

Supplementary Materials

Triglyceride-glucose waist-to-weight index and bone microarchitecture in type 2 diabetes: a machine-learning and regression analysis

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Supplementary Table 1. Index of TyG and derived indices

Index	Calculation formula
TyG	$TyG = \ln [TG(mg/dL) \times FBG(mg/dL) / 2]$
TyG-BMI	$TyG-BMI = TyG \times BMI$
TyG-WC	$TyG-WC = TyG \times WC$
TyG-WHtR	$TyG-WHtR = TyG \times (WC / Height)$
TyG-BRI	$TyG-BRI = TyG \times BRI$ $BRI = 364.2 - 365.5 \times \sqrt{(1 - [WC(cm)/(2\pi)]^2 / [0.5 \times Height(cm)]^2)}$
TyG-ABSI	$TyG-ABSI = TyG \times ABSI$ $ABSI = WC(m) / [BMI^{(2/3)} \times Height(m)^{(1/2)}]$
TyG-WWI	$TyG-WWI = TyG \times WWI$ $WWI = WC(cm) / \sqrt{Weight(kg)}$ Unit: cm/ $\sqrt{kg}$
TyG-LAP	$TyG-LAP = TyG \times LAP$ $LAP = [WC(cm) - (65 \text{ male} / 58 \text{ female})] \times TG(mmol/L)$
TyG-CI	$TyG-CI = TyG \times CI$ $CI = WC(m) / [0.109 \times \sqrt{(Weight(kg)/Height(m))}]$
TyG-BSI	$TyG-BSI = TyG \times BSI$ $BSI = WC(m) / \sqrt{(BMI \times Height(m))}$ $TyG-RFM = TyG \times RFM$
TyG-RFM	$RFM = 64 - (20 \times Height/WC) + (12 \times Sex)$ (Sex: male = 0, female = 1)

ABSI: A Body Shape Index; BMI: body mass index; BRI: body roundness index; BSI: body shape index; CI: conicity index; FBG: fasting blood glucose; LAP: lipid accumulation product; RFM: relative fat mass; TG: triglyceride; TyG: triglyceride-glucose; WC: waist circumference; WHtR: waist-to-height ratio; WWI: weight-adjusted waist index

Supplementary Table 2. Random forest-based covariate selection for Model 3

Rank	Variable	%IncMSE	Role in final model	Reason
1	Age	≈ 19.7	Included	A priori covariate in Model 2/3
2	Sex	10.8009746	Included	A priori covariate in Model 2/3
3	TyG-WWI	5.7918378	Included	Main exposure variable
4	SCr (μmol/L)	4.4490959	Included	RF-selected covariate
5	25-(OH)VitD (ng/mL)	2.9574260	Included	RF-selected covariate
6	BUN (mmol/L)	2.7896324	Included	RF-selected covariate
7	Urinary albumin (mg/L)	1.9389261	Not included	Redundant with UACR-related albuminuria indicator
8	P1NP	1.7986393	Included	RF-selected covariate
9	Albumin	1.6880901	Included	RF-selected covariate
10	PTH	1.3655882	Included	RF-selected covariate
11	Smoking	1.1406393	Included	RF-selected covariate
12	γ-GGT	1.0992021	Included	RF-selected covariate
13	UACR (mg/g)	1.0495109	Included	RF-selected covariate; representative albuminuria indicator
14	Serum phosphorus	1.0161963	Included	RF-selected covariate
15	Blood Calcium	0.8504552	Not included	%IncMSE ≤ 1.0
16	Fasting C peptide	0.8488615	Not included	%IncMSE ≤ 1.0
17	Peripheral neuropathy	0.8405793	Not included	%IncMSE ≤ 1.0
18	HbA1c	0.6694324	Not included	%IncMSE ≤ 1.0
19	Drinking	0.6168361	Not included	%IncMSE ≤ 1.0
20	Retinal disease	0.4372574	Not included	%IncMSE ≤ 1.0
21	UA	0.4358664	Not included	%IncMSE ≤ 1.0
22	Chronic kidney disease	0.3420949	Not included	%IncMSE ≤ 1.0
23	LDL	0.1091429	Not included	%IncMSE ≤ 1.0

24	N_terminal osteocalcin	-0.1203480	Not included	Low RF importance
25	TC	-0.1237702	Not included	Low RF importance
26	ALT	-0.3777302	Not included	Low RF importance
27	Hypertension	-0.5297641	Not included	Low RF importance
28	Insulin	-0.6728580	Not included	Low RF importance
29	β -CTX	-0.6904986	Not included	Low RF importance
30	Antidiabetic drugs	-0.7309711	Not included	Low RF importance
31	TBIL ($\mu\text{mol/L}$)	< 0	Not included	Low RF importance
32	Duration of diabetes	< 0	Not included	Low RF importance
33	Hyperlipidemia	< 0	Not included	Low RF importance

SCr: Serum creatinine; 25-(OH)VitD: 25-hydroxyvitamin D; BUN: blood urea nitrogen; PINP: procollagen type I N-terminal propeptide; PTH: parathyroid hormone; γ -GGT: gamma-glutamyl transferase; UACR: urine albumin-creatinine ratio; HbA1c: glycated hemoglobin; UA: uric acid; LDL: low-density lipoprotein cholesterol; TC: total cholesterol; ALT: alanine aminotransferase; β -CTX: β -C-terminal telopeptide; TBIL: total bilirubin.

