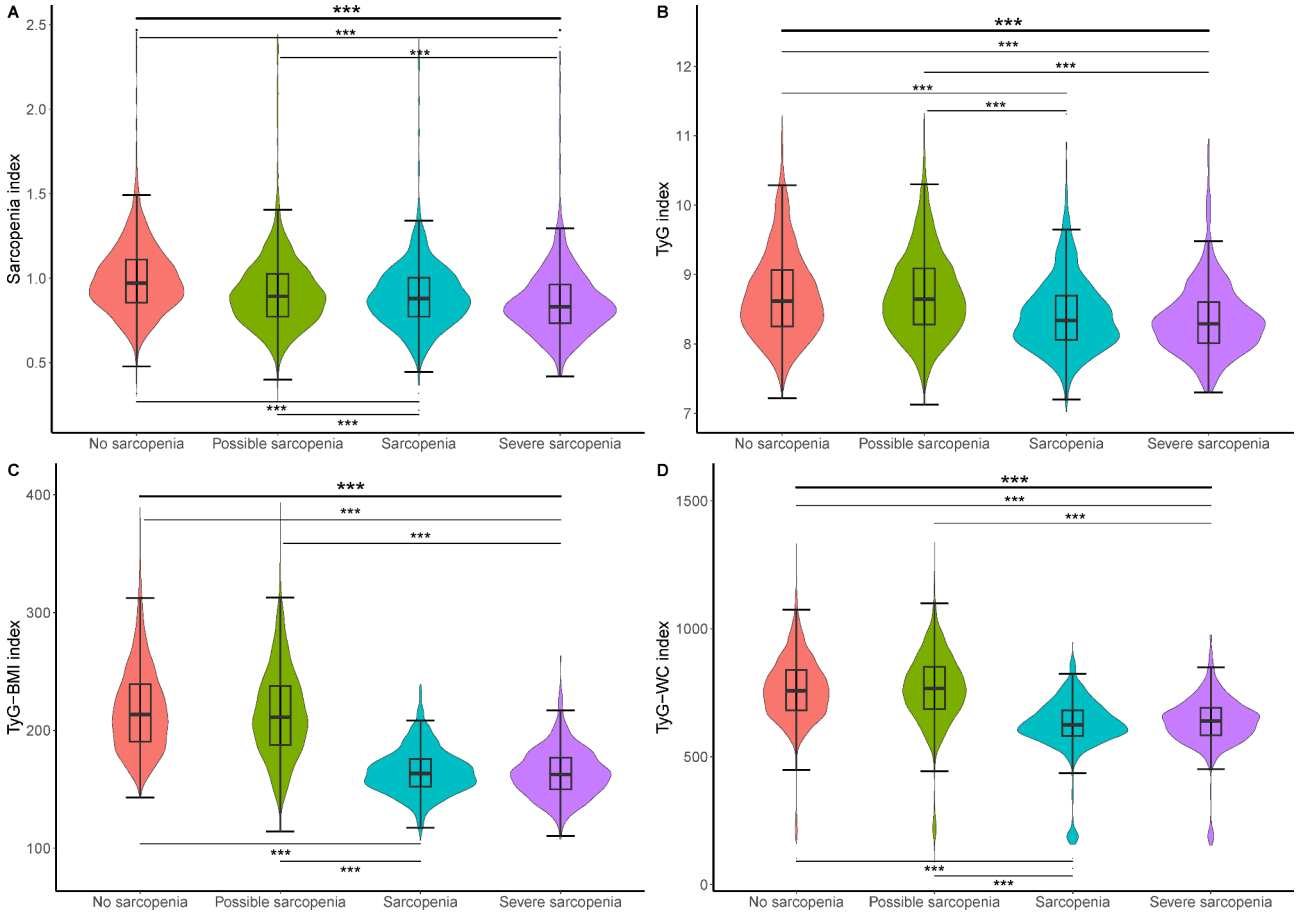

Fig. 1. Difference in TyG related index as well as sarcopenia index between sarcopenia categories. (**A**) sarcopenia index is associated with sarcopenia. (**B**) TyG index is associated with sarcopenia. (**C**) TyG-BMI index is associated with sarcopenia. (**D**) TyG-WC index is associated with sarcopenia. Abbreviations: TyG, Triglyceride-Glucose index; BMI, Body mass index; WC, Waist circumference.

