American Heart Journal Plus: Cardiology Research and Practice 61 (2026) 100684

Contents lists available at ScienceDirect

American Heart Journal Plus: Cardiology Research and Practice

journal homepage: www.sciencedirect.com/journal/american-heart-journal-plus-cardiology-research-and-practice

Research Paper

Triglyceride–glucose index predicts early, short-term, and long-term mortality after transcatheter aortic valve replacement

Haitham Abu Khadija [a], Duha Najajra [b], Mohammad Masu'd [b], Nizar Abu Hamdeh [b], Omar Ayyad [a], Ameer Mahamid [a], Max Bagan [c], Ali Abdullah [d,e], Jebrin Alkrinawi [a], Alaa Zayed [b], Abdalaziz Darwish [b], Aesha L.E. Enairat [b], Alena Kirzhner [f], Tal Schiller [g], Mohammad Alnees [a,b,h,*]

[a] Heart Center, Kaplan Medical Center, Rehovot, affiliated with the Hebrew University, Jerusalem, Israel
[b] Palestinian Clinical Research Center, Bethlehem, Palestine
[c] Adelson School of Medicine, Ariel University, Ariel, Israel
[d] Institute of Gastroenterology and Liver Disease, Kaplan Medical Center, affiliated with the Hebrew University, Jerusalem, Israel
[e] Department of Internal Medicine B, Kaplan Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel
[f] Department of Internal Medicine A, Kaplan Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Jerusalem, Israel
[g] Department of Diabetes, Endocrinology and Metabolism, Wolfson Medical Center and Gray Faculty of Medical and Health Sciences, Tel Aviv University, Israel
[h] Harvard Medical School, Postgraduate Medical Education, Global Clinical Scholar Research Training Program, Boston, United States

ARTICLE INFO

Keywords:
Transcatheter aortic valve replacement
TyG index
Insulin resistance
Mortality
Risk stratification

ABSTRACT

Background: Despite transforming care for severe aortic stenosis, TAVR is still followed by early and late mortality. The triglyceride–glucose (TyG) index, an insulin-resistance marker from routine triglyceride and glucose levels, may flag high-risk patients in Ashkenazi-Jewish and Mediterranean individuals. We examined whether baseline TyG predicts all-cause mortality at 30 days, 1 year, and 3 years post-TAVR.

Methods: We retrospectively studied patients with severe symptomatic aortic stenosis who underwent TAVR at a single tertiary center between 2010 and 2024. The TyG index was calculated from baseline triglyceride and glucose values. The primary endpoint was all-cause mortality at 1 year, with secondary endpoints of all-cause mortality at 30 days and 3 years. Cox proportional hazards models evaluated the association between TyG (per 1-unit increase) and mortality, adjusting for major clinical risk factors. Additionally, ROC curves were used to derive cohort-specific TyG thresholds for short-term and long-term mortality.

Results: Results: A total of 821 TAVR patients were included. All-cause mortality was 3.4 % at 30 days, 10.9 % at 1 year, and 19.7 % at 3 years. Higher baseline TyG was associated with significantly increased mortality risk at all time points. After multivariable adjustment, each 1-unit increase in TyG index conferred a higher hazard of 1-year death (adjusted HR 1.62, 95 % CI 1.21–2.16) and remained predictive of mortality at 30 days (HR 1.92, 95 % CI 1.08–3.42) and 3 years (HR 1.42, 95 % CI 1.14–1.77). ROC analysis identified distinct TyG thresholds for short-term and long-term outcomes, with an optimal cut-point of 9.012 for 30-day mortality, 9.15 for 1-year mortality, and 8.700 for 3-year mortality.

Conclusions: Baseline TyG index is an independent predictor of early, short-term, and long-term mortality after TAVR. The identification of cohort-specific TyG cut-points highlights population-specific metabolic risk calibration and supports the use of TyG as a simple and informative biomarker for refining risk stratification and follow-up intensity in TAVR recipients.

* Corresponding author at: Harvard Medical School, Postgraduate Medical Education, Global Clinical Scholar Research Training Program, Boston, United States.
E-mail address: a2011z2012z2013@gmail.com (M. Alnees).

https://doi.org/10.1016/j.ahjo.2025.100684
Received 20 September 2025; Received in revised form 16 November 2025; Accepted 24 November 2025
Available online 25 November 2025

1. Introduction

Transcatheter aortic valve replacement (TAVR) has redefined the management of severe aortic stenosis, expanding eligibility to lower-risk and younger patients and yielding excellent early outcomes with durable clinical benefit. Nonetheless, clinically meaningful adverse events still occur during the initial 30 days, including death. Contemporary registry data among low-risk patients records ~0.6–0.8 % 30-day mortality, and ~ 3–5 % mortality at 1 year; randomized and registry cohorts show sustainable benefits or non-inferiority versus surgery at 3 years for composite end points of death [1–3].

The triglyceride–glucose (TyG) index, expressed as ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL) / 2], is a convenient biomarker tracking insulin resistance and the downstream state of atherogenic dyslipidemia, endothelial dysfunction, and low-grade inflammation [4]. In cardiometabolic and cardiovascular populations, elevated TyG consistently links to elevated short- and long-term mortality [4,5]. Recent TAVR registries now link elevated baseline TyG to poor prognosis after valve implantation: multicenter and single-centered studies delineate stepwise hazards of all-cause mortality and major adverse cardiovascular events (MACE) through ~1 year, with incremental discrimination beyond clinical models; landmark analysis also attributes separation of early (≤30-day) outcomes by TyG categories [6–8]. High TyG denotes a state of greater insulin resistance with an adverse metabolic milieu (atherogenic dyslipidemia, endothelial dysfunction, low-grade inflammation); conversely, low TyG reflects more favorable insulin sensitivity and lower risk [7]. These associations provide a rationale for testing TyG as a 30-day, short-term (1 year), and long-term (3 years) prognostic marker in TAVR.

Within this context, metabolic and inflammatory biomarkers have emerged as promising tools for risk prediction. The TyG index, a composite parameter derived from fasting triglyceride and glucose levels, reflects underlying insulin resistance and broader metabolic dysfunction. Previous studies have suggested its value in cardiovascular risk stratification; however, its role in predicting adverse outcomes among TAVR recipients remains incompletely understood [6–8].

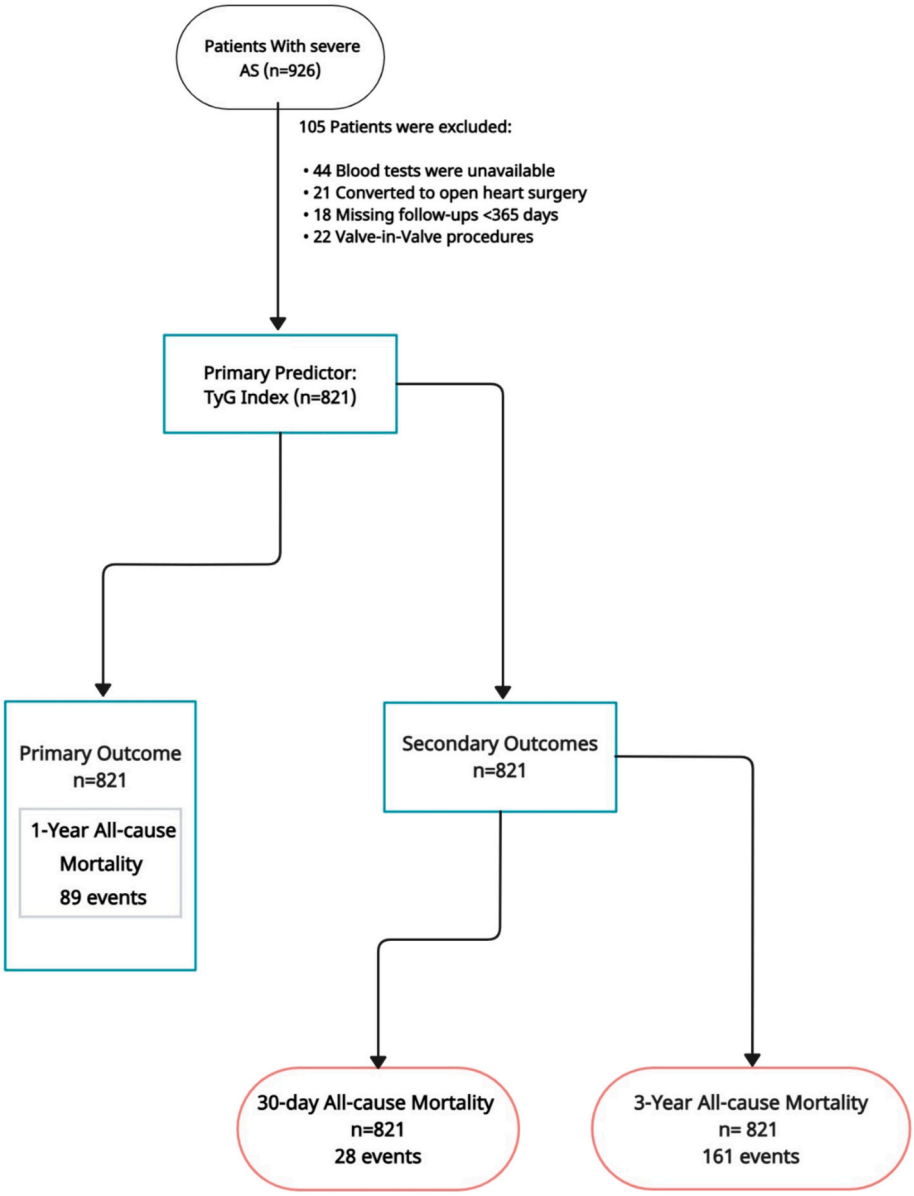

Fig. 1. Flowchart of patient inclusion, exclusion, and follow-up for primary and secondary. outcomes.