Supplementary Table 3. TyG-WWI and TBS: interaction effects with age and sex

Term	Estimate	Std.error	Statistic	P value	Conf.low	Conf.high
TyG_WWI:	0.0006387	0.0009141	0.6986953	0.4852947	-	0.0024378
SexWomen	14	53	58	53	0.0011603	27
					98	
TyG_WWI:	-	3.81399E-	-	0.5754543	-	5.36783E-
Age	2.13837E-	05	0.5606629	29	9.64456E-	05
	05		7		05	

CI: Confidence interval; .TBS: trabecular bone score; TyG-WWI: triglyceride-glucose waist-to-weight index; Conf. low: lower limit of the 95% confidence interval; Conf. high: upper limit of the 95% confidence interval.

Supplementary Table 4. Restricted cubic spline (RCS) analysis of the TyG-WWI and TBS

Term	d.f.	Partial SS	MS	<i>F</i>	<i>P</i>
TyG-WWI	3	0.14381999	0.047939997	5.696166602	0.000839255
Nonlinear	2	0.014459837	0.007229918	0.85904928	0.424628577
Age	1	0.314888065	0.314888065	37.41458078	3.04947E-09
Sex	1	0.233917003	0.233917003	27.79370697	2.62397E-07
SCr (μmol/L)	1	0.015753015	0.015753015	1.871752297	0.172322777
25-(OH)VitD (ng/mL)	1	0.003192831	0.003192831	0.379367924	0.538419882
BUN (mmol/L)	1	0.009191917	0.009191917	1.09217135	0.296852022
P1NP	1	0.004038559	0.004038559	0.479856197	0.489036128
Albumin (g/L)	1	0.000424258	0.000424258	0.050409786	0.822508235
PTH	1	0.008259481	0.008259481	0.98138053	0.322675597
Smoking	1	0.008411461	0.008411461	0.999438573	0.318271297
γ-GGT	1	0.00240644	0.00240644	0.285930002	0.593246104
UACR (mg/g)	1	0.0230165	0.0230165	2.734789877	0.099255341
Serum phosphorus	1	0.003185716	0.003185716	0.378522537	0.538872563
TOTAL	15	1.224772001	0.081651467	9.701718601	0
ERROR	293	2.465942452	0.008416186		

SCr: Serum creatinine; 25-(OH)VitD: 25-hydroxyvitamin D; BUN: blood urea nitrogen; P1NP: procollagen type I N-terminal propeptide; PTH: parathyroid hormone; γ-GGT: gamma-glutamyl transferase; UACR: urine albumin-creatinine ratio.

Supplementary Table 5. Multivariable logistic regression analysis of TyG-WWI and TBS deterioration

Index	Model	N	OR (95%CI)	P-value	AUC	AUC_95CI	Threshold_predicted_probability	Sensitivity	Specificity	Youden_J
TyG-WWI	Model 1	309	1.044 (1.021-1.067)	0.000149	0.636	0.563-0.708	0.28	0.543	0.711	0.254
TyG-WWI	Model 2	309	1.034 (1.008-1.06)	0.009985	0.819	0.765-0.874	0.42	0.617	0.899	0.516
TyG-WWI	Model 3	309	1.033 (1.006-1.061)	0.017026	0.83	0.778-0.883	0.361	0.667	0.868	0.535

Model 1: TyG-WWI only; Model 2: TyG-WWI + sex + age; Model 3: TyG-WWI + sex + age + RF-selected covariates (SCr ($\mu\text{mol/L}$), 25-(OH)VitD (ng/mL), BUN (mmol/L), P1NP, albumin (g/L), PTH, Smoking, γ -GGT, UACR (mg/g), serum phosphorus). N: Sample size; OR: odds ratio; CI: confidence interval; AUC: area under the receiver operating characteristic curve; Youden J: Youden index.

Supplementary Table 6. Logistic regression and ROC analysis of the association between TyG-WWI and TBS deterioration among postmenopausal women

Stratum	Model	N	Event_N	Non_event_N	Used_variables	OR	CI_Lower	CI_Upper	P_value	AUC	AUC_CI_Lower	AUC_CI_Upper
Postmenopausal	Model 1	13963	63	76	TyG-WWI	1.035	1.007	1.065	0.015	0.33	0.619	0.524
	2											
Postmenopausal	Model 2	13963	63	76	TyG-WWI + Age	1.026	0.994	1.058	0.110	0.3	0.758	0.676
	3											
Postmenopausal	Model 3	13963	63	76	TyG-WWI + Age + SCr (μmol/L) + 25-(OH)VitD (ng/mL) + BUN (mmol/L) + P1NP+ albumin (g/L) + PTH+γ-GGT + UACR (mg/g) +serum phosphorus	1.025	0.992	1.059	0.135	0.39	0.784	0.707

N: Sample size; Event_N: number of events; Non_event_N: number of non-events; OR: odds ratio; CI: confidence interval; AUC: area under the receiver operating characteristic curve.