Predictive potential of TyG related index for incident Sarcopenia

We utilized ROC curves to examine whether the TyG related index could predict sarcopenia. For the TyG index, the AUC was 0.659, with a cutoff value of 8.564, sensitivity of 69.40%, and specificity of 54.80%. For the TyG-BMI index, the AUC was 0.903, with a cutoff value of 182.558, sensitivity of 83.80%, and specificity of 81.70%. As for the TyG-WC index, the AUC was 0.819, with a cutoff value of 700.899, sensitivity of 80.50%, and specificity of 69.90% (Fig. 3B-D). Furthermore, a 5-fold cross-validation showed that the TyG-BMI index had the highest AUC among the four indices, with an AUC of 0.826, sensitivity of 95.20%, and specificity of 69.90% (**Supplementary Table 4**). Our subgroup analyses revealed that TyG related index had a larger area under the AUC curve than the overall area in men, the late-ife, and those with hyperglycaemia, hyperlipidaemia, hypertension and heart disease (**Supplementary Table 5**). In particular, TyG-BMI showed a good predictive effect in the whole as well as in different subgroups.

TyG related index and Incident Sarcopenia Risk

We divided TyG related index into two groups based on cutoff values, and survival analyses showed significant differences in incidence between the two groups at the 4-year follow-up time (**Supplementary Fig. 2**). The Cox proportional risk model showed that the risk of sarcopenia was reduced by 37.3% (HR 0.623[0.502,0.774]), 4.8% (HR 0.952[0.947,0.958]), 0.4% (HR 0.996[0.995,0.996]) for each one-unit increase in the TyG index, TyG-BMI index and TyG-WC index, respectively. When grouped according to cutoff values, the risk was reduced by 35.9% (HR 0.641[0.505,0.814]); 86.7% (HR 0.133[0.104,0.171]); and 81.6% (HR 0.184[0.142,0.238]) for groups larger than the cutoff value, respectively, compared with groups below the cutoff value (Table 3). The TyG-BMI index and TyG-WC index did not differ significantly between subgroups. In the sensitivity analysis, we conducted subgroup analyses based on healthy physical activity, and still did not observe any significant differences between the groups (**Supplementary Table 6**). RCS results revealing nonlinear associations between the TyG-BMI index and the TyG-WC index with sarcopenia, whereas the nonlinear associations between TyG index and sarcopenia were not significant (Fig. 4B-D).

Variance	TyG index		TyG-BMI index		TyG-WC index		Sarcopenia index	
	OR(95%CI)	*P*	OR(95%CI)	*P*	OR(95%CI)	*P*	OR(95%CI)	*P*
ALL	0.961(0.955,0.968)	**2.00E-16**	0.872(0.867,0.878)	**2.00E-16**	0.896(0.890,0.902)	**2.00E-16**	0.988(0.982,0.995)	**4.03E-4**
Sex								
Male	0.963(0.953,0.973)	**1.45E-13**	0.882(0.873,0.890)	**2.00E-16**	0.901(0.892,0.910)	**2.00E-16**	0.978(0.969,0.987)	**1.43E-6**
Female	0.996(0.957,0.976)	**2.10E-11**	0.884(0.875,0.893)	**2.00E-16**	0.904(0.895,0.913)	**2.00E-16**	0.979(0.970,0.988)	**3.88E-6**
Age								
Mid-life	0.984(0.978,0.991)	**9.58E-7**	0.926(0.920,0.932)	**2.00E-16**	0.940(0.934,0.946)	**2.00E-16**	0.983(0.977,0.988)	**4.52E-9**
Late-life	0.911(0.896,0.928)	**2.00E-16**	0.753(0.742,0.764)	**2.00E-16**	0.814(0.801,0.827)	**2.00E-16**	0.967(0.951,0.983)	**5.08E-5**
Hypertension								
No	0.966(0.958,0.974)	**2.00E-16**	0.871(0.865,0.878)	**2.00E-16**	0.900(0.893,0.907)	**2.00E-16**	0.987(0.979,0.994)	**6.88E-4**
Yes	0.967(0.955,0.979)	**4.90E-8**	0.887(0.877,0.897)	**2.00E-16**	0.902(0.892,0.913)	**2.00E-16**	0.996(0.985,1.008)	0.515
Hyperlipidemia								
No	0.964(0.957,0.971)	**2.00E-16**	0.874(0.868,0.880)	**2.00E-16**	0.900(0.893,0.906)	**2.00E-16**	0.987(0.980,0.994)	**3.63E-4**
Yes	0.974(0.959,0.989)	**7.08E-4**	0.892(0.879,0.904)	**2.00E-16**	0.905(0.892,0.918)	**2.00E-16**	0.999(0.984,1.014)	0.932
Hyperglycemia								
No	0.965(0.958,0.972)	**2.00E-16**	0.875(0.869,0.881)	**2.00E-16**	0.901(0.895,0.907)	**2.00E-16**	0.987(0.981,0.994)	**2.72E-4**
Yes	0.973(0.953,0.994)	**0.012**	0.878(0.861,0.897)	**2.00E-16**	0.887(0.869,0.905)	**2.00E-16**	1.002(0.981,1.023)	0.857
Cardiology								
No	0.967(0.960,0.974)	**2.00E-16**	0.872(0.866,0.879)	**2.00E-16**	0.901(0.895,0.908)	**2.00E-16**	0.988(0.981,0.995)	**7.34E-4**
Yes	0.954(0.936,0.971)	**2.90E-7**	0.882(0.67,0.897)	**2.00E-16**	0.882(0.867,0.898)	**2.00E-16**	0.994(0.977,1.011)	0.477
Stroke								
No	0.962(0.955,0.968)	**2.00E-16**	0.873(0.867,0.879)	**2.00E-16**	0.897(0.891,0.903)	**2.00E-16**	0.988(0.982,0.995)	**4.88E-4**