Although prior studies from Chinese TAVR cohorts have demonstrated an association between the TyG index and adverse outcomes, these data are limited to East Asian populations and short- to mid-term follow-up [9,10]. Important ethnic and metabolic differences suggest that TyG-related risk thresholds may not be directly generalizable to Western patients. Building on this background, the present study extends the existing evidence by evaluating the prognostic impact of TyG in a Western TAVR population of Ashkenazi-Jewish and Mediterranean origin, with dedicated analyses of 30-day, 1-year, and 3-year mortality and the derivation of population-specific TyG cut-off values using ROC methodology.

2. Method

2.1. Study design and population

This study is a retrospective, longitudinal cohort analysis of consecutive patients who underwent TAVR at the Heart Center of Kaplan Medical Center, Israel, between December 2010 and March 2024. Inclusion criteria were age $\geq$ 18 years, severe symptomatic aortic stenosis treated with TAVR during the study period, and availability of baseline pre-procedural triglyceride and glucose measurements from which the triglyceride–glucose (TyG) index was computed as ln ([triglycerides (mg/dL) $\times$ glucose (mg/dL)]/2). We excluded 105 patients for the following reasons: 44 without the requisite baseline blood tests (precluding TyG calculation), 21 who converted to open-heart surgery before or during the index procedure, 18 with insufficient follow-up (<365 days) for 1-year survival ascertainment, and 22 who underwent valve-in-valve procedures. The final analytic cohort comprised 821 patients for the 30-day and 1-year endpoints. For the 3-year endpoint, 266 patients lacked complete 3-year follow-up and were excluded, yielding a 3-year analysis cohort of 555 patients. The cohort assembly is shown in Fig. 1.

2.2. Procedural details

All TAVR procedures were performed via the transfemoral approach using the safety-wire technique. Vascular access and closure were achieved with the Prostar XL vascular closure system (Abbott Vascular, Redwood City, CA, USA). Procedures were conducted in hybrid operating rooms under either general anesthesia or local anesthesia with conscious sedation, with the latter being the standard approach.

Procedure duration was defined as the time from arterial puncture ("skin") to vascular closure ("skin"). After femoral access, unfractionated heparin was administered to maintain an activated clotting time (ACT) >250 s; when indicated, Protamine sulfate was given at the time of vascular closure (maximum dose 50 mg; 1 mg per 100 units of heparin administered). In accordance with European Society of Cardiology guidelines, dual antiplatelet therapy (DAPT) with Aspirin 100 mg or Clopidogrel 75 mg was initiated one day before the procedure, unless patients were already on chronic antiplatelet or oral anticoagulation therapy. Valve deployment was guided fluoroscopically, aiming for a final implantation depth of approximately 2–3 mm below the annular plane, consistent with current best practices.

2.3. Study endpoints

The primary endpoint was all-cause mortality at 1 year following TAVR. Secondary endpoints included all-cause mortality at 30 days (early mortality) and at 3 years (long-term mortality). Mortality was defined as death from any cause, and survival time was calculated from the date of the TAVR procedure to the date of death or last known follow-up. Outcomes at 30 days and 1 year were assessed in all 821 patients, while 3-year outcomes were evaluated in patients with available longer follow-up. The median follow-up duration for the study cohort was 2189 days (IQR: 643–2189 days), with a mean of 1510.9 $\pm$ 852.6 days.

2.4. Rationale for maintaining a separate 1-year mortality model

One-year mortality after TAVR was analyzed in a dedicated Cox model because it represents a clinically distinct and internationally standardized benchmark endpoint. Major TAVR trials and registries—including PARTNER 1 & 2, and the STS/ACC TVT Registry—consistently report 30-day and 1-year mortality as standalone clinical outcomes, as these intervals reflect early and mid-term procedural performance, patient selection, and peri-procedural physiology distinct from long-term prognosis [11–13].

Predictors of 1-year mortality often differ from those that drive outcomes beyond the first year, as later mortality is more strongly influenced by chronic comorbidities, heart-failure progression, and long-term metabolic risk profiles [14,15]. Therefore, integrating the 1-year period into a single 3-year model may obscure meaningful changes in risk trajectories. For these reasons, and in alignment with international standards (VARC-3 criteria) [16].

2.5. Primary predictor: TyG Index

The primary Predictor variable is the **Triglyceride-Glucose (TyG) index**, a continuous measure calculated from each patient's preoperative lab values. For each patient, we obtained the fasting triglyceride (TG) level (in mg/dL) and fasting plasma glucose (FPG) level (in mg/dL) from routine preoperative evaluation. Using these, TyG can be computed as:

$$\text{TyG index} = \text{Ln}\,(\text{fasting triglycerides [mg/dL] x fasting glucose [mg/dL]})/2 \text{ or TyG index} = \text{Ln}\,(\text{fasting triglycerides [mmol/L] x 88.57 x fasting glucose [mmol/L] x 18})/2)$$

where ln is the natural logarithm [17]. This formula (originally proposed by Guerrero-Romero et al.) effectively combines the two values; higher TyG indicates higher TG and glucose, thus more pronounced insulin resistance [18].

Although the TyG index was analyzed as a continuous variable in all primary and secondary analyses, for visualization purposes, we categorized the TyG index into tertiles (low, medium, high) and generated Kaplan–Meier survival curves for 1-year all-cause mortality.

2.6. Statistical analysis

All statistical analyses were performed using Stata (version 17; StataCorp, College Station, TX, USA). A two-sided p-value <0.05 was considered statistically significant. Continuous variables were assessed for normality using visual inspection of Box plots and the Shapiro–Wilk test. Normally distributed variables were presented as mean $\pm$ standard deviation (SD) and compared using Student's t-test, while non-normally distributed variables were summarized as median (Q1-Q3) and compared using the Mann–Whitney U test. Categorical variables were presented as counts (percentages) and compared using Fisher's exact test or Chi-square test, as appropriate.

For the primary endpoint of 1-year all-cause mortality, 89 events were observed, and the multivariable model included 9 covariates, resulting in an EPV of approximately 9.8. This satisfies commonly accepted methodological criteria for model stability and precision. *Supplement 1, eAppendix 1*.

TyG cut-off values for 30-day, 1-year, and 3-year mortality were derived using ROC analysis and Youden's J statistic, yielding thresholds of 9.01, 9.15, and 8.70, respectively. Full details are provided in Supplement 1, eAppendix 2.

For survival analysis, time-to-event data were calculated from the date of TAVR to death or censoring at the last follow-up. The primary

endpoint was 1-year all-cause mortality; secondary endpoints were 30-day and 3-year all-cause mortality.

Univariate Cox proportional hazards regression models were first fitted to explore associations between each candidate predictor and 1-year all-cause mortality. Variables with $p < 0.10$ in univariate analyses and those with strong clinical relevance were considered for multivariable modeling [19–22]. The main predictor of interest, the Triglyceride-Glucose index (TyG index), was analyzed as a continuous variable (per 1-unit increase).

To avoid model overfitting and account for the limited number of events (89 deaths), the ratio of at least 10 events per covariate was maintained. In addition, a Least Absolute Shrinkage and Selection Operator (LASSO) regression with 10-fold cross-validation was performed to aid in variable selection and reduce collinearity. Candidate covariates identified from LASSO and univariate analyses were entered into **multivariable Cox proportional hazards models** adjusted for age, atrial fibrillation, total cholesterol, septum thickness, mean aortic valve gradient, procedural time, PR interval, annulus area, and annulus perimeter.

Hazard ratios (HR) with 95 % confidence intervals (CI) were reported. Proportional hazards were evaluated using Schoenfeld residuals for all Cox models. The primary exposure, the TyG index modeled as a continuous variable, fulfilled the proportional hazards assumption. For visualization purposes, the TyG index was additionally categorized into tertiles and plotted using Kaplan–Meier survival curves to compare survival across groups. To explore the functional form of the continuous TyG index, we fitted adjusted restricted cubic spline Cox proportional hazards models. Because spline modeling requires adequate statistical power to ensure stable estimation, we performed this analysis using the 3-year mortality outcome, which provided 161 events, exceeding commonly recommended thresholds (>100 events) for flexible spline modeling. Endpoints 30-day and 1-year mortality were not analyzed using splines due to insufficient event counts, which would increase the risk of overfitting and unstable curvature. Following established recommendations, four knots were placed at the empirical percentiles of the TyG index distribution (5th, 35th, 65th, 95th), corresponding to values 5.616, 8.178, 8.739, and 9.622. This specification balances flexibility with parsimony and ensures sensitivity to potential curvature without introducing unnecessary model complexity. The spline was incorporated into the adjusted Cox regression model using three spline components (k–1), and the model was adjusted for the same covariates used in multivariable analysis to maintain comparability.

Only 0.3 % had missing values in baseline covariates included in the multivariable models. Given the extremely low proportion of missingness, these values were imputed using mean substitution, an approach considered acceptable when missingness is minimal and unlikely to affect model estimates. Finally, all models' reporting followed TRIPOD guidance for multivariable prediction modeling [23].

2.7. Ethical considerations

The study was approved by the local IRB committee (0091–20-KMC), with a waiver of informed consent due to the retrospective use of de-identified clinical data. All procedures were in accordance with the ethical standards of the Helsinki Declaration. The conduct and reporting of this observational study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Patient confidentiality was maintained throughout, and all data were stored on secure servers with access limited to the research team.

3. Results

Of the 821 included patients, 732 survived and completed the full follow-up period of 365 days, while 89 patients died during follow-up with a median follow-up of 89 days [IQR 20–236]. Baseline characteristics stratified by 1-year all-cause mortality are shown in Table 1.