Supplementary Table 7. Sensitivity analysis of the association between TyG-WWI and TBS in linear regression models

Variable	Model	Estimate	Std_Beta	Conf.low	Conf.high	P value	R2	Adj_R2	RMSE
TyG_WWI	Model 1	-0.0025	-0.2701	-0.0034	-0.0015	0.00000145	0.073	0.0699	0.1052
TyG_WWI	Model 2	-0.0018	-0.2022	-0.0027	-0.001	0.0000368	0.3035	0.2966	0.0912
TyG_WWI	Model 3	-0.0018	-0.1983	-0.0027	-0.0009	0.000109	0.3279	0.2983	0.0896
TyG_WWI	Model 3_Antidiabetic	-0.0018	-0.1981	-0.0027	-0.0009	0.000098	0.3466	0.3131	0.0883

Model 1 was unadjusted. Model 2 was adjusted for age and sex; Model 3: TyG-WWI + sex + age + RF-selected covariates [SCr ($\mu\text{mol/L}$), 25-(OH)VitD (ng/mL), BUN (mmol/L), P1NP, albumin (g/L), PTH, Smoking, γ -GGT, UACR (mg/g), serum phosphorus]. The sensitivity model was additionally adjusted for antidiabetic drugs based on Model 3. The stability of the association was evaluated by comparing the effect estimate of TyG-WWI between Model 3 and the sensitivity model. Std_Beta: Standardized beta coefficient; Conf. low: lower confidence limit; Conf. high: upper confidence limit; R²: coefficient of determination; Adj_R²: adjusted coefficient of determination; RMSE: root mean square error.

Supplementary Table 8. Multivariable linear regression analysis of TyG-WWI and Lumbar spine BMD (T-score)

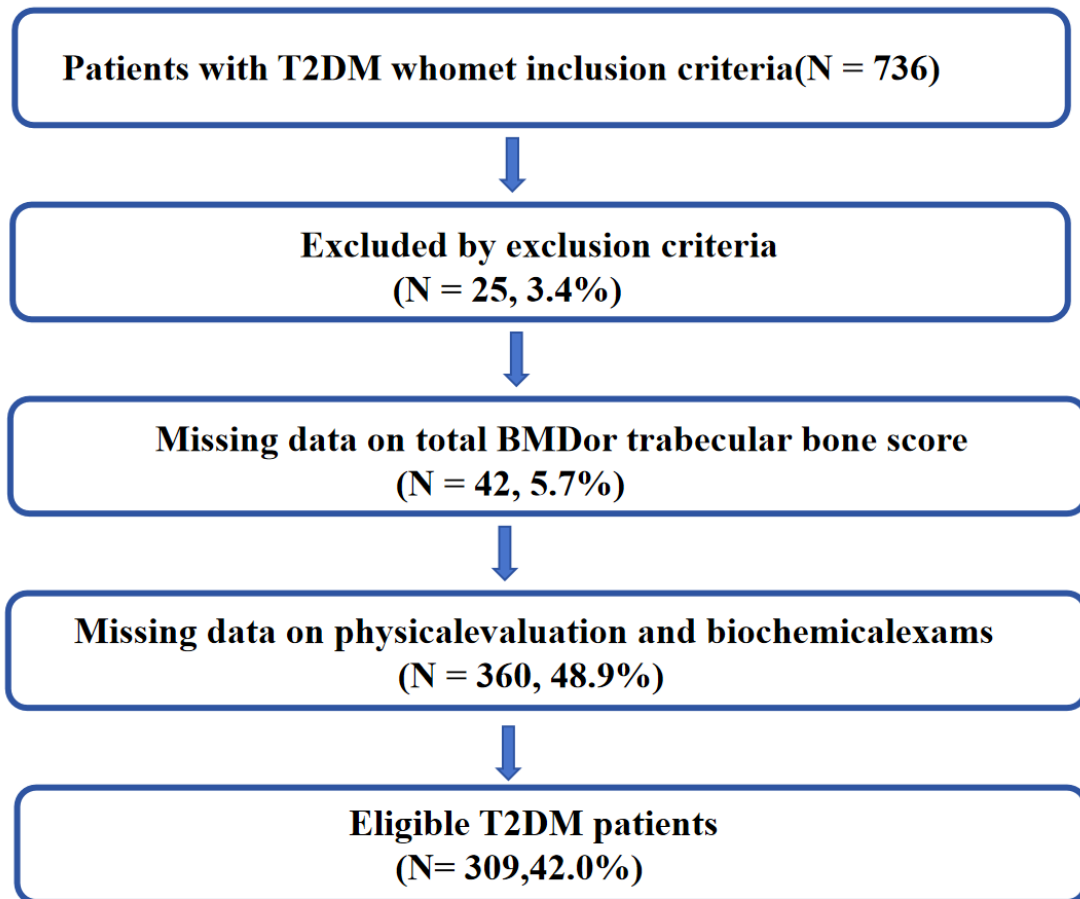
Model	Term	β (95%CI)	<i>P</i> value
Model 1	TyG-WWI	-0.0048 (-0.0193 to 0.0096)	0.509
Model 2	TyG-WWI	0.001 (-0.0128 to 0.0148)	0.883
	Sex: women	-0.861 (-1.196 to -0.526)	7.45E-07***
	Age	-0.021 (-0.037 to -0.006)	0.008*
Model 3	TyG-WWI	0.0007 (-0.0137 to 0.015)	0.926
	Age	-0.025 (-0.042 to -0.008)	0.0036**
	Sex: women	-1.001 (-1.447 to -0.556)	1.38E-05***
	SCr (μ mol/L)	-0.0005 (-0.001 to 0.0001)	0.113
	25-(OH)VitD (ng/mL)	-0.0065 (-0.0288 to 0.0159)	0.57
	BUN (mmol/L)	0.0476 (-0.0311 to 0.1263)	0.235
	P1NP	-0.0105 (-0.0204 to -0.0006)	0.0376*
	Albumin(g/L)	-0.0291 (-0.0773 to 0.019)	0.235
	PTH	-0.0018 (-0.0106 to 0.007)	0.684
	Smoking: yes	-0.2673 (-0.752 to 0.217)	0.278
	γ -GGT	-0.0015 (-0.0084 to 0.0054)	0.66
	UACR (mg/g)	-0.0002 (-0.0005 to 0.0001)	0.118
	Serum_phosphorus	0.0442 (-0.200 to 0.288)	0.721

