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High triglyceride-to-high-density lipoprotein cholesterol ratio predicts poor prognosis in new-onset heart failure: a retrospective study

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Abstract

Background There is limited research on the relationship between the triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio and outcomes in new-onset heart failure (HF). Therefore, this study aimed to explore the association between TG/HDL-C ratio and clinical outcomes in these patients.

Methods A retrospective cohort of 614 adults with new-onset HF hospitalized at The First Affiliated Hospital of Nanchang University between July 2021 and December 2022 was analyzed. The primary endpoint was major adverse cardiovascular events (MACE), defined as cardiovascular (CV) death and HF rehospitalizations within 12 months after discharge. Kaplan–Meier (K–M) curves, restricted cubic spline (RCS) analysis, and Cox regression evaluated the association between TG/HDL-C ratio and MACE risk.

Results Patients were divided into four quartiles (Quartile 1, 2,3 and 4) based on their TG/HDL-C ratios. The mean age was 68.94 ± 14.34 years, with 59.12% male. The mean left ventricular ejection fraction (LVEF) was 46.59 ± 10.89%, with 45.11% having an LVEF ≤ 40%. During the 12-month follow-up, 156 patients experienced MACE, comprising 18 CV deaths and 138 HF rehospitalizations. The Quartile 4 group had the highest MACE risk incidence compared to other groups ($P < 0.001$). K–M analysis confirmed that the Quartile 4 group was associated with an increased cumulative incidence of MACE, HF rehospitalization, and CV death (all $P < 0.001$). RCS analysis revealed a positive nonlinear relationship between the TG/HDL-C ratio and MACE risk (P for nonlinear = 0.026), with a sharp risk increase above a ratio of 1.08. After adjustment, TG/HDL-C ratio was independently associated with MACE (HR: 1.44, 95% CI: 1.29–1.60). Compared to Quartile 1, adjusted HRs were significantly higher in Quartiles 2, 3, and 4 (all $P < 0.005$).

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Conclusions The TG/HDL-C ratio is independently associated with 12-month MACE risk in new-onset HF patients. It may serve as a simple, cost-effective marker to improve early risk stratification and guide closer monitoring and tailored management in this high-risk population.

Keywords Triglyceride-to-high-density lipoprotein cholesterol ratio, New-onset heart failure, Poor prognosis, Nonlinear association

Background

Heart failure (HF) arises from a wide range of cardiac and noncardiac conditions and is characterized by a high incidence and poor prognosis. Globally, over 64 million people are currently diagnosed with HF. As population age, the prevalence of chronic conditions such as coronary atherosclerotic disease (CAD), hypertension, diabetes, and obesity continue to rise, leading to increased HF incidence, prevalence, and mortality rates [1–3]. This underscores the urgent need for research to improve the treatment and prognosis of HF, thereby reducing its societal and familial burden.The primary pathophysiological basis of HF is myocardial remodeling—a complex process often accompanied by metabolic disturbances, including insulin resistance, dyslipidemia, and altered fatty acid metabolism [4–8]. As metabolic dysfunction is an important driver of HF pathophysiology, evaluating these metabolic abnormalities and HF prognosis through novel biomarkers is crucial for improving clinical outcomes [9].

Lipid profiling, a commonly used tool, provides insights into metabolic health and risks for conditions such as fatty liver, pancreatitis, metabolic syndrome, insulin resistance, and cardiovascular disease. Elevated Triglycerides (TG), contributes to lipotoxicity and oxidative stress, are a significant risk factor for cardiovascular disease [10, 11]. Meanwhile, low high-density lipoprotein cholesterol (HDL-C) levels impair cholesterol transport and reduce HDL-C's protective anti-inflammatory and antioxidant functions [12–14]. The TG/HDL-C ratio, which integrates these two lipid markers, has been recognized as a marker of insulin resistance and metabolic syndrome [15–17]. In addition, elevated TG/HDL-C ratios have been associated with increased cardiovascular risk, particularly in patients with coronary artery disease (CAD) [16, 18]. Although metabolic dysfunction plays a key role in HF progression, the prognostic value of the TG/HDL-C ratio in HF, particularly in new-onset cases, remains unclear. As a recognized marker of insulin resistance and metabolic syndrome, the TG/HDL-C ratio may help predict adverse outcomes in this population. This study aimed to assess its prognostic significance in new-onset HF by evaluating its association with major adverse cardiovascular events (MACE), including cardiovascular (CV) death and HF rehospitalization.