Table 1
Baseline demographics, comorbidities, laboratory, echocardiographic, procedural, and electrocardiographic characteristics stratified by 1-year all-cause mortality.

Variable	Category	1-year all-cause mortality		
		Alive $N = 732$ (%)	Dead $N = 89$(%)	*P* value
Demographic data				
Age, y	**Mean ± SD**	80.825 ± 7.175	82.820 ± 6.348	**0.012[a]**
Gender n, %	**Female**	399(54.51)	40(44.94)	0.092[b]
BMI, kg/m^2	**Mean ± SD**	28.33 ± 5.086	27.439 ± 5.384	0.121[a]
BSA, m^2	**Mean ± SD**	1.838 ± 0.210	1.833 ± 0.220	0.846[a]
STS Score	**Mean ± SD**	6.8 ± 4.2	7.2 ± 4.5	0.45[a]
Medical history				
Diabetes mellitus	**Yes**	324 (44.3)	46 (51.69)	0.203[b]
Hypertension	**Yes**	649 (88.7)	79 (88.76)	0.884[b]
Smoker	**Yes**	113 (15.4)	14 (15.73)	0.963[b]
Dyslipidemia	**Yes**	574 (78.4)	69 (77.53)	0.756[b]
Atrial fibrillation	**Yes**	206 (28.1)	45 (50.56)	**<0.001[b]**
Coronary artery disease (CAD)	**Yes**	303 (41.4)	41 (46.07)	0.429[b]
Peripheral vascular disease (PVD)	**Yes**	97 (13.3)	17 (19.10)	0.139[b]
Medication				
Insulin	**Yes**	66 (9.0 %)	6 (6.7 %)	0.464[b]
Oral diabetic	**Yes**	228 (31.1 %)	18 (20.2 %)	0.064[b]
Statins	**Yes**	549 (75.0 %)	70 (78.7 %)	0.477[b]
Statin intensity (only among users)				
Low/moderate	**Yes**	318 (57.9 %)	38 (54.3 %)	0.562 b
High	**Yes**	231 (42.1 %)	32 (45.7 %)	
Adherence (3 months)	**Yes**	559 (95.9 %)	62 (95.4 %)	0.849b
Laboratory				
White blood cells (K/μL)	**Mean ± SD**	5.54 ± 3.71	6.44 ± 4.36	**0.035[a]**
Platelets (K/μL)	**Mean ± SD**	198.0 ± 71.6	190.1 ± 94.2	0.343[a]
Total cholesterol (mg/dl)	**Mean ± SD**	139.0 ± 39.2	129.8 ± 40.6	**0.036[a]**
Total protein (g/dl)	**Mean ± SD**	6.19 ± 1.03	6.11 ± 0.85	0.476[a]
Creatinine (mg/dl)	**Mean ± SD**	1.12 ± 0.78	1.30 ± 0.91	**0.043[a]**
TyG Index	**Mean ± SD**	7.958 ± 1.436	8.460 ± 1.289	**0.001[a]**
Echocardiography				
Septum thickness (mm)	**Mean ± SD**	11.13 ± 4.02	12.09 ± 3.51	**0.032[a]**
LVEF%	**Median(Q1-Q3)**	55 (44–60)	50 (33–55)	0.865[C]
Aortic valve peak **gradient (mm Hg)**	**Median(Q1-Q3)**	54 (38–60)	71 (51–71)	**<0.001[C]**
Aortic valve mean **gradient (mm Hg)**	**Median(Q1-Q3)**	64 (43–82)	70 (53–80)	0.143[C]
Aortic valve area (cm^2)	**Median(Q1-Q3)**	0.7 (0.6–0.8)	0.7 (0.6–0.8)	0.841[C]
Procedural parameters				
Valve type	**SEV vs. BEV**	490 (66.9)	61 (68.5)	0.762[b]
Valve size	**Mean ± SD**	27.2 ± 2.7	27.1 ± 2.8	0.683[a]
Post dilatation	**Yes**	206 (28.1)	32 (36.0)	0.125b
Procedural time (m)	**Median(Q1-Q3)**	73 (60–94)	81 (61–110)	**0.018[a]**
Contrast medium volume (mL)	**Median(Q1-Q3)**	100 (80–140)	119 (70–150)	0.527[a]
Electrocardiography & CT				
PR Interval (ms)	**Mean ± SD**	185.4 ± 23.8	192.7 ± 23.2	**0.006[a]**
QTc Interval (ms)	**Mean ± SD**	440.3 ± 26.2	443.5 ± 26.3	0.269[a]

(*continued on next page*)

Table 1 (*continued*)

Variable	Category	1-year all-cause mortality		
		Alive $N = 732$ (%)	Dead $N = 89$(%)	*P* value
RBBB	**Yes**	18 (2.5)	2 (2.3)	0.903[b]
LBBB	**Yes**	16 (2.2)	4 (4.5)	0.182[b]
LAHB	**Yes**	82 (11.2)	12 (13.5)	0.523[b]
QRS duration	**Mean ± SD**	106.8 ± 21.9	111.5 ± 22.8	0.060[a]
LVOT calcification	None/Mild Moderate/ Severe	651 (88.9) 81 (11.1)	85 (95.5) 4 (4.5)	0.064[b]
Annulus area (mm2)	Mean ± SD	336.4 ± 148.1	397.2 ± 111.4	**<0.001[a]**
Annulus perimeter (mm)	Mean ± SD	59.3 ± 19.1	66.9 ± 14.9	**<0.001[a]**

Values are expressed as mean ± SD, median (IQR), or No. (%). P values were calculated using t test[a], Fisher's exact test[b], or Mann–Whitney U test[c], as appropriate.

Patients who died were older (82.8 ± 6.3 vs 80.8 ± 7.2 years, $p = 0.012$) and had a higher prevalence of atrial fibrillation (50.6 % vs 28.1 %, $p < 0.001$). Laboratory data showed higher creatinine (1.30 ± 0.91 vs 1.12 ± 0.78 mg/dl, $p = 0.043$) and higher TyG index (8.46 ± 1.29 vs 7.96 ± 1.44, $p = 0.001$) among non-survivors, whereas total cholesterol was lower (129.8 ± 40.6 vs 139.0 ± 39.2 mg/dl, $p = 0.036$).

On echocardiography, non-survivors demonstrated greater septal thickness (12.1 ± 3.5 vs 11.1 ± 4.0 mm, $p = 0.032$), larger annulus area (397.2 ± 111.4 vs 336.4 ± 148.1 mm^2, $p < 0.001$), and larger annulus perimeter (66.9 ± 14.9 vs 59.3 ± 19.1 mm, $p < 0.001$). Aortic valve peak gradient was also higher (71 vs 54 mmHg, $p < 0.001$). Procedural time was longer in the mortality group (median 81 vs 73 min, $p = 0.018$).

Electrocardiographic analysis revealed a significantly longer PR interval (192.7 ± 23.2 vs 185.4 ± 23.8 ms, $p = 0.006$). Although QRS duration was slightly longer in non-survivors (111.5 ± 22.8 vs 106.8 ± 21.9 ms), the difference did not reach statistical significance ($p = 0.060$).

Fig. 2 shows the Kaplan–Meier survival curves for 1-year all-cause mortality stratified by TyG index tertiles (Low, Medium, High). Patients were categorized into three groups based on their baseline TyG index: group 1 (TyG < 8.14, $n = 272$), group 2 (8.14 ≤ TyG ≤ 8.75, n = 272), and group 3 (TyG > 8.75, n = 272). Patients in the highest TyG tertile exhibited a notably lower survival probability compared with those in the medium and low tertiles throughout the follow-up period. For the TyG index assessed as a continuous predictor, the proportional hazards assumption was not violated (Schoenfeld test $\chi^2 = 0.58$, $p = 0.445$). In contrast, the tertile-based TyG groups showed evidence of non-proportionality, consistent with the limitations of arbitrary categorization.

Table 2 presents Univariate Cox regression that identified several predictors of 1-year all-cause mortality. Age (HR 1.04, 95 % CI 1.01–1.08, $p = 0.011$), atrial fibrillation (HR 2.34, 95 % CI 1.54–3.54, $p < 0.001$), higher TyG index (HR 1.34, 95 % CI 1.11–1.61, $p = 0.002$), septal thickness (HR 1.06, 95 % CI 1.01–1.13, $p = 0.032$), AV mean gradient (HR 1.03, 95 % CI 1.02–1.03, $p < 0.001$), longer procedural time (HR 1.008, 95 % CI 1.003–1.013, $p = 0.003$), prolonged PR interval (HR 1.010, 95 % CI 1.003–1.018, $p = 0.006$), larger annulus area (HR 1.003, 95 % CI 1.001–1.005, $p < 0.001$), and perimeter (HR 1.028, 95 % CI 1.013–1.043, $p < 0.001$) were significantly associated with increased mortality. Conversely, higher total cholesterol was inversely associated with risk (HR 0.99, 95 % CI 0.99–1.00, $p = 0.034$). Other variables, including BMI, hypertension, CAD, and LVEF, did not reach statistical significance.

During follow-up, all-cause mortality occurred in 28 patients (3.4 %) at 30 days, 89 patients (10.9 %) at 1 year, and 161 patients (19.7 %) at 3 years after TAVR. In unadjusted Cox regression analyses, a higher TyG index was significantly associated with an increased risk of death at all time points (30-day HR 1.76, 95 % CI 1.17–2.64; 1-year HR 1.34, 95 % CI 1.11–1.61; 3-year HR 1.40, 95 % CI 1.21–1.61).