Table 2. Associations of TyG-related index as well as Sarcopenia index with Sarcopenia. Abbreviations: TyG, Triglyceride-Glucose index; BMI, Body mass index; WC, Waist circumference; OR, odd ratio; CI, confidence interval. All factors adjusted for age, sex, residence, education, hyperlipidemia, hypertension, hyperglycemia, heart disease, stroke, systolic, diastolic, high-density lipoprotein and low-density lipoprotein expect itself.

Variance	TyG index		TyG-BMI index		TyG-WC index		Sarcopenia index	
	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*	HR(95%CI)	*P*
ALL	0.623(0.502,0.774)	**1.88E-05**	0.952(0.947,0.958)	**2.00E-16**	0.996(0.995,0.996)	**2.00E-16**	0.812(0.473,1.394)	0.450
Group2*	0.641(0.505,0.814)	**2.66E-4**	0.133(0.104,0.171)	**2.00E-16**	0.184(0.142,0.238)	**2.00E-16**	1.007(0.785,1.292)	0.957
Sex								
Male	0.449(0.320,0.628)	**2.98E-6**	0.940(0.931,0.949)	**2.00E-16**	0.995(0.993,0.996)	**2.00E-16**	0.753(0.353,1.606)	0.463
Female	0.816(0.612,1.085)	**2.00E-16**	0.959(0.952,0.965)	**2.00E-16**	0.996(0.995,0.997)	**2.00E-16**	0.740(0.443,1.234)	0.248
Age								
Mid-life	0.795(0.553,1.142)	0.215	0.964(0.955,0.973)	**3.33E-14**	0.996(0.995,0.997)	**4.07E-11**	0.917(0.391,2.149)	0.842
Late-life	0.625(0.483,0.808)	**3.28E-4**	0.955(0.949,0.961)	**2.00E-16**	0.996(0.995,0.997)	**2.00E-16**	0.410(0.185,0.909)	**0.028**
Hypertension								
No	0.573(0.438,0.749)	**4.53E-4**	0.951(0.945,0.958)	**2.00E-16**	0.996(0.995,0.996)	**2.00E-16**	0.524(0.239,1.146)	0.106
Yes	0.732(0.504,1.064)	0.102	0.953(0.943,0.963)	**2.00E-16**	0.996(0.994,0.997)	**8.03E-14**	1.480(0.719,3.048)	0.287
Hyperlipidemia								
No	0.760(0.415,1.393)	0.375	0.939(0.921,0.958)	**7.08E-10**	0.997(0.995,0.999)	**6.40E-4**	0.233(0.022,2.518)	0.230
Yes	0.623(0.494,0.787)	**6.89E-5**	0.953(0.948,0.959)	**2.00E-16**	0.995(0.995,0.959)	**2.00E-16**	0.863(0.496,1.501)	0.601
Hyperglycemia								
No	0.543(0.470,0.748)	**1.09E-5**	0.951(0.946,0.957)	**2.00E-16**	0.996(0.995,0.996)	**2.00E-16**	0.788(0.447,1.388)	0.409
Yes	0.834(0.458,1.521)	0.554	0.957(0.939,0.976)	**1.30E-5**	0.995(0.992,0.998)	**0.002**	0.939(0.152,5.823)	0.946
Cardiology								
No	0.635(0.500,0.806)	**1.90E-4**	0.952(0.946,0.957)	**2.00E-16**	0.996(0.995,0.996)	**2.00E-16**	0.714(0.386,1.322)	0.284
Yes	0.537(0.317,0.911)	**0.021**	0.953(0.939,0.967)	**7.55E-11**	0.996(0.995,0.998)	**1.08E-5**	1.632(0.506,5.205)	0.416
Stroke								
No	0.630(0.506,0.786)	**4.18E-5**	0.953(0.948,0.958)	**2.00E-16**	0.996(0.995,0.996)	**2.00E-16**	0.824(0.478,1.421)	0.487