* $P < 0.05$; ** $P < 0.01$; and *** $P < 0.001$. SCr: Serum creatinine; 25-(OH)VitD: 25-hydroxyvitamin D; BUN: blood urea nitrogen; P1NP: procollagen type I N-terminal propeptide; PTH: parathyroid hormone; γ -GGT: gamma-glutamyl transferase; UACR: urine albumin-creatinine ratio.

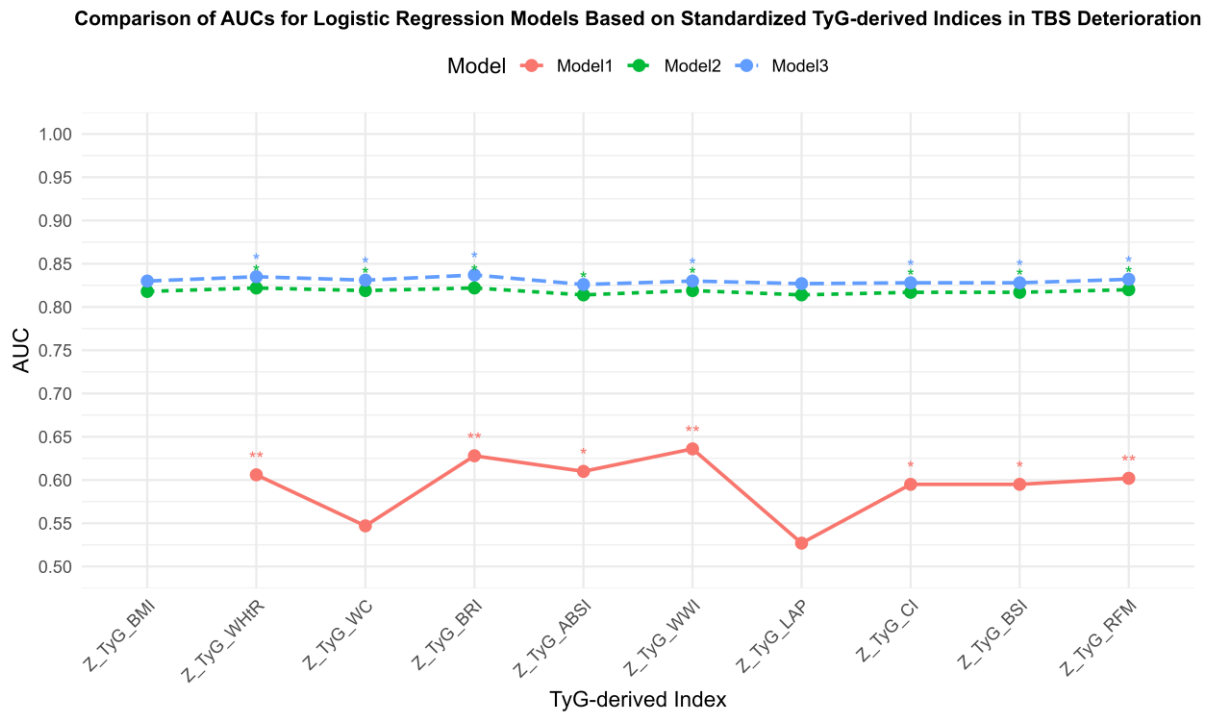
Supplementary Table 9. Analysis of the interaction of TyG-WWI and BMD with sex and age

Term	Estimate	Std.error	Statistic	<i>P</i> value	Conf.low	Conf.high
TyG- WWI:SexWo men	0.0169271 78	0.0144821 2	1.1688328 81	0.2434178 04	- 0.0115745 85	0.0454289 42
TyG- WWI:Age	- 0.0002217 4	0.0006053 03	- 0.3663296 51	0.7143825 86	- 0.0014130 16	0.0009695 36