Materials and methods

Study design and participants

This study included 982 consecutive adult patients with new-onset HF hospitalized at the Department of Cardiology at The First Affiliated Hospital of Nanchang University between July 2021 and December 2022. Inclusion were: (1) aged18–90 years; (2) confirmed diagnosis of HF on the basis of the 2021 ESC guidelines [19], characterized by symptoms (e.g., dyspnea, fatigue), signs (e.g., jugular venous distension, edema), N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels ≥ 125 pg/mL, and echocardiographic evidence of structural or functional cardiac abnormalities. Exclusion criteria included: (1) loss to follow-up; (2) missing critical clinical data (e.g., TG, HDL-C, and NT-proBNP); (3) hematologic diseases, autoimmune diseases, or malignant tumors; (4) severe disease affecting major organs, such as liver or kidney dysfunction (estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2 or transaminase levels > 5 times the upper limit of normal); (5) recent glucocorticoid use; (6) suspected familial hypertriglyceridemia (fasting TG ≥ 5.65 mmol/L); (7) extreme body mass index (BMI) values (BMI ≥ 45 kg/m^2). Patients with missing critical clinical data were excluded from the final analysis. Given the small proportion of missing data, no data imputation was performed. Based on these criteria, 614 individuals were included (Fig. 1).

Data collection

Data were extracted from a retrospective HF database containing demographic, laboratory, imaging, and clinical details. Fasting venous blood samples were collected on the second hospitalization day, and laboratory analyses adhered to standard protocols. Key parameters included TG, HDL-C, fasting blood glucose (FBG), like left ventricular ejection fraction (LVEF), and QRS duration (QRSd), along with comorbidities such as diabetes mellitus (DM), coronary artery disease (CAD).

Follow-up arrangements

Patients were monitored for 12 months post-discharge through phone calls or outpatient visits every 3 months. To enhance data accuracy, reported HF rehospitalizations were cross-checked with hospital electronic medical records. The primary study endpoint was the first occurrence of major adverse cardiovascular events (MACE). The time to the first occurrence of MACE was