Table 3. Risk factors associated with sarcopenia development using Cox regression. Abbreviations: HR, hazard ratio; CI, confidence interval; TyG, Triglyceride-Glucose index; BMI, Body mass index; WC, Waist circumference. All factors adjusted for age, sex, residence, education, hyperlipidemia, hypertension, hyperglycemia, heart disease, stroke, systolic, diastolic, high-density lipoprotein and low-density lipoprotein expect itself. *Grouped according to the cutoff value, with the group below the cutoff value as the reference.

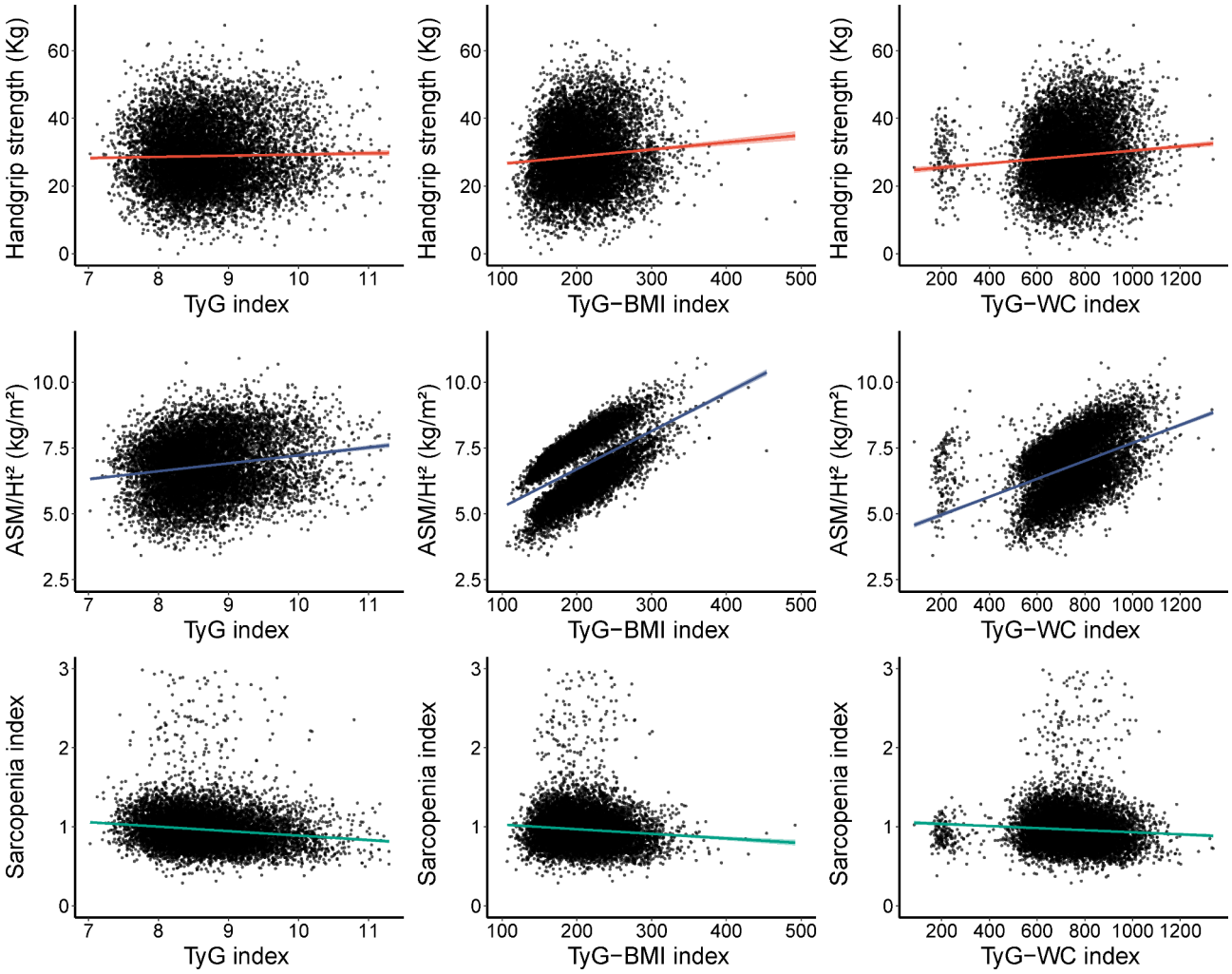

Fig. 2. Associations of TyG related index with handgrip strengthen, ASM/Ht^2 and sarcopenia index. Abbreviations: ASM/Ht2, appendicular skeletal muscle mass divided by the square of the height; TyG, Triglyceride-Glucose index; BMI, Body mass index; WC, Waist circumference. All factors adjusted for age, sex, residence, education, hyperlipidemia, hypertension, hyperglycemia, heart disease, stroke, systolic, diastolic, high-density lipoprotein and low-density lipoprotein.

Discussion

Our study found an association between the TyG related index and sarcopenia in a large cohort in China. Compared with the TyG index, the TyG-BMI and TyG-WC indices, which combine BMI and WC, have better predictive value for sarcopenia. In particular, the TyG-BMI index demonstrated an area under the ROC curve of 0.903, with corresponding sensitivity and specificity values of 83.80% and 81.70%, respectively. We conducted a 5-fold cross-validation, which suggested that the TyG-BMI index is a valuable predictor of sarcopenia. In the general population, the relationship between SI and sarcopenia was not significant, and the function of prediction of sarcopenia was limited.

Studies have shown an association between IR and sarcopenia, but reports of the relationship between TyG index and sarcopenia remain controversial. Yang et al.[23] found a positive association between the TyG index and sarcopenia in a large cohort, suggesting that higher TyG levels may increase the risk of sarcopenia. A positive association between IR and sarcopenia was found in elderly patients undergoing dialysis treatment[24]. Similarly TG/HDL, which is another index for IR, was found to be negatively associated with sarcopenia in the CHARLS database, which is consistent with our results[25]. The reason for this phenomenon is that the effect of BMI was not taken into account. Studies that also used the CHARLS database to investigate the correlation between the TyG index and sarcopenia have reported that each one-unit increase in the TyG index, as a continuous variable, is associated with a 26% reduction in the risk of sarcopenia (HR 0.74 [0.61,0.89]), but the correlation between TyG index and sarcopenia was not significant when the effect of BMI was considered (HR 0.90 [0.68,1.82]). They also discovered that BMI acted as a significant mediator in the relationship between the TyG index and sarcopenia[26]. Similar findings held true in the Korean cohort, who found a positive association between IR and ASM/Ht^2, but a negative association between IR and ASM/Ht^2 after adjusting for BMI[27]. The association between muscle strength and IR was also influenced by BMI, with muscle mass being negatively associated with IR in low-fat