After multivariable adjustment for major clinical, laboratory,

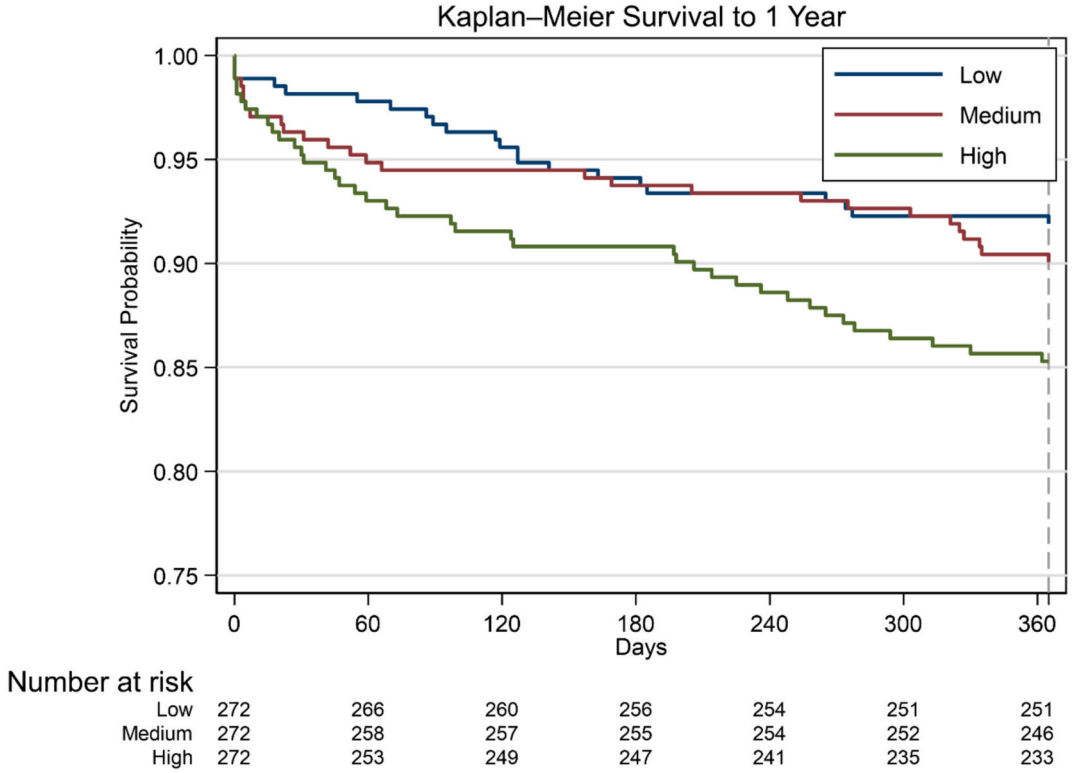

Fig. 2. Kaplan–Meier survival curves by TyG Index tertiles.

Table 2
Univariate Cox regression analysis for predictors of 1-year all-cause mortality after TAVR.

Variable	References	1-year all-cause mortality	
		HR (95 % CI)	P value
Demographic data			
Age, y (per year)		1.04 (1.01–1.08)	**0.011**
Gender n, %	**Female**	1.42 (0.93–2.15)	0.101
BMI, kg/m^2 (per unit)		0.97 (0.92–1.01)	0.116
BSA, m^2 (per unit)		0.89 (0.33–2.38)	0.814
Medical history			
Diabetes mellitus	**No**	1.29 (0.85–1.96)	0.228
Hypertension	**No**	0.96 (0.50–1.85)	0.896
Smoker	**No**	1.01 (0.57–1.79)	0.966
Dyslipidemia	**No**	0.92 (0.56–1.52)	0.752
Atrial fibrillation	**No**	2.34 (1.54–3.54)	**<0.001**
Coronary artery disease (CAD)	**No**	1.17 (0.77–1.78)	0.449
Peripheral vascular disease (PVD)	**No**	1.48 (0.87–2.51)	0.148
Laboratory			
White blood cells (K/μL, per unit)		1.06 (1.01–1.13)	**0.029**
Platelets (K/μL, per unit)		1.00 (0.995–1.002)	0.363
Total cholesterol (mg/dl, per unit)		0.99 (0.99–1.00)	**0.034**
Total protein (g/dl, per unit)		0.93 (0.76–1.14)	0.470
Creatinine (mg/dl, per unit)		1.18 (1.00–1.39)	0.054
TyG Index (per unit)		1.34 (1.11–1.61)	**0.002**
Echocardiography			
Septum thickness (mm)		1.06 (1.01–1.13)	**0.032**
LVEF%		0.99 (0.97–1.01)	0.157
Aortic valve peak **gradient (mm Hg)**		1.00 (0.99–1.01)	0.228
Aortic valve mean **gradient (mm Hg)**		1.03 (1.02–1.03)	**<0.001**
Aortic valve area(mm)		1.40 (0.65–3.01)	0.392
Procedural parameters			
Valve type	SEV vs BEV	0.935 (0.598–1.462)	0.767
Valve size		0.982 (0.908–1.062)	0.652
Post dilatation	**No**	1.412 (0.916–2.177)	0.118
Procedural time (m)		**1.008 (1.003–1.013)**	**0.003**
Contrast medium volume (mL)		1.001 (0.997–1.005)	0.653
Electrocardiography & CT			
PR Interval (ms, per ms)		**1.010 (1.003–1.018)**	**0.006**
QTc Interval (ms, per ms)		1.004 (0.997–1.012)	0.241
RBBB	**No**	0.938 (0.231–3.809)	0.928
LBBB	**No**	2.104 (0.772–5.735)	0.146
LAHB	**No**	1.227 (0.668–2.254)	0.510
QRS duration (ms, per ms)		1.008 (1.000–1.017)	0.060
LVOT calcification (moderate/severe vs none/mild)		0.391 (0.143–1.065)	0.066
Annulus area (mm^2, per mm^2)		**1.003 (1.001–1.005)**	**<0.001**
Annulus perimeter (mm, per mm)		**1.028 (1.013–1.043)**	**<0.001**

Values are presented as Hazard Ratio (HR) with 95 % Confidence Interval (CI).

echocardiographic, and procedural variables, the TyG index remained independently associated with mortality. The adjusted hazard ratios were 1.92 (95 % CI 1.08–3.42) for 30-day mortality, 1.62 (95 % CI 1.21–2.16) for 1-year mortality, and 1.42 (95 % CI 1.14–1.77) for 3-year mortality. These results present Table 3 and Fig. 3.

The full adjusted models for each endpoint are reported in Supplement 1 (eTables 1–3).

In Kaplan–Meier analysis, patients with higher TyG index exhibited substantially lower 3-year survival compared with those in the low and medium TyG groups (Fig. 4). Survival curves separated early during follow-up and continued to diverge over time. The log-rank test confirmed a significant difference in 3-year all-cause mortality across TyG categories ($p < 0.001$).

The findings of the spline analysis are summarized in Table 4 and visualized in Fig. 5. None of the individual spline components reached statistical significance, and the formal test for non-linearity was not statistically significant ($p = 0.123$). This indicates that there is no strong evidence supporting a non-linear association. However, the overall effect of TyG index remained statistically significant ($p = 0.001$), confirming a robust relationship between higher TyG values and increased 3-year mortality risk. The extremely wide confidence interval of the highest spline term is a known artifact of spline modeling when few observations exist at the upper tail of the distribution. This reflects numerical instability rather than a clinically meaningful signal. The spline curve (Fig. 5) shows a relatively flat risk profile at lower-to-mid TyG values, with a gradual upward trajectory beginning near the median (TyG = 8.65). Although visually suggestive of mild curvature, the formal statistical test indicates that a linear specification adequately describes the association.

4. Discussion

This study demonstrates that a readily obtainable metabolic marker, the triglyceride–glucose (TyG) index, conveys clinically relevant prognostic information across the full post-TAVR horizon. In a contemporary TAVR cohort, higher baseline TyG was independently and consistently associated with greater early (30-day) mortality, worse short-term (1-year) outcomes, and higher long-term (3-year) mortality. In contrast, lower TyG tracked with more favorable trajectories.

Pathobiologically, an elevated TyG index denotes systemic insulin resistance that amplifies three interlocking axes of risk highly relevant to post-TAVR prognosis. First, it drives atherogenic dyslipidemia via hepatocellular de-novo lipogenesis and SREBP-1c–mediated VLDL overproduction, coupled with adipose-tissue insulin resistance that impairs lipoprotein-lipase–mediated triglyceride clearance; cholesteryl-ester transfer then enriches LDL with triglycerides, accelerating hepatic lipase–dependent remodeling into small, dense LDL and attenuating HDL functionality (reduced cholesterol efflux capacity and paraoxonase-1 activity). These apoB-laden particles and dysfunctional HDL contribute to diffuse and complex coronary atherosclerosis, a substrate that independently predicts adverse survival after TAVR and is associated with higher TyG in clinical cohorts [6,7,24]. Second, hyperglycemia and excess free fatty acids promote endothelial dysfunction through reactive-oxygen–mediated nitric-oxide quenching and eNOS uncoupling, PKC activation, and AGE–RAGE signaling, with concomitant glycocalyx shedding and a prothrombotic shift (PAI-1, von Willebrand factor); concordantly, endothelial-injury biomarker profiles (e.g., vWF) correlate with increased 1-year mortality after TAVR [25,26]. Third, insulin-resistant adipose and innate-immune activation sustain low-grade inflammation (NF-κB/NLRP3 signaling with downstream IL-6, TNF-α, and CRP), impairing myocardial energetic recovery and vascular remodeling; in TAVR populations, elevated pre-procedural CRP, higher CRP-to-albumin ratio, and peri-procedural systemic inflammatory responses each associate with greater mortality during follow-up [27–37]. Taken together, these data support TyG as a proxy for a high-risk metabolic–endothelial–inflammatory milieu not fully

Table 3
Association of TyG Index with all-cause mortality after TAVR.