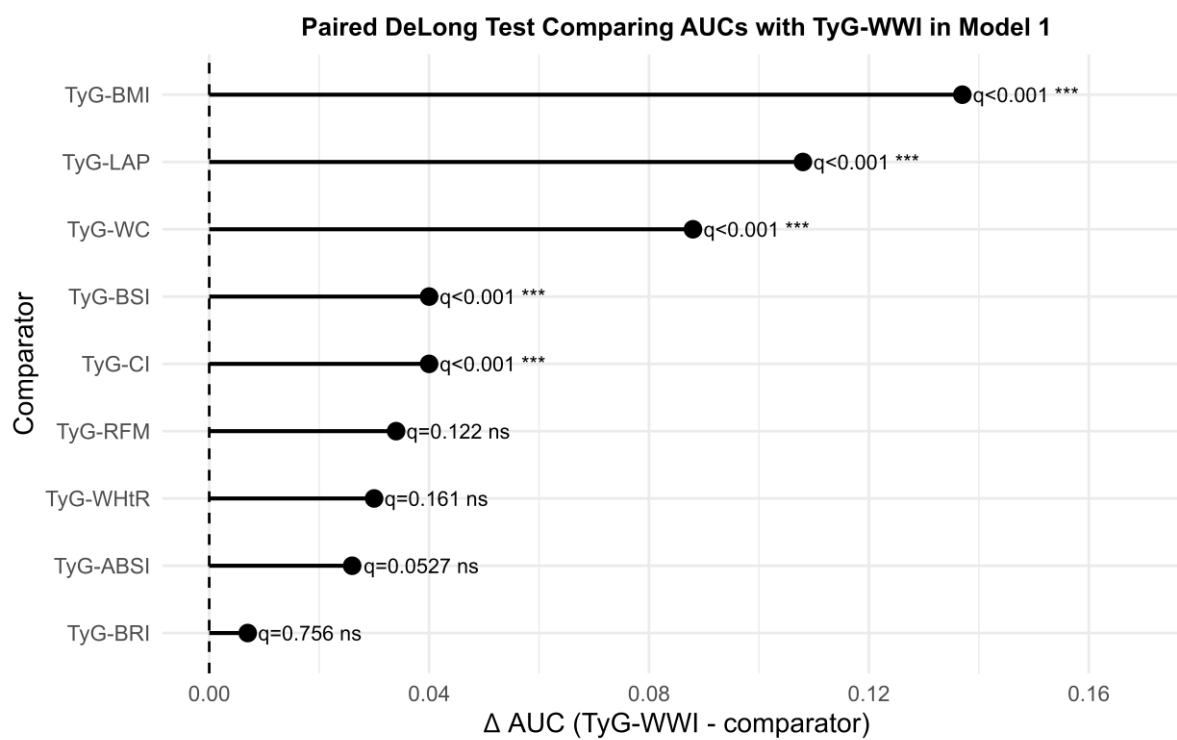
Std. error: Standard error; Conf. low: lower limit of the 95% confidence interval; Conf. high: upper limit of the 95% confidence interval.



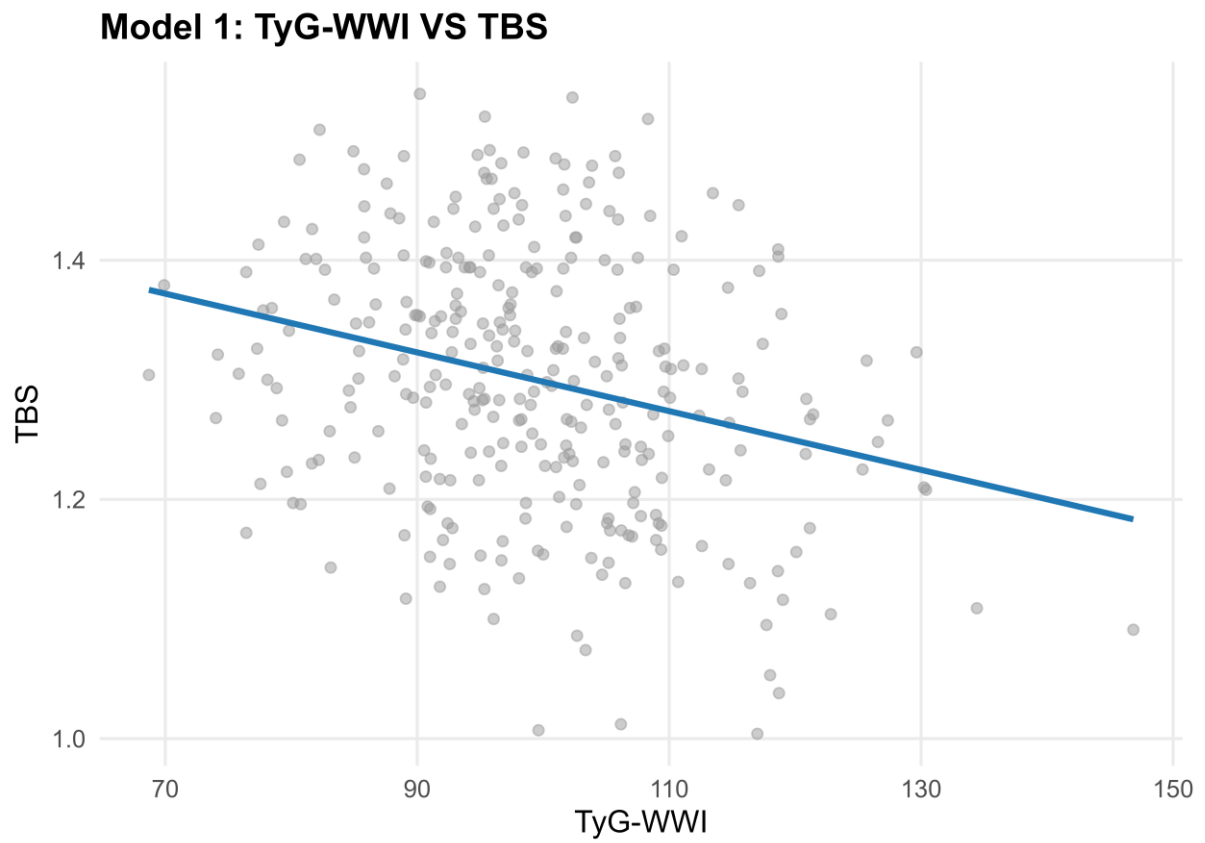
Supplementary Figure 1. Flowchart of recruitment.