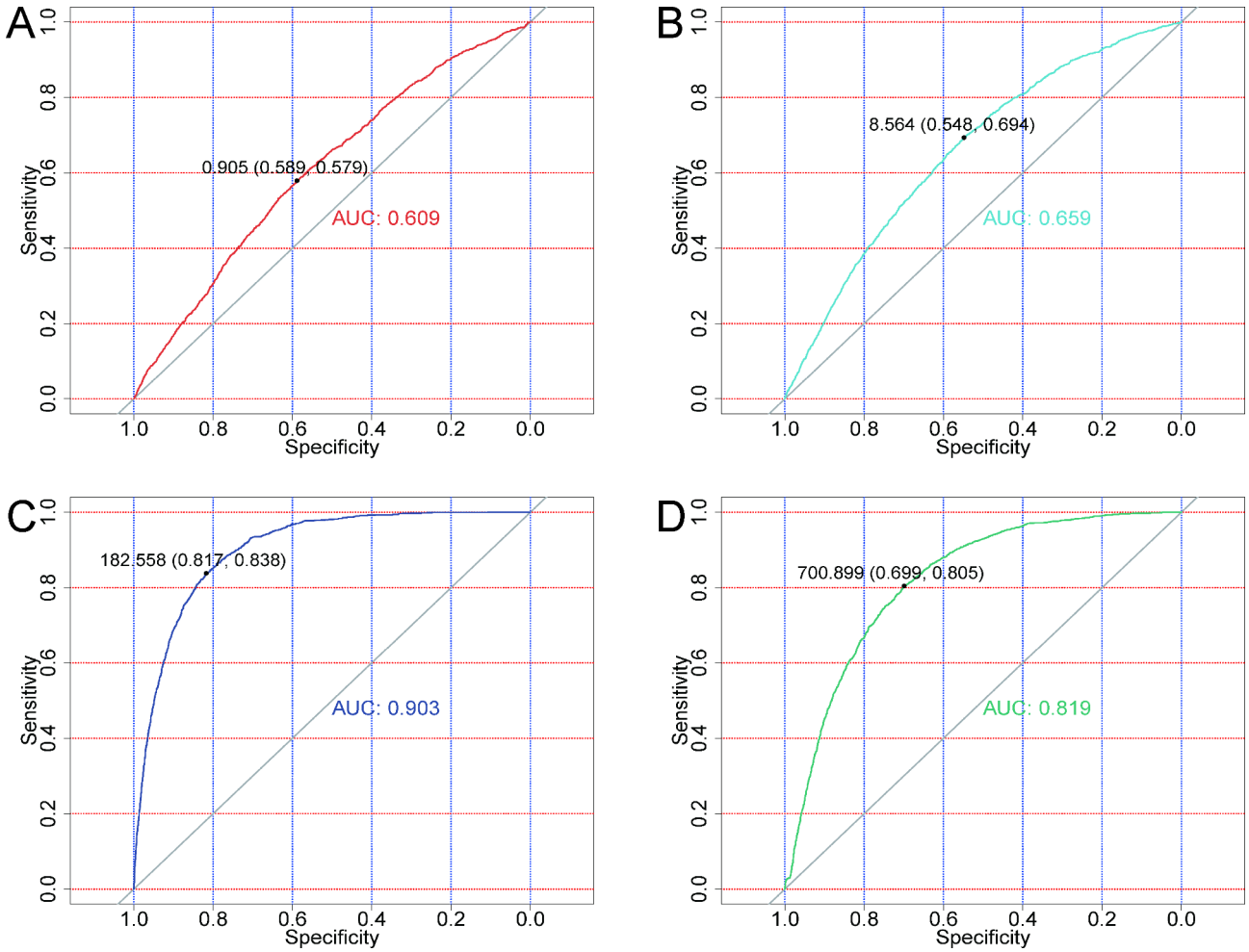

Fig. 3. ROC curves pertaining to the TyG related index and sarcopenia index for the sarcopenic. (A) ROC curves of the sarcopenia index. (B) ROC curves of the TyG index. (C) ROC curves of the TyG-BMI index. (**D**) ROC curves of the TyG-WC index. Abbreviations: HR, hazard ratio; CI, confidence interval; TyG, Triglyceride-Glucose index; BMI, Body mass index; WC, Waist circumference

individuals, and the protective association of muscle mass with IR diminishing as fat mass increased[28]. Our main objective was to evaluate whether TyG-related index could be a valid predictor of sarcopenia, and to avoid multicollinearity, we did not consider the effect of BMI in our correlation analysis.