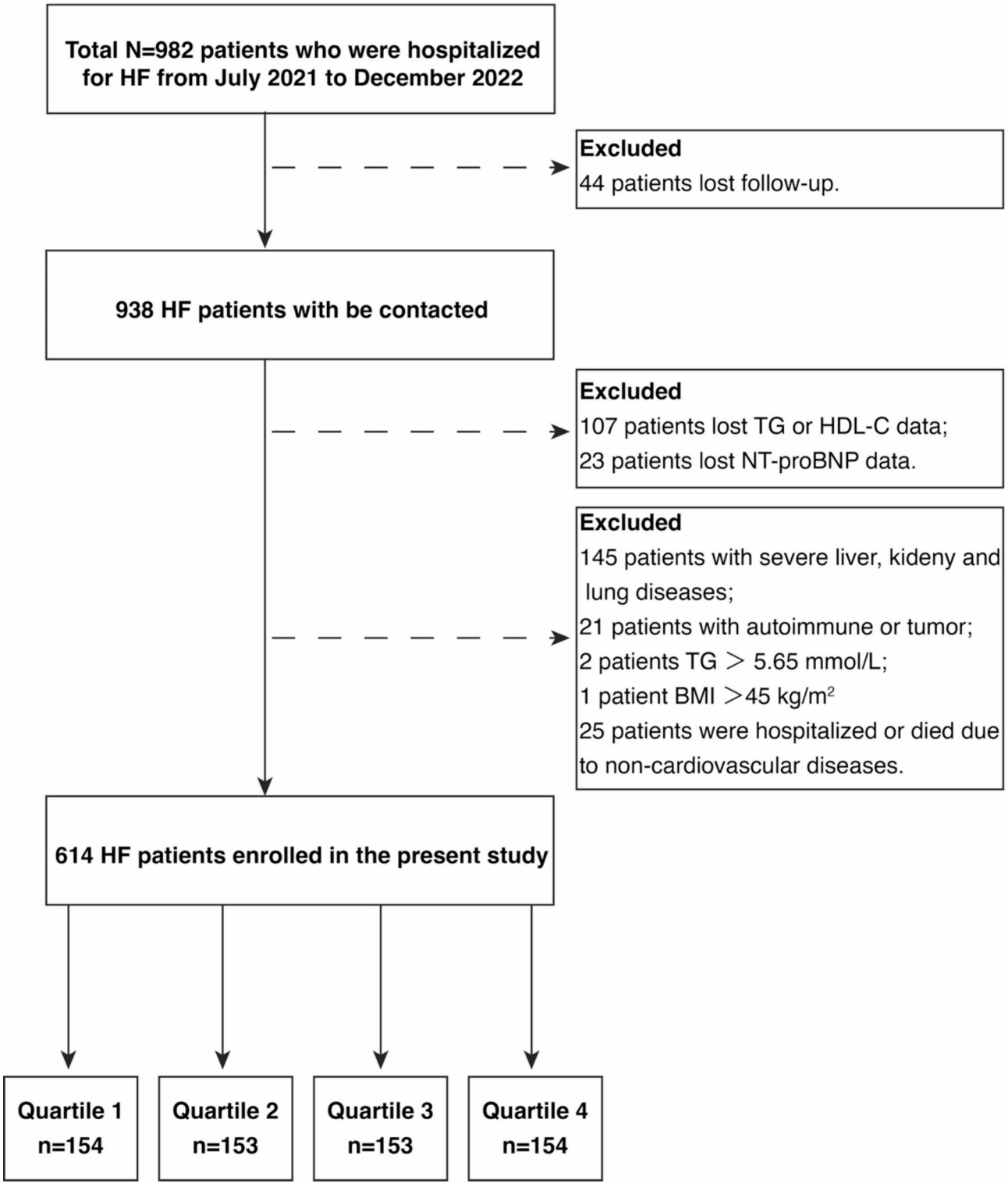

Fig. 1 Flow diagram of the study population
HF: heart failure; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; BMI: body mass index; NT-proBNP: N-terminal pro-B-type natriuretic peptide

recorded as the endpoint time. Trained researchers confirmed events via patient interviews and medical records.

Definitions

TG/HDL-C ratio The fasting serum triglyceride level (mmol/L) divided by the high-density lipoprotein cholesterol level (mmol/L).

Body mass index (BMI) Calculated as body weight (kg) divided by height squared (m^2).

New York heart association (NYHA) functional classification Symptoms and physical activity limitations were categorized into four classes (I, II, III, and IV) based on severity, following the 2021 ESC Guidelines [19].

Estimated Glomerular Filtration Rate (eGFR) Calculated via using the formula: eGFR (ml/min/1.73 m^2) = 175 × [Scr (mg/dL) – 1.234] × [age (years) – 0.179] × 0.79, which is based on the Modification of Diet in Renal Disease (MDRD) equation as defined by the Chinese eGFR Investigation Collaboration [20].

Major adverse cardiovascular events (MACE) Defined as HF rehospitalization (due to worsening HF) and CV death (e.g., death caused by myocardial infarction, stroke, or other cardiovascular events).

Ethics statement

This study adhered to the Helsinki Declaration and was approved by the Ethical Review Board of The First Affiliated Hospital of Nanchang University (Ethical Number: IIT2024402). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study, and all data were anonymized and handled with strict confidentiality.

Statistical analysis

SPSS 24.0 and R 4.2.3 were used for analyses. Continuous variables were tested for normality and expressed as mean ± SD or medians with interquartile ranges. Comparisons were conducted using t-tests, Mann-Whitney U tests, χ^2 tests, or Fisher's exact tests. Kaplan-Meier curves and Cox proportional hazards models assessed associations between TG, HDL-C, and TG/HDL-C ratio with MACE risk. Pairwise comparisons between quartiles were not performed. Restricted cubic splines (RCS) were employed to analyze non-linear relationships. Sensitivity analyses validated findings. A two-sided P value < 0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 982 patients were initially diagnosed with HF and admitted to our department. Of these, 318 patients were excluded for the following reasons: 38 were lost to follow-up, 107 had missing TG or HDL-C data, 23 had missing NT-proBNP data, and 194 had severe comorbidities, including severe liver, kidney, or lung diseases; autoimmune disorders; or tumors. Ultimately, 614 patients met the inclusion criteria and were included in the study.