	All-cause mortality					
	30-day all-cause mortality *N* = 821[a] 28 events		1-year all-cause mortality *N* = 821[a] 89 events		3-year all-cause mortality N = 821[a] 161 events	
Predictor	HR (95 % CI)	P value	HR (95 % CI)	P value	HR (95 % CI)	P value
Crude						
TyG index	1.76 (1.17–2.64)	0.007	1.34 (1.11–1.61)	0.002	1.40 (1.21–1.61)	<0.001
Adjusted						
TyG index	1.92 (1.08–3.42)	0.027	1.62 (1.21–2.16)	0.001	1.42 (1.14–1.77)	0.002

[a] Adjusted for age, atrial fibrillation, total cholesterol, septum thickness, mean aortic valve gradient, procedural time, PR interval, annulus area, and annulus perimeter.

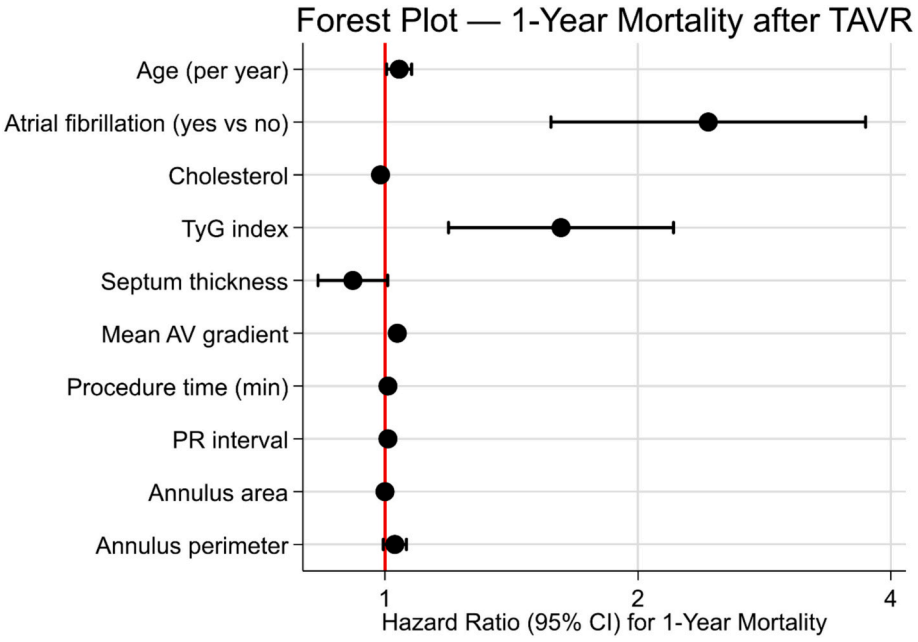

Fig. 3. Forest plot of multivariable Cox regression predictors of 1-year all-cause mortality after TAVR.

captured by standard risk scores. Our study, therefore, prespecified early (30-day), short-term (1-year), and long-term (3-year) horizons to test whether baseline TyG independently stratifies mortality across the post-TAVR continuum and adds incremental prognostic value to contemporary clinical models, thereby informing pragmatic, low-cost triage, metabolic optimization, and surveillance pathways.

4.1. 30-day mortality after TAVR

Aligned with our aim, baseline TyG independently predicted 30-day all-cause mortality after TAVR [6,7,38]. High TyG reflects residual metabolic–endothelial–inflammatory risk beyond STS/EuroSCORE II and VARC-3, consistent with pathways that precipitate early complications. Fan et al. reported a 41 % higher adjusted risk of death per 1-unit TyG increase (HR 1.41, 95 % CI 1.03–1.93) and separation of high- vs low-TyG survival even after excluding ≤30-day deaths (HR 1.53, 95 % CI 1.08–2.17) [7]. Li et al. showed in their cohort that per-unit TyG strongly related to mortality (adjusted HR 5.41, 95 % CI 4.01–7.32), identified an optimal threshold near 8.4, and improved discrimination (IDI 0.11; NRI 0.32) [6]. Extending to moderate–severe aortic stenosis, Huang et al. found TyG predicted mortality (HR 1.62, 95 % CI 1.09–2.42) with a cut-off around 8.47 and better reclassification [38]. In contrast, Moscarelli et al. observed no difference in in-hospital mortality or major complications by metabolic-syndrome status within a multicenter TAVR subgroup (12.3 % of cases), suggesting that broad syndromic labels can obscure the specific insulin-resistance signal captured by TyG [39]. In contrast, Moscarelli et al. observed no difference in in-hospital mortality or major complications by metabolic-syndrome status within a multicenter TAVR subgroup (12.3 % of cases), suggesting that broad syndromic labels can obscure the specific insulin-resistance signal captured by TyG.

4.2. Short-term (1-year) mortality after TAVR

In accordance with our predefined objective, we found that higher baseline TyG independently stratified 1-year mortality after TAVR. External evidence is congruent across high-risk cohorts: Xie et al. observed in 959 dialysis patients with CAD that the highest TyG tertile had greater 1-year MACE risk than the lowest (HR 1.63, 95 % CI 1.14–2.35) and that each 1-unit increase conferred a 37 % rise in risk (HR 1.37, 95 % CI 1.13–1.66) [40]; Tao et al. reported in 810 patients with CHD and hypertension that the top TyG quartile independently predicted 1-year MACEs (adjusted OR 1.47, 95 % CI 1.07–2.02) with a non-linear pattern and a threshold near 8.85 [41]; and Khalaji et al. showed in a 13,542-patient ACS-PCI registry that each 1-unit TyG increment related to higher MACE (adjusted HR 1.18, 95 % CI 1.08–1.30), with Q4 vs Q1 adding risk (HR 1.29, 95 % CI 1.08–1.53) [42]. In contrast, Boukhris et al. found no difference in 1-year survival across BMI strata in a single-center TAVR cohort ($n = 412$; log-rank $p = 0.925$), a result likely reflecting BMI's limitations as an anthropometric

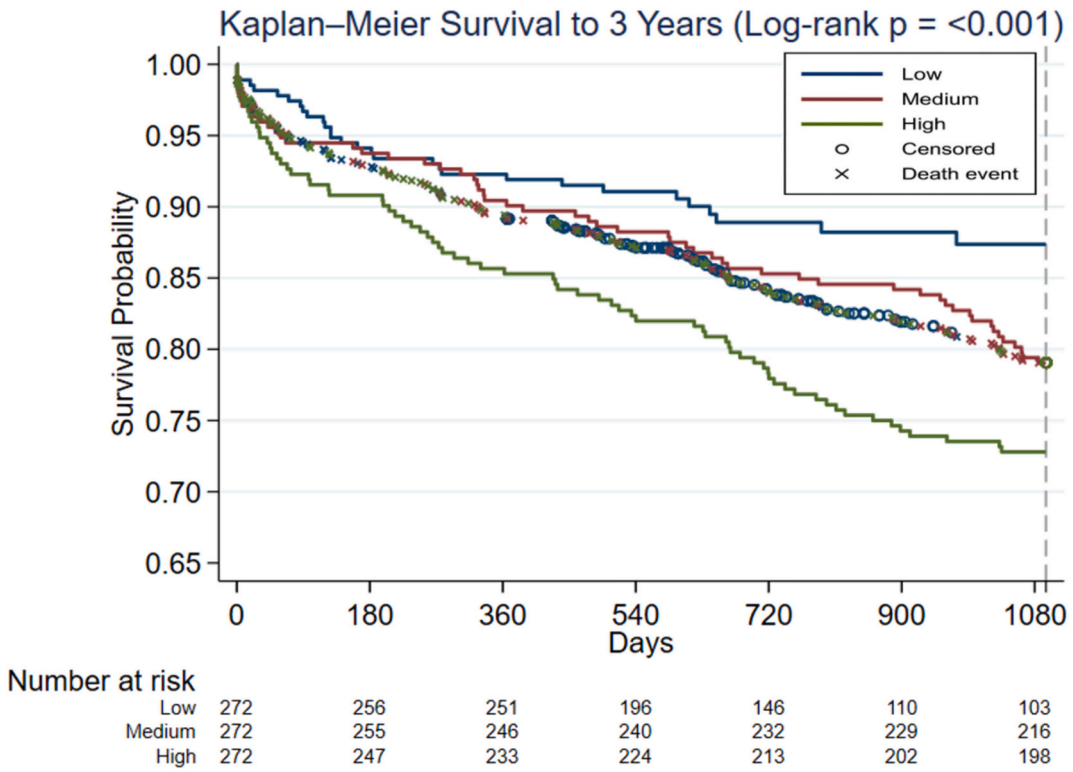

Fig. 4. Kaplan–Meier survival curves to 3 years according to TyG Index categories.

Table 4
Restricted cubic spline model for the association between TyG Index and 3-year all-cause mortality.

Parameter	HR (95 % CI)	p-Value
rcs_TyG1	**1.08 (0.67–1.73)**	0.753
rcs_TyG2	**1.15 (0.52–2.55)**	0.728
rcs_TyG3	**6.64 (0.00–1.14 × 10^6)**	0.758
Non-linearity test	–	**0.123**
Overall effect of TyG	–	**0.001**

proxy in older, sarcopenic patients rather than the absence of a biochemical insulin-resistance signal such as TyG [43]. Taken together with our findings, these data support TyG as a pragmatic, low-cost biomarker to refine 1-year risk stratification, enable targeted pre-procedural metabolic optimization (glycemic control and triglyceride–apoB lowering), prioritize structured follow-up and inform shared decision-making for patients with high-risk TyG profiles.