Between-group differences and the presence of nonlinear relationships may also account for the controversial relationship of muscle strength, muscle mass as well as physical performance to IR. Our research revealed that elevated TyG related indices were correlated with a decreased prevalence of sarcopenia, as well as lower levels of muscle strength, muscle mass, and reduced physical performance.

One study found that when IR was grouped by quartiles (Q). In comparison to the Q1 group, there was a positive correlation observed with skeletal muscle treatment in the Q2 group, but conversely, a negative correlation was noted in the Q3 and Q4 groups, suggesting a possible nonlinear relationship between IR and muscle mass[29]. We found nonlinear associations of TyG-BMI index and TyG-WC index with the risk of developing sarcopenia using RCS. The association of IR with grip strength was significant in males but not in females, suggesting that there may be gender differences. Studies using CHARLS in the absence of hypertension, hypertension as well as hyperlipidemia with increased cognitive TyG index the risk of sarcopenia, which is the same as what we observed[26]. However, no between-group differences were observed for TyG-BMI index and TyG-WC index.

In the general population, the TyG index and SI were less effective than the TyG related index in predicting sarcopenia. Our AUC for the TyG index using the 2015 version of the data was 0.659, whereas other studies using the 2011 version of the data yielded an AUC of 0.628[26]. In non-diabetic participants, the AUC for the TyG index reached only 0.707[30]. Although the TyG index showed slightly better predictive performance in non-diabetic participants, it still lags behind the TyG-BMI index and TyG-WC index. SI is a poor predictor of sarcopenia relative to the TyG index in the general population, probably because creatinine is derived mainly from the metabolites of muscle cells, whereas cystatin C is derived from all nucleated cells. In ICU patients, the association between creatinine and muscle mass is more pronounced due to factors such as malnutrition, muscle