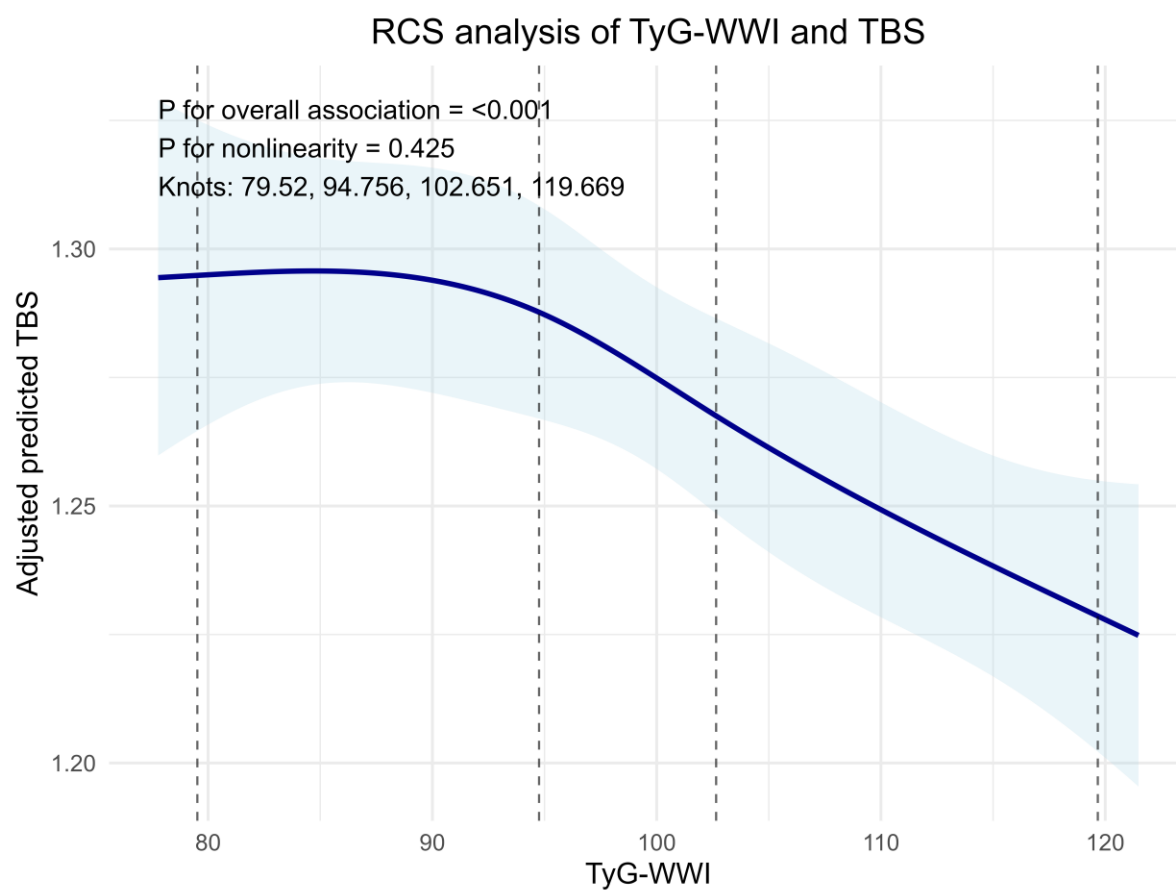
Supplementary Figure 2. Comparison of AUCs among logistic regression models based on standardized TyG-derived indices for identifying TBS deterioration.