4.3. Long-term (3-year) mortality after TAVR

Consistent with our a priori hypothesis, we found that higher baseline TyG independently predicted 3-year mortality after TAVR. Over this longer interval, the cumulative consequences of insulin resistance: progressive atherogenic dyslipidemia, endothelial–microvascular injury, and chronic low-grade inflammation, likely foster late atherosclerotic events, heart-failure progression, renal decompensation, and infection-related deaths. External evidence is congruent: Li et al. analyzed 1810 cardiac-surgery patients and showed per-unit TyG predicted mortality (HR 1.206, 95 % CI 1.121–1.297) with strong time-dependent discrimination (AUC 0.857 at 3 years; 0.801 at 5 years) [44]. D'Elia et al. reported in 12,275 hypertensive adults a 33 % higher cardiovascular-mortality risk per one-SD increase in TyG and a 67 % higher risk above a data-driven threshold of 4.54; over 10.5 years, cardiovascular mortality was 9.3 % for TyG >4.54 vs 5.6 % for TyG ≤4.54 (adjusted HR 1.31, 95 % CI 1.11–1.55; competing-risk SHR 1.19–1.29) [45]. In a U.S. population cohort, Yue et al. identified threshold effects whereby TyG ≥9.47 was associated with a 40.6 % higher all-cause mortality per unit and TyG ≥9.427 with a 79.5 % higher cardiovascular-mortality risk per unit [46]. In contrast, De Palma et al. found in a single-center TAVR cohort that BMI >25 kg/m^2 associated with lower 3-year mortality (HR 0.68, 95 % CI 0.50–0.93) and that pre-procedural weight loss predicted higher 1-year mortality (HR 1.64, 95 % CI 1.06–2.30), implying that frailty, not adiposity per se, may dominate longer-term risk [47]. Collectively, these data, together with our results, support incorporating TyG into long-term risk models to target intensive atherothrombotic prevention.

4.4. Ethnic and temporal variation in optimal TyG cut-points

ROC analysis identified distinct TyG thresholds for short- and long-term mortality. The optimal cut-points were 9.01 for 30-day mortality (adjusted AUC = 0.68), 9.15 for 1-year mortality (adjusted AUC = 0.66), and 8.70 for 3-year mortality (adjusted AUC = 0.71). When compared with Chinese TAVR cohorts, our cut-points are meaningfully higher, and this difference is biologically coherent. Fan et al. [10] identified a 1-year mortality TyG cut-point of 6.88, and Li et al. [9] reported an optimal 1-year threshold of 8.40, both of which are notably lower than the corresponding 1-year cut-point observed in our Western cohort of

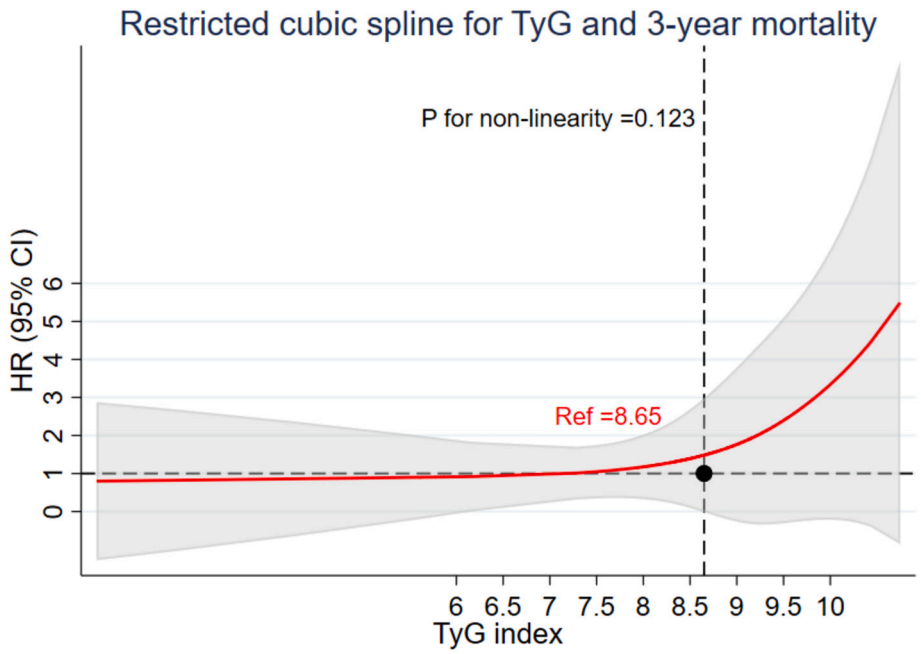

Fig. 5. Restricted cubic spline plot describing the adjusted association between continuous TyG index and 3-year all-cause mortality.

Ashkenazi-Jewish and Mediterranean patients. Clinically, this indicates that Western TAVR patients require a higher triglyceride–glucose burden before manifesting an equivalent increase in mortality risk, suggesting that TyG does not operate on a universal risk scale but rather follows population-specific metabolic thresholds.

Decades of metabolic research show that East Asians develop insulin resistance and type 2 diabetes at a lower BMI and with more visceral adiposity at matched body size compared with Europeans [48]. Moreover, ethnic differences exist in the hyperbolic compensation curve between insulin sensitivity and insulin secretion, where East Asians exhibit earlier β-cell exhaustion and weaker compensatory responses during rising triglyceride and glucose load [49]. Consequently, a lower TyG value already represents advanced metabolic dysfunction in East Asian populations, explaining why risk thresholds in Chinese cohorts lie in the 6.88–8.40 range. In contrast, Western populations, including Ashkenazi Jewish and Mediterranean individuals, generally show stronger β-cell reserve and different triglyceride-glucose coupling, requiring higher TyG values to reach equivalent metabolic stress.

These findings collectively demonstrate that TyG calibration is population-specific and that cut-points derived from Asian cohorts cannot be directly applied to Western TAVR patients. The higher short-term and long-term thresholds observed in our study reflect Western variations in visceral adiposity, hepatic insulin resistance, and β-cell reserve, all of which shift the TyG–risk relationship upward. Clinically, this means that reliance on East-Asian TyG thresholds would underestimate risk in Western patients and misclassify metabolic severity. Our data, therefore, provide the first validated TyG cut-points for Western TAVR recipients, offering a more accurate, ethnically appropriate framework for integrating TyG into structural-heart risk stratification and for guiding future risk-model calibration efforts.

4.5. *A structurally informed and procedurally calibrated TyG analysis*

In our study, the multivariable framework was expanded to include CT-derived annular measures (annulus area, annulus perimeter, and LVOT calcification), along with conduction-system indices (PR and QRS intervals) and procedure duration. These variables capture structural anatomy, conduction vulnerability, and intraprocedural complexity factors increasingly recognized as important contributors to TAVR outcomes. Incorporating these parameters allowed us to evaluate the TyG index within a more structurally and procedurally detailed context. Notably, TyG remained an independent predictor even after adjustment for these higher-resolution characteristics, suggesting that our findings add a complementary layer of understanding to the existing literature and help position TyG within a more comprehensive, physiologically integrated risk model.

The decision to retain a separate 1-year mortality model was driven by its established importance as an independent performance benchmark in TAVR research. Multiple pivotal trials and national registries report 1-year mortality as a distinct endpoint because it represents a transitional phase between peri-procedural risk and long-term prognosis [11–13]. Early post-TAVR mortality is predominantly influenced by procedural factors, frailty, and acute hemodynamic changes, whereas survival beyond one year reflects longer-term cardiac and metabolic trajectories [14,15]. Collapsing these intervals into a single long-term model could obscure time-dependent differences in risk relationships, particularly for metabolic markers such as the TyG index. Our approach is consistent with VARC-3 recommendations and ensures clear clinical interpretability of both early and long-term outcomes.

4.6. *Strengths*

This investigation addresses a clinically pertinent gap by evaluating the triglyceride–glucose (TyG) index across prespecified, practice-relevant horizons early (30 days), short term (1 year), and long term (3 years), thereby aligning biomarker performance with decision points that guide peri-procedural care and longitudinal follow-up. The exposure is simple, inexpensive, and widely available, enhancing scalability and bedside applicability. Analytical choices emphasized clinical translation by examining TyG both as a continuous measure and by clinically interpretable strata, and by assessing its added prognostic contribution beyond established clinical and procedural covariates. The

directionally consistent associations across all time windows strengthen the internal coherence of the findings and support the biological plausibility that a metabolic–inflammatory substrate influences outcomes after TAVR. Although the Kaplan–Meier curves for TyG tertiles display some crossing, this reflects the categorized version of the exposure rather than the underlying continuous TyG index. Arbitrary categorization is well known to distort the functional form of continuous predictors and may introduce apparent non-proportionality. In our analysis, the continuous TyG index, the main exposure used in all multivariable Cox models, fully satisfied the proportional hazards assumption. The observed crossing of tertile curves should therefore be interpreted cautiously and not as evidence of violation of model assumptions. Modeling the TyG index as a continuous exposure using restricted cubic splines did not provide evidence of a statistically significant non-linear relationship. Although the curve demonstrated a gradual increase in risk at higher TyG levels, the non-linearity test was not significant, suggesting that the association may be appropriately represented by a linear term. The widening of the confidence bands at the upper end reflects sparse data rather than increased biological uncertainty. Taken together, the findings support the prognostic relevance of TyG as a continuous marker, even in the absence of strong non-linear behavior.

4.7. Limitations

As an observational, the study is susceptible to residual confounding and selection bias despite multivariable adjustment. TyG was derived from a single baseline measurement; lack of serial assessments precludes evaluation of intra-individual variability, treatment effects, or trajectories over time. While mortality is robust, cause-specific events and nonfatal complications (e.g., stroke, rehospitalization, valve thrombosis) were not comprehensively analyzed, limiting mechanistic inference. Early (30-day) event counts are intrinsically low in contemporary practice, which can widen confidence intervals and limit subgroup precision. Finally, the spline analysis was limited by sparse data at very high TyG levels, resulting in unstable estimates at the upper tail of the distribution. Restricted cubic spline modeling also requires a sufficient number of events, which restricted its application to the 3-year mortality endpoint only. The absence of statistically significant non-linearity suggests that a linear specification may adequately reflect the association.