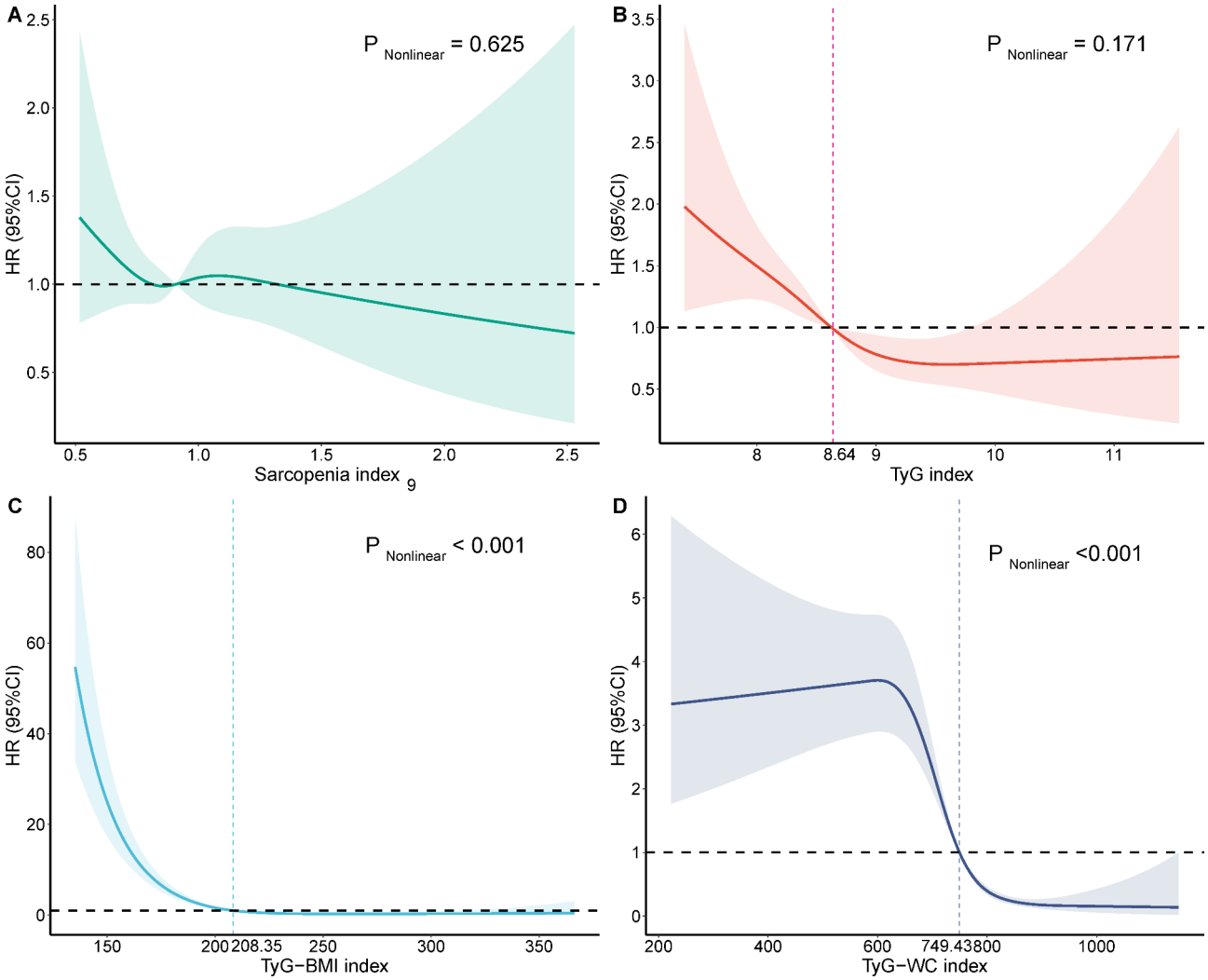

Fig. 4. Restricted cubic spline curve for the TyG-related index and sarcopenia index hazard ratio. Abbreviations: HR, hazard ratio; CI, confidence interval; TyG, Triglyceride-Glucose index; BMI, Body mass index; WC, Waist circumference.

proteolysis and muscle wasting. However, in the general population, who are usually able to maintain a good nutritional status and a relatively stable physiological state, the ratio of creatinine to cystatin C may be more significantly influenced by renal function than by muscle mass and nutritional status[15,31].

We think that TyG-BMI index can predict sarcopenia may be related to a few factors. The first is the interaction between adipose tissue and muscle mass[32]. In the obese state, adipose tissue releases large amounts of fatty acids, inflammatory factors, and hormones, and these metabolites may directly or indirectly affect the metabolism and function of muscle tissue[33,34]. For example, excess fatty acids may interfere with insulin signaling within muscle cells, thereby promoting muscle proteolysis[35]. In addition, inflammatory mediators may affect muscle tissue metabolism and function by activating inflammatory responses and inhibiting growth factor signaling pathways in muscle cells[36,37]. Another factor is the effect of IR on muscle metabolic pathways. In a state of IR, muscle cells have a reduced response to insulin, leading to inhibition of glucose uptake and utilization, which increases the burden of muscle proteolysis and energy metabolism[38]. In addition, IR may promote the oxidative metabolism of fatty acids, causing muscle cells to rely more on fat as an energy source, which leads to increased muscle proteolysis and accelerated loss of muscle mass[39,40].

