

UC San Diego

Biomarkers Symposium 2026

Title

Association between Triglyceride-Glucose Index and Heart Failure Risk by Body MassIndex in a Multi-Ethnic Cohort

Permalink

<https://escholarship.org/uc/item/76t7g659>

Authors

Thakkar, Nandan

Hong, Kimberly

Shapiro, Michael D.

et al.

Publication Date

2026-05-15

Association between Triglyceride-Glucose Index and Heart Failure Risk by Body Mass Index in a Multi-Ethnic Cohort

Nandan Thakkar, MD, MSc¹; Kimberly Hong, MD,MHSA²; Michael D. Shapiro, DO,MCR³; Alain G. Bertoni, MD, MPH⁴; Harpreet S. Bhatia, MD, MAS,FACC²

¹ Department of Medicine, University of California San Diego, La Jolla, CA
² Division of Cardiovascular Medicine, Department of Medicine, University of California San Diego, La Jolla, CA
³ Center for Preventive Cardiology, Wake Forest University School of Medicine, Winston-Salem, NC
⁴ Department of Internal Medicine and Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC

Introduction

Heart failure (HF) remains a leading cause of morbidity and mortality in the U.S., driven by heterogeneous pathophysiology. Insulin resistance (IR) contributes to HF risk, even in the absence of diabetes, via:

- Metabolic dysregulation
- Systemic inflammation
- Adverse myocardial remodeling

Common anthropometric markers of adiposity (e.g., BMI) may fail to identify individuals with insulin resistance, particularly when excess adiposity is visceral or ectopic (e.g., liver, heart) rather than central. The triglyceride-glucose (TyG) index—a simple, routine lab-based measure—is a reliable surrogate for IR that may better capture this metabolic risk.

Study aims:

- Assess the association between TyG and incident HF
- Determine if this relationship varies by BMI and HF subtype

Materials and Methods

Study design & population

- Prospective cohort analysis (MESA)
- 6,683 participants free of heart failure (HF) at baseline

Exposure

- TyG index = $\ln(\text{fasting triglycerides [mg/dL]} \times \text{fasting glucose [mg/dL]}/2)$

Outcome

- Incident HF (adjudicated; median follow-up 15.2 years)

Statistical analysis

- Primary: Multivariable Cox proportional hazards models (HR per 1-unit $\uparrow$ in TyG)
- Covariates: Age, sex, race/ethnicity, systolic BP, total cholesterol, HDL-C, eGFR, diabetes status, CRP, antihypertensives, lipid-lowering therapy, smoking status

Effect Modification & Subgroup Analysis

- BMI as effect modifier (interaction testing) with results stratified by non-obese (<30) vs. obese (≥ 30 kg/m²)
- Subgroup analyses by HF subtype with HFpEF (EF $\geq 50\%$) & HFrEF (EF $<50\%$)

Results

- Over a median follow-up of 15.2 years, 502 HF events occurred. In fully adjusted models, higher TyG was associated with increased HF risk (HR 1.24, 95% CI 1.02–1.50, $p=0.032$).

Variable	HR for HF (95% CI)	p
TyG index (per 1-unit increase)	1.24 (1.02–1.50)	0.032*
Age	1.07 (1.06–1.08)	<0.001*
Female Gender (Ref: Male)	1.49 (1.22–1.83)	<0.001*
Race/ethnicity (Ref: White)		
Chinese	0.57 (0.39–0.82)	0.002*
Black	0.95 (0.75–1.19)	0.658
Hispanic	0.81 (0.63–1.04)	0.098
Systolic BP (per 1 mmHg)	1.01 (1.01–1.01)	<0.001*
Total cholesterol (per 1 mg/dl)	1.00 (0.99–1.00)	0.192
HDL cholesterol (per 1 mg/dl)	1.00 (0.99–1.01)	0.978
eGFR (per unit)	1.00 (0.99–1.00)	0.214
Diabetes (Ref: Non-diabetic)	1.84 (1.45–2.34)	<0.001*
CRP (per unit)	1.02 (1.01–1.03)	<0.001*
Antihypertensive use	1.57 (1.29–1.91)	<0.001*
Lipid-lowering therapy use	0.84 (0.67–1.06)	0.139
Smoking status (Ref: Never)		
Former	1.22 (1.00–1.48)	0.049*
Current	1.83 (1.38–2.44)	<0.001*
BMI (Obese ≥ 30)	1.23 (1.01–1.49)	0.043*

Table 1. Multivariable Cox Proportion Hazard Model for HF (all subtypes).

- TyG, HF association was modified by BMI (with BMI-TyG interaction test: $p = 0.010$) and restricted to non-obese participants.