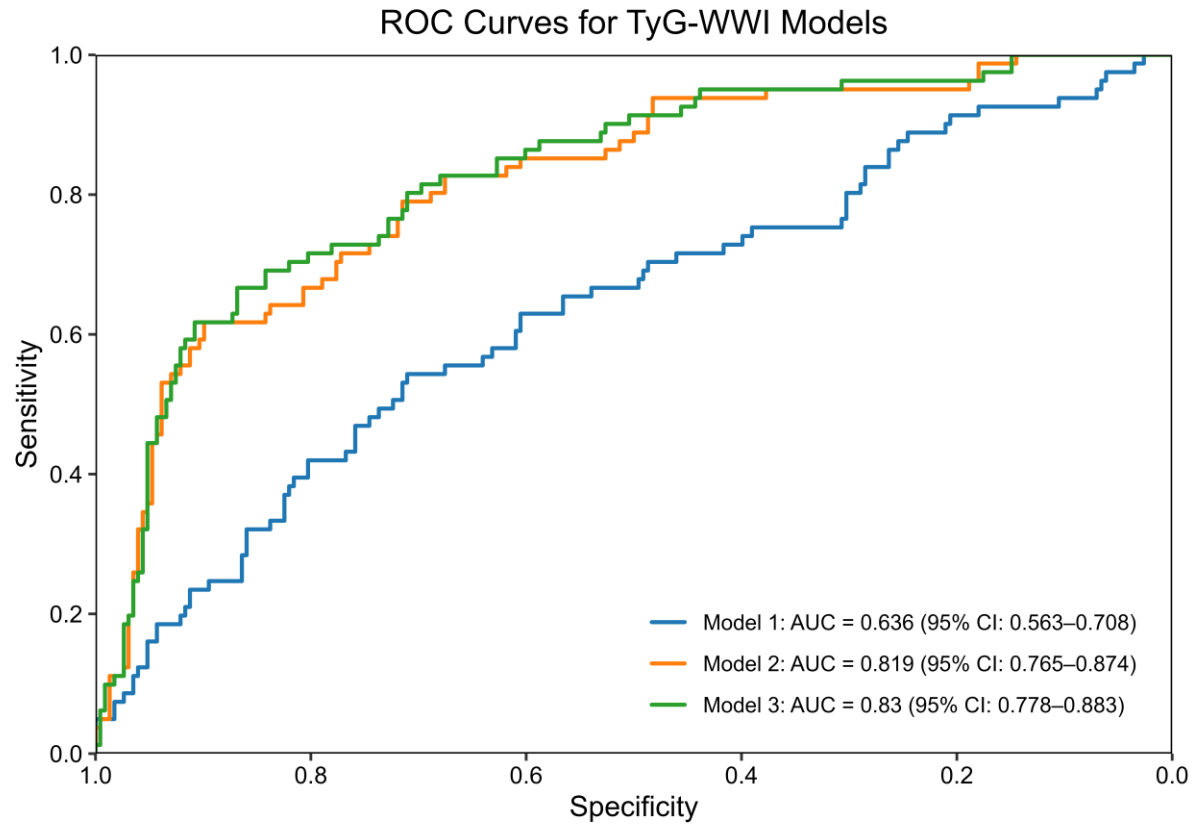
Supplementary Figure 3. Paired DeLong test comparing the AUC of TyG-WWI with other TyG-derived indices in Model 1.



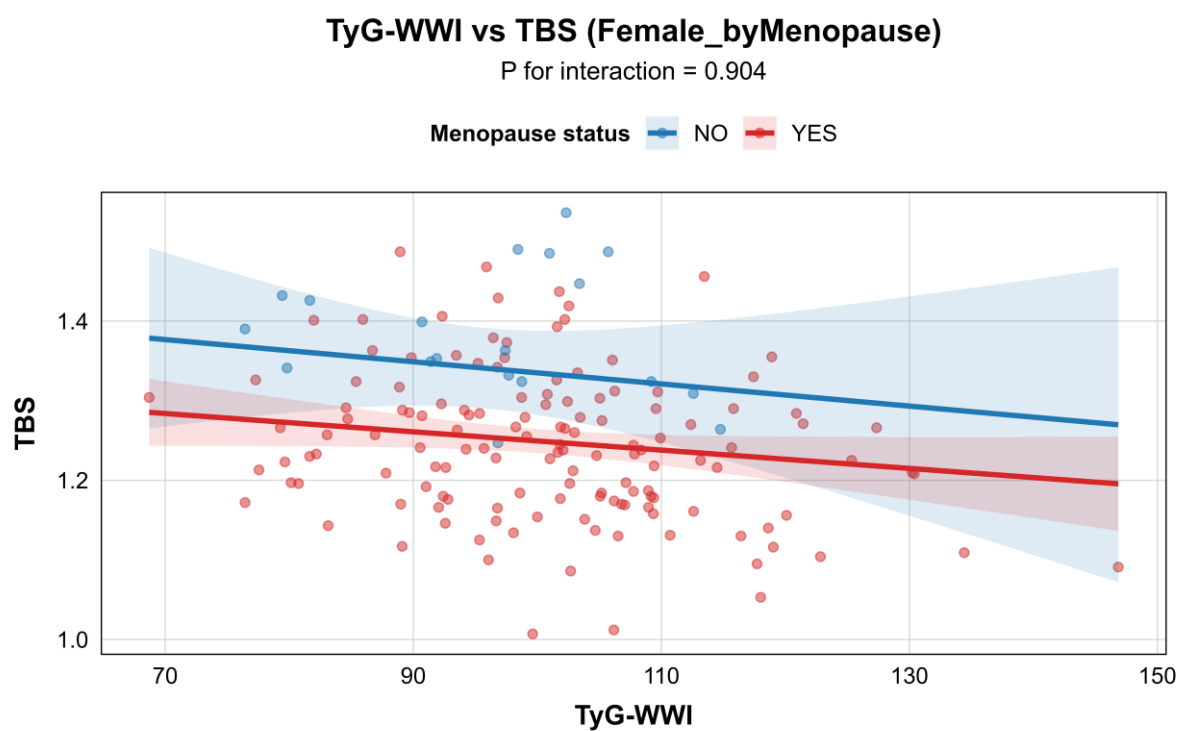
Supplementary Figure 4. Multivariable linear regression models evaluating the association between TyG-WWI and TBS.