Based on TG/HDL-C ratios, the 614 patients were divided into four groups: Quartile 1 ($n = 154$), Quartile 2 ($n = 153$), Quartile 3 ($n = 153$), and Quartile 4 ($n = 154$). Baseline characteristics of these groups are summarized in Table 1(see Table 1 at the end of the document). The mean age of all patients was 68.94 ± 14.34 years, with 59.12% being male. Causes of HF included ischemic heart disease (34.04%), myocardial disease (6.03%), valvular disease (20.03%), and other causes (39.9%). The mean LVEF was 46.59 ± 10.89%, with heart failure with preserved ejection fraction(HFpEF, LVEF ≥ 50%)), heart failure with mildly reduced ejection fraction(HFmrEF, 41%< LVEF < 50%) and heart failure with reduced ejection fraction(HFrEF, LVEF ≤ 40%) accounting for 28.18%, 26.71% and 45.11% of cases, respectively. No significant differences in LVEF distribution were observed among the four quartile groups ($P = 0.14$). Patients in the Quartile 4 group tended to be younger and exhibited lower LVEF, and exhibited a more adverse metabolic profile, including higher BMI, hemoglobin (Hb), total cholesterol (TC), fasting blood glucose (FBG), and glycated hemoglobin (HbA1c%) levels (all $P < 0.05$). Additionally, Quartile 4 patients also had significantly higher rates of DM, and sodium-glucose cotransporter-2 (SGLT2) inhibitor use, at 27.92% and 36.36%, respectively (all $P < 0.05$), highlighting a close link between metabolic dysregulation and HF risk.

TG/HDL-C ratio and outcomes

During the 12-month follow-up, 154 patients (25.41%) experienced MACE, including 138 HF rehospitalization (22.48%) and 18 CV death (2.93%) (Table 1). Patients in Quartile 4 (highest TG/HDL-C ratio) had the highest MACE incidence (40.38%), significantly exceeding the rates observed in Quartiles 1–3 ($P < 0.001$). Compared to those who did not experience these events, patients in the MACE, HF rehospitalization, and CV death groups exhibited higher TG/HDL-C ratios (Additional file 1: Table S1; Additional file 2: Table S2; Additional file 3: Table S3).

Kaplan-Meier survival curve indicated that patients in the Quartile 4 group had a significantly higher risk of MACE, HF rehospitalization, and CV death (all Log-rank $P < 0.001$, Fig. 2). In subgroup analyses, TG levels in

Table 1 Baseline characteristics of the study population according to the TG/HDL-C ratio quartiles