4.8. Take-home message

The TyG index (derived from triglyceride and glucose levels) is an easily obtainable biomarker that stratifies risk after TAVR. Patients with higher TyG indices had significantly higher mortality in the early, short-term, and longer-term follow-up, underscoring the importance of metabolic risk in TAVR outcomes and the potential benefit of targeted interventions for high-risk in Ashkenazi-Jewish and Mediterranean individuals.

5. Conclusion

The TyG index is a simple measure of insulin resistance, was independently associated with all-cause mortality at 30 days, 1 year, and 3 years after TAVR. This metabolic risk marker adds incremental prognostic value beyond conventional risk factors and may help clinicians identify TAVR recipients at higher risk. Incorporating the TyG index into post-TAVR risk assessment could inform targeted metabolic optimization and closer surveillance to potentially improve long-term outcomes in in Ashkenazi-Jewish and Mediterranean patients.

Abbreviation list

AIC	Akaike Information Criterion
AUC	area under the receiver-operating characteristic curve
CI	confidence interval
CKD	chronic kidney disease
CRP	C-reactive protein
eGFR	estimated glomerular filtration rate
HR	hazard ratio
IQR	interquartile range
IR	insulin resistance
LVEF	left ventricular ejection fraction
NRI	net reclassification improvement
OR	odds ratio
ROC	receiver-operating characteristic
SD	standard deviation
STS	Society of Thoracic Surgeons risk score
TyG	triglyceride–glucose index
VARC-3	Valve Academic Research Consortium-3
TAVR	transcatheter aortic valve replacement

CRediT authorship contribution statement

Haitham Abu Khadija: Project administration, Methodology. **Duha Najajra:** Formal analysis, Data curation. **Mohammad Masu'd:** Investigation, Funding acquisition. **Nizar Abu Hamdeh:** Investigation, Funding acquisition. **Omar Ayyad:** Resources, Project administration. **Ameer Mahamid:** Investigation, Funding acquisition. **Max Bagan:** Supervision, Software. **Ali Abdullah:** Project administration, Methodology. **Jebrin Alkrinawi:** Validation, Supervision. **Alaa Zayed:** Methodology, Investigation. **Abdalaziz Darwish:** Formal analysis, Data curation. **Aesha L.E. Enairat:** Methodology, Investigation. **Alena Kirzhner:** Investigation, Funding acquisition. **Tal Schiller:** Software, Resources. **Mohammad Alnees:** Investigation, Conceptualization.

Ethical considerations

The study was approved by the local IRB committee (0091-20-KMC), with a waiver of informed consent due to the retrospective use of de-identified clinical data. All procedures were in accordance with the ethical standards of the Helsinki Declaration. The conduct and reporting of this observational study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Patient confidentiality was maintained throughout, and all data were stored on secure servers with access limited to the research team.

Funding information

This research received no specific grant from any public, commercial, or not-for-profit funding agency. The study was carried out using institutional resources and in-kind support from the participating centers principally the Heart Center, Kaplan Medical Center, and the Palestinian Clinical Research Center including access to clinical databases, infrastructure, and staff time. These institutions had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to submit the article for publication.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We thank the patients and their families, as well as the interventional cardiology physicians, catheterization laboratory nursing staff, and allied health professionals at the Heart Center, Kaplan Medical Center, for their commitment to patient care and their support of the TAVR registry.

We are grateful to the echocardiography and clinical biochemistry laboratories for assistance with measurements and data retrieval, and to the medical records and information-technology teams for secure data extraction. We also acknowledge methodological and editorial input from colleagues at the Palestinian Clinical Research Center. The individuals acknowledged did not meet ICMJE authorship criteria, had no role in study design, data analysis, data interpretation, or the decision to submit the manuscript, and have provided permission to be named.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahjo.2025.100684.

Data availability

The data sets supporting the current research results are available from the corresponding authors upon request.

References

[1] A.M. Vekstein, Z.K. Wegermann, P. Manandhar, M.J. Mack, D.J. Cohen, G. C. Hughes, et al., Outcomes of Transcatheter aortic valve replacement in low-risk patients in the United States: a report from the STS/ACC TVT registry, Circulation 151 (16) (2025 Apr) 1134–1146.

[2] J.K. Forrest, G.M. Deeb, S.J. Yakubov, H. Gada, M.A. Mumtaz, B. Ramlawi, et al., 3-year outcomes after transcatheter or surgical aortic valve replacement in low-risk patients with aortic stenosis, J Am Coll Cardiol 81 (17) (2023 May) 1663–1674.

[3] F. Zahr, B. Ramlawi, M.J. Reardon, G.M. Deeb, S.J. Yakubov, H.K. Song, et al., 3-year outcomes from the evolut low risk TAVR bicuspid study, JACC Cardiovasc Interv 17 (14) (2024 Jul) 1667–1675.

[4] H. Cheng, W. Huang, X. Huang, W. Miao, Y. Huang, Y. Hu, The triglyceride glucose index predicts short-term mortality in non-diabetic patients with acute heart failure, Adv Clin Exp Med 33 (2) (2024 Feb) 103–110.

[5] T. Li, C. Yang, J. Yang, J. Jing, C. Ma, Elevated triglyceride-glucose index predicts mortality following endovascular abdominal aortic aneurysm repair, Front Nutr 10 (2023).

[6] W. Li, H. Li, S. Peng, J. Li, Y. Feng, Y. Peng, et al., Prognostic effect of the TyG index on patients with severe aortic stenosis following transcatheter aortic valve replacement: a retrospective cohort study, Cardiovasc Diabetol 23 (1) (2024 Aug) 312.

[7] J. Fan, A. Aihemaiti, A. Yidilisi, X. Liu, J. Wang, Association between triglyceride-glucose index and all-cause mortality in patients underwent transcatheter aortic valve replacement, BMC Cardiovasc Disord 24 (1) (2024 Sep) 508.

[8] E. Altuntas, A.E. Tırnaksız, K. Sadıkoğlu, S. Aslan, G. Demirci, A.A. Yalcın, et al., Prognostic value of the triglycerides-glucose index for major adverse cardiac events in severe aortic stenosis patients after TAVI, Angiology 33197251328773 (2025 Mar).

[9] W. Li, H. Li, S. Peng, J. Li, Y. Feng, Y. Peng, et al., Prognostic effect of the TyG index on patients with severe aortic stenosis following transcatheter aortic valve replacement: a retrospective cohort study, Cardiovasc Diabetol 23 (1) (2024) 1–10 [Internet]. 2024 Aug 24 [cited 2025 Nov 12]. Available from: https://cardiab.biomedcentral.com/articles/10.1186/s12933-024-02414-9.

[10] J. Fan, A. Aihemaiti, A. Yidilisi, X. Liu, J. Wang, Association between triglyceride-glucose index and all-cause mortality in patients underwent transcatheter aortic valve replacement, BMC Cardiovasc Disord [Internet] 24 (1) (2024 Dec 1) [cited 2025 Nov 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/39313838/.

[11] J.D. Carroll, M.J. Mack, S. Vemulapalli, H.C. Herrmann, T.G. Gleason, G. Hanzel, et al., STS-ACC TVT registry of transcatheter aortic valve replacement, J Am Coll Cardiol 76 (21) (2020 Nov) 2492–2516.

[12] M.B. Leon, C.R. Smith, M.J. Mack, R.R. Makkar, L.G. Svensson, S.K. Kodali, et al., Transcatheter or surgical aortic-valve replacement in intermediate-risk patients, N Engl J Med 374 (17) (2016 Apr 28) 1609–1620.

[13] C.R. Smith, M.B. Leon, M.J. Mack, D.C. Miller, J.W. Moses, L.G. Svensson, et al., Transcatheter versus surgical aortic-valve replacement in high-risk patients, N Engl J Med 364 (23) (2011 Jun 9) 2187–2198.

[14] T. Pilgrim, A. Franzone, S. Stortecky, F. Nietlispach, A.G. Haynes, D. Tueller, et al., Predicting mortality after transcatheter aortic valve replacement, Circ Cardiovasc Interv 10 (11) (2017 Nov).

[15] S. Kiani, A. Stebbins, V.H. Thourani, J. Forcillo, S. Vemulapalli, A.S. Kosinski, et al., The effect and relationship of frailty indices on survival after transcatheter aortic valve replacement, JACC Cardiovasc Interv 13 (2) (2020 Jan) 219–231.

[16] P. Généreux, N. Piazza, M.C. Alu, T. Nazif, R.T. Hahn, P. Pibarot, et al., Valve academic research consortium 3: updated endpoint definitions for aortic valve clinical research, J Am Coll Cardiol 77 (21) (2021 Jun) 2717–2746.

[17] L.B. Kurniawan, Triglyceride-glucose index as a biomarker of Insulin resistance, diabetes mellitus, metabolic syndrome, and cardiovascular disease: a review, EJIFCC [Internet] 35 (1) (2024) 44 [cited 2025 Aug 24]. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC11063788/.

[18] F. Guerrero-Romero, L.E. Simental-Mendía, M. González-Ortiz, E. Martínez-Abundis, M.G. Ramos-Zavala, S.O. Hernández-González, et al., The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp, J. Clin. Endocr. Metab 95 (7) (2010) 3347–3351 [cited 2025 Aug 24]. Available from: https://pubmed.ncbi.nlm.nih.gov/20484475/.