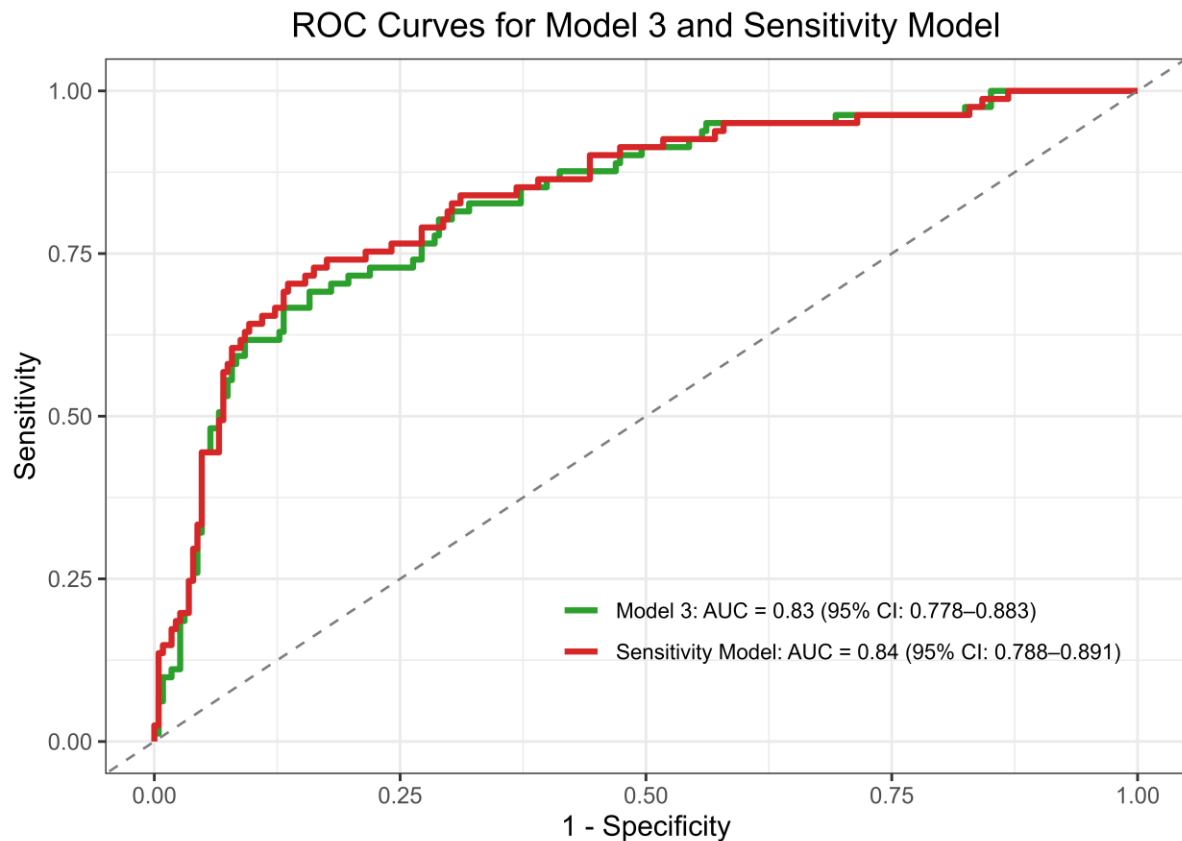
Supplementary Figure 5. Restricted cubic spline analysis of the association between TyG-WWI and TBS.



Supplementary Figure 6. ROC analysis of TyG-WWI for TBS deterioration.



Supplementary Figure 7. Interaction analysis of TyG-WWI and TBS by menopausal status.



Supplementary Figure 8. ROC curves for Model 3 and the sensitivity model in predicting TBS deterioration. Model 3: TyG-WWI + sex + age + RF-selected covariates (SCr ($\mu\text{mol/L}$), 25-(OH)VitD (ng/mL), BUN (mmol/L), P1NP, albumin (g/L), PTH, Smoking, γ -GGT, UACR (mg/g), serum phosphorus). The sensitivity model was additionally adjusted for antidiabetic drugs based on Model 3. The AUCs were comparable between Model 3 and the sensitivity model, suggesting stable predictive performance after further adjustment.