There are several limitations in our study. Firstly, the results we obtained need validation in larger cohorts. Additionally, the diagnosis of the disease relied on self-reporting, which may introduce recall bias. Finally, although we observed a non-linear correlation between the TyG-BMI index and TyG-WC index with sarcopenia risk, we are unable to establish a causal relationship between IR and sarcopenia.

Conclusions

In our study, we identified an association between the TyG related index and sarcopenia, with the TyG-BMI index demonstrating good predictive efficacy for sarcopenia. Nevertheless, there are limitations in the utility of SI for predicting sarcopenia in the general population. The TyG-BMI index exhibited high accuracy and

reliability in predicting sarcopenia, enabling the timely identification of high-risk individuals and facilitating appropriate interventions to prevent or delay the onset of sarcopenia.

Data availability

The datasets generated for this study are available on request to the corresponding author.

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Author contributions
ZH-Z contributed to the conception or design of the work. All authors were responsible for the acquisition, analysis and interpretation of data. ZH-Z and X-C drafted the manuscript. N-J participated in the revision of the manuscript and provided financial support. Critical revision of the manuscript for important intellectual content were performed by all authors. All author agreed with the content of the article to be submitted. All authors reviewed and approved the final manuscript.

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Declarations

Ethics approval and consent to participate
This study was complied with the ethical guidelines of the Declaration of Helsinki, and was approved by the Ethics Committee of Peking University (approval number: IRB00001052-13074). The participants provided their written informed consent to participate in this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Additional information
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