[19] J.W. Luo, W.H. Duan, Y.Q. Yu, L. Song, D.Z. Shi, Prognostic significance of triglyceride-glucose index for adverse cardiovascular events in patients with coronary artery disease: a systematic review and meta-analysis, Front Cardiovasc Med [Internet] 8 (2021) [cited 2025 Sep 12]. 774781. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC8674619/.

[20] H.W. Zhao, Y. Wang, C.F. Wang, Q.K. Meng, Association between triglyceride glucose index and adverse clinical outcomes in patients with acute myocardial infarction and LDL-C≤1.8 mmol/L who underwent percutaneous coronary intervention: a prospective cohort study, Front Endocrinol (Lausanne) 18 (14) (2023 Jan) 1323615.

[21] L. Wang, H.L. Cong, J.X. Zhang, Y.C. Hu, A. Wei, Y.Y. Zhang, et al., Triglyceride-glucose index predicts adverse cardiovascular events in patients with diabetes and acute coronary syndrome, Cardiovasc Diabetol [Internet] 19 (1) (2020 Jun 13) 80 [cited 2025 Sep 12]. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC7293784/.

[22] A. Khalaji, A.H. Behnoush, Y. Pasebani, A. Rafati, T. Mahmoodi, A. Arzhangzadeh, et al., Triglyceride-glucose index as a predictor of cardiac adverse events in acute coronary syndrome patients undergoing percutaneous coronary intervention: role of diabetes, BMC Cardiovasc Disord [Internet] 24 (1) (2024 Dec 1) [cited 2025 Sep 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/39333881/.

[23] G.S. Collins, J.B. Reitsma, D.G. Altman, K.G.M. Moons, Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD), Circulation 131 (2) (2015 Jan 13) 211–219.

[24] S. Khodaei, L. Garber, M. Abdelkhalek, N. Maftoon, A. Emadi, Z. Keshavarz-Motamed, Reducing long-term mortality post transcatheter aortic valve replacement requires systemic differentiation of patient-specific coronary hemodynamics, J Am Heart Assoc 12 (11) (2023 Jun 6) e029310.

[25] R.N. Sánchez-Santillán, M.P. Sierra-Vargas, D. González-Islas, O.G. Aztatzi-Aguilar, R. Pérez-Padilla, A. Orea-Tejeda, et al., Endothelial biomarkers (Von willebrand factor, BDCA3, urokinase) as predictors of mortality in COVID-19 patients: cohort study, BMC Pulm Med 24 (1) (2024 Jul) 325.

[26] B. Redfors, A. Furer, B.R. Lindman, D. Burkhoff, G. Marquis-Gravel, D.P. Francese, et al., Biomarkers in aortic stenosis: a systematic review, Structural Heart 1 (1) (2017) 18–30.

[27] A.L.S. Sousa, L.A.F. Carvalho, C.G. Salgado, R.L. de Oliveira, L.C.C.L.E. Lima, N.D. F.G. de Mattos, et al., C-reactive protein as a prognostic marker of 1-year mortality after transcatheter aortic valve implantation in aortic stenosis, Arq Bras Cardiol 117 (5) (2021 Nov) 1018–1027.

[28] Y. Avci, A.R. Demir, M. Duran, U. Bulut, G. Demirci, B. Uygur, et al., The prognostic value of C-reactive protein to albumin ratio in patients undergoing transcatheter aortic valve implantation, Acta Cardiol 77 (10) (2022 Dec) 930–936.

[29] J.M. Sinning, A.C. Scheer, V. Adenauer, A. Ghanem, C. Hammerstingl, R. Schueler, et al., Systemic inflammatory response syndrome predicts increased mortality in patients after transcatheter aortic valve implantation, Eur Heart J 33 (12) (2012) 1459–1468.

[30] A. Kirzhner, H. Green, R. Koren, H. Abu Khadija, D. Sapojnik, T. Schiller, Diabetes and acute decompensated heart failure: a comprehensive analysis of in-hospital outcomes, Isr Med Assoc J 27 (2) (2025 Feb) 103–109.

[31] H. Abu Khadija, G. Gandelman, O. Ayyad, L. Poles, M. Jonas, O. Paz, et al., Comparative analysis of the kinetic behavior of systemic inflammatory markers in patients with depressed versus preserved left ventricular function undergoing transcatheter aortic valve implantation, J Clin Med 10 (18) (2021 Sep 15).

[32] H.A. Khadija, M. Welt, G. Gendelman, A. Hamode, L. Poles, M. Jonas, et al., Systemic inflammatory markers in elderly patients undergoing transcatheter aortic valve replacement, J Geriatr Cardiol 19 (11) (2022 Nov 28) 811–821.

[33] H. Abu Khadija, O. Ayyad, D. Haberman, G. Gandelman, L. Poles, M. Jonas, et al., Contemporary transcatheter aortic valve implantation related thrombocytopenia, Catheter Cardiovasc Interv 98 (1) (2021 Jul 1) E139–E144.

[34] H. Abu Khadija, G. Gandelman, O. Ayyad, M. Jaber, L. Poles, M. Jonas, et al., Differential systemic inflammatory responses after TAVI: the role of self versus balloon expandable devices, PLoS One 16 (10) (2021 Oct 26) e0258963.

[35] H. Abu Khadija, G. Gandelman, O. Ayyad, M. Jaber, L. Poles, M. Jonas, et al., Differential systemic inflammatory responses after TAVI: the role of self versus balloon expandable devices, PLoS One 16 (10) (2021) e0258963.

[36] H.A. Khadija, M. Alnees, G. Gandelman, M. Awwad, T. Schiller, Y. Hamdan, et al., Clinical Impact of Glucose Levels on Patient Outcome after Transcatheter Aortic Valve Replacement [Internet], Available from: https://doi.org/10.31083/?, 2025.

[37] H.A. Khadija, M. Alnees, O. Ayyad, G. Gandelman, G. Sella, N.A. Hamdeh, et al., Pre-procedural neutrophil-to-lymphocyte ratio: a novel predictor of permanent pacemaker implantation in self-expandable vs. balloon-expandable valve cohorts following transcatheter aortic valve implantation, Heart Rhythm O2 6 (6) (2025 Mar) 766–780.

[38] R. Huang, X. Xu, C. Xu, S. Zhang, Z. Xiong, M. Liu, et al., Association between the insulin resistance and all-cause mortality in patients with moderate and severe aortic stenosis: a retrospective cohort study, Cardiovasc Diabetol 22 (1) (2023) 238.

[39] M. Moscarelli, D. Paparella, G.D. Angelini, F. Giannini, G. Contegiacomo, A. Marchese, et al., The influence of metabolic syndrome in heart valve intervention. A multi-centric study, J Card Surg 37 (12) (2022 Dec) 5063–5072.

[40] E. Xie, Z. Ye, Y. Wu, X. Zhao, Y. Li, N. Shen, et al., The triglyceride-glucose index predicts 1-year major adverse cardiovascular events in end-stage renal disease patients with coronary artery disease, Cardiovasc Diabetol 22 (1) (2023 Oct) 292.
[41] S. Tao, L. Yu, J. Li, L. Huang, X. Huang, W. Zhang, et al., Association between the triglyceride-glucose index and 1-year major adverse cardiovascular events in patients with coronary heart disease and hypertension, Cardiovasc Diabetol 22 (1) (2023) 305.
[42] A. Khalaji, A.H. Behnoush, Y. Pasebani, A. Rafati, T. Mahmoodi, A. Arzhangzadeh, et al., Triglyceride-glucose index as a predictor of cardiac adverse events in acute coronary syndrome patients undergoing percutaneous coronary intervention: role of diabetes, BMC Cardiovasc Disord 24 (1) (2024) 514.
[43] M. Boukhris, J. Forcillo, J. Potvin, N. Noiseux, L.M. Stevens, M. Badreddine, et al., Does "obesity paradox" apply for patients undergoing transcatheter aortic valve replacement? Cardiovasc Revasc Med 38 (2022 May) 1–8.
[44] H. Li, F. Xiao, H. Ren, F. Xu, H. Che, H. Zhu, et al., Triglyceride index as a predictor of mortality after cardiac surgery, iScience 27 (11) (2024 Nov) 111107.
[45] L. D'Elia, F. Galletti, M. Maria, A. Virdis, E. Casiglia, V. Tikhonoff, et al., Triglyceride-glucose index threshold for cardiovascular mortality in hypertensive individuals - URRAH project, Am J Prev Cardiol 23 (2025 Sep) 101053.
[46] C.Y. Yue, H.S. Dong, H.X. Liu, A.M. Xie, J. Wang, Association between triglyceride-glucose index and all-cause and cardiovascular mortality in US adults: a cohort study, Medicine 104 (34) (2025 Aug) e43897.
[47] R. De Palma, J. Ivarsson, K. Feldt, N. Saleh, A. Ruck, R. Linder, et al., The obesity paradox: an analysis of pre-procedure weight trajectory on survival outcomes in patients undergoing transcatheter aortic valve implantation, Obes Res Clin Pract 12 (1) (2018) 51–60.
[48] R.C.W. Ma, J.C.N. Chan, Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States, Ann N Y Acad Sci [Internet] 1281 (1) (2013 Apr 1) 64–91 [cited 2025 Nov 15]. Available from: https://nyaspubs.onlinelibrary.wiley.com/doi/pdf/10.1111/nyas.12098.
[49] K. Kodama, D. Tojjar, S. Yamada, K. Toda, C.J. Patel, A.J. Butte, Ethnic differences in the relationship between insulin sensitivity and insulin response: a systematic review and meta-analysis, Diabetes Care [Internet] 36 (6) (2013 Jun 1) 1789–1796 [cited 2025 Nov 12]. Available from, https://doi.org/10.2337/dc12-1235.