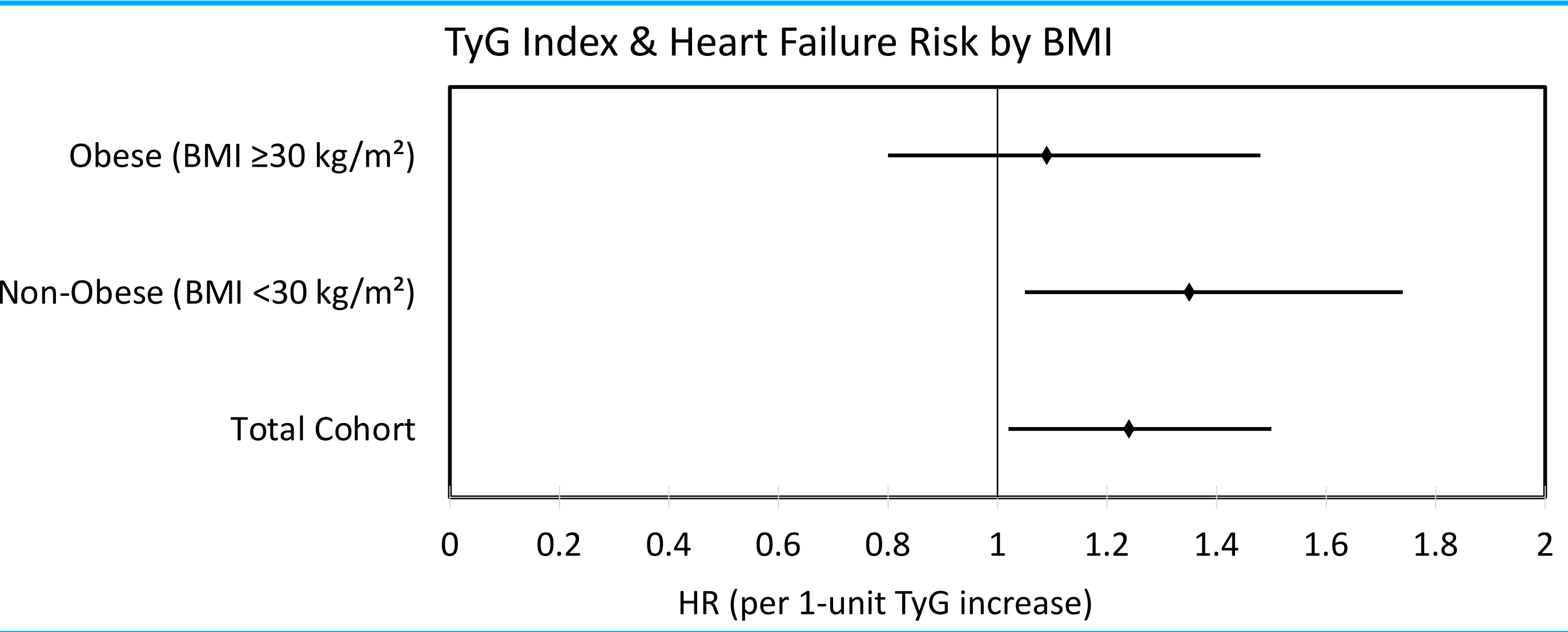


Figure 1. Triglyceride-glucose index hazard ratios for HF (all subtypes), stratified by BMI.

Population	N	HF Events	TyG HR (per 1-unit increase)	p
Total Cohort	6,683	502	1.24 [CI: 1.02-1.50]	0.032*
Non-Obese (BMI <30)	4,544	302	1.35 [CI: 1.05-1.74]	0.018*
Obese (BMI ≥ 30)	2,139	200	1.09 [CI: 0.80-1.48]	0.60

Table 2. Triglyceride-glucose index hazard ratios for HF (all subtypes), stratified by BMI

- In HF subtype analyses, TyG demonstrated a trend toward association with HFpEF but not HFrEF.

Outcome	Events*	TyG HR (per 1-unit increase)	p
HFpEF (EF $\geq 50\%$)	193	1.32 [CI: 0.96-1.82]	0.085
HFrEF (EF $<50\%$)	234	1.03 [CI: 0.78-1.37]	0.81

Table 3. Triglyceride-glucose index hazard ratios by HF subtype
**Among 502 HF events, 75 missing subtype adjudication*

Conclusion

- TyG index is associated with incident HF independent of traditional risk factors.
- This association appears to be modified by BMI, with a significant association observed among non-obese individuals.
- Among non-obese individuals, higher TyG may reflect underlying insulin resistance in the absence of central adiposity. Findings suggest that insulin resistance markers such as TyG could complement traditional anthropometric measures to identify at-risk individuals with potentially atypic phenotypes.

References

Banerjee, D., Biggs, M.L., Mercer, L., Mukamal, K., Kaplan, R., Barzilay, J., Kuller, L., Kizer, J.R., Djousse, L., Tracy, R. and Ziemann, S., 2013. Insulin resistance and risk of incident heart failure: Cardiovascular Health Study. *Circulation: Heart Failure*, 6(3), pp.364-370.

Bild, D.E., Bluemke, D.A., Burke, G.L., Detrano, R., Diez Roux, A.V., Folsom, A.R., Greenland, P., Jacobs Jr, D.R., Kronmal, R., Liu, K. and Nelson, J.C., 2002. Multi-ethnic study of atherosclerosis: objectives and design. *American journal of epidemiology*, 156(9), pp.871-881.

Ingelsson, E., Sundström, J., Ärnlöv, J., Zethelius, B. and Lind, L., 2005. Insulin resistance and risk of congestive heart failure. *Jama*, 294(3), pp.334-341.

Khan, S.S., Matsushita, K., Sang, Y., Ballew, S.H., Grams, M.E., Surapaneni, A., Blaha, M.J., Carson, A.P., Chang, A.R., Ciemins, E. and Go, A.S., 2024. Development and validation of the American Heart Association’s PREVENT equations. *Circulation*, 149(6), pp.430-449.