Variables	Total (*n* = 614)	Quartile 1 (*n* = 154)	Quartile 2 (*n* = 153)	Quartile 3 (*n* = 153)	Quartile 4 (*n* = 154)	*P*-value
		TG/ HDL-C ≤ 0.71	0.71< TG/ HDL-C ≤ 1.12	1.12< TG/ HDL-C ≤ 1.80	1.80< TG/HDL-C	
Age (years), Mean ± SD	68.94 ± 14.34	73.85 ± 11.09	70.29 ± 13.52	67.67 ± 15.08	63.94 ± 15.52	**< 0.001***
Male, n (%)	363 (59.12)	85 (55.19)	87 (56.86)	90 (58.82)	101 (65.58)	0.264
Smoke, n (%)	100 (16.29)	22 (14.29)	26 (16.99)	23 (15.03)	29 (18.83)	0.702
NYHA class, n (%)						0.12
II	206 (33.55)	53 (34.42)	50 (32.68)	51 (33.33)	52 (33.77)	
III	313 (50.98)	86 (55.84)	69 (45.10)	77 (50.33)	81 (52.60)	
IV	95 (15.47)	15 (9.74)	34 (22.22)	25 (16.34)	21 (13.64)	
LVEF-based HF classification, n (%)						0.14
HFpEF (LVEF ≥ 50%)	173 (28.18)	36 (23.38)	39 (25.49)	50 (32.68)	48 (31.17)	
HFmrEF (41%< LVEF < 49%)	164 (26.71)	34 (22.08)	45 (29.41)	41 (26.80)	44 (28.57)	
HFrEF (LVEF ≤ 40%)	277 (45.11)	84 (54.55)	69 (45.10)	62 (40.52)	62 (40.26)	
HF causes, n (%)						0.066
Ischemic	209 (34.04)	51 (33.12)	45 (29.41)	52 (33.99)	61 (39.61)	
Myocardial disease-related	37 (6.03)	5 (3.25)	7 (4.58)	12 (7.84)	13 (8.44)	
Valvular disease-related	123 (20.03)	40 (25.97)	28 (18.30)	33 (21.57)	22 (14.29)	
Others (as arrhythmias etc.)	245 (39.90)	58 (37.66)	73 (47.71)	56 (36.60)	58 (37.66)	
Length of Stay (Days), Mean ± SD	8.71 ± 4.56	7.93 ± 3.86	9.29 ± 5.44	8.60 ± 4.00	9.00 ± 4.69	0.051
Weight (kg), Mean ± SD	59.72 ± 13.53	55.71 ± 10.99	59.50 ± 13.22	60.49 ± 14.60	63.20 ± 14.10	**< 0.001***
BMI (kg/m2), Mean ± SD	22.44 ± 4.17	21.25 ± 3.57	22.43 ± 4.24	22.67 ± 4.29	23.42 ± 4.28	**< 0.001***
Laboratory parameters						
RBC (10^12/L), Mean ± SD	4.13 ± 0.78	3.95 ± 0.70	4.06 ± 0.72	4.26 ± 0.84	4.23 ± 0.82	**0.001***
Hb (g/L), Mean ± SD	121.93 ± 23.15	118.45 ± 21.02	120.18 ± 22.21	123.16 ± 23.97	125.93 ± 24.74	**0.024***
CRP (mg/L), M (Q_1, Q_3)	6.96 (2.36, 16.74)	5.26 (1.98, 15.46)	8.96 (4.99, 15.10)	5.83 (1.73, 17.62)	6.78 (3.48, 18.77)	0.176
NT-ProBNP (pg/ml), M (Q_1, Q_3)	2956.50 (1275.95, 6985.50)	2146.35 (1137.50, 5055.65)	3466.50 (1852.40, 9213.30)	3141.00 (1330.00, 6292.60)	2660.30 (1055.03, 7695.00)	**0.046***
TC (mmol/L), Mean ± SD	3.89 ± 1.10	3.83 ± 0.97	3.72 ± 1.09	3.90 ± 1.07	4.12 ± 1.23	**0.014***
TG (mmol/L), Mean ± SD	1.36 ± 0.91	0.70 ± 0.21	0.94 ± 0.27	1.37 ± 0.48	2.44 ± 1.07	**< 0.001***
HDL-C (mmol/L, Mean ± SD	1.06 ± 0.36	1.40 ± 0.35	1.03 ± 0.26	0.97 ± 0.31	0.83 ± 0.23	**< 0.001***

Table 1 **(continued)**

Variables	Total (*n* = 614)	Quartile 1 (*n* = 154)	Quartile 2 (*n* = 153)	Quartile 3 (*n* = 153)	Quartile 4 (*n* = 154)	*P*-value
		TG/ HDL-C ≤ 0.71	**0.71< TG/ HDL-C ≤ 1.12**	**1.12< TG/ HDL-C ≤ 1.80**	**1.80< TG/HDL-C**	
LDL-C (mmol/L), Mean ± SD	2.28 ± 0.88	2.33 ± 0.91	2.19 ± 0.89	2.31 ± 0.94	2.29 ± 0.78	0.501
eGFR [ml/ (min*1.73m^2)], M (Q_1, Q_3)	0.37 (0.27, 0.45)	0.38 (0.30, 0.45)	0.36 (0.24, 0.44)	0.36 (0.28, 0.45)	0.37 (0.27, 0.46)	0.132
CK-MB, M (Q_1, Q_3)	18.00 (13.80, 23.40)	18.00 (14.00, 22.80)	18.30 (13.20, 25.00)	18.00 (14.00, 23.90)	17.15 (13.07, 22.40)	0.514
FPG (mmol/L), Mean ± SD	6.69 ± 2.87	5.91 ± 2.08	6.35 ± 2.55	6.74 ± 2.50	7.73 ± 3.76	**< 0.001***
HbA1c (%), Mean ± SD	6.32 ± 1.14	6.07 ± 0.75	6.12 ± 0.94	6.41 ± 1.12	6.69 ± 1.51	**< 0.001***
LVEF (%), Mean ± SD	46.59 ± 10.89	48.81 ± 10.28	46.78 ± 10.70	45.50 ± 11.46	45.28 ± 10.84	**0.017***
LVEDD (mm), Mean ± SD	54.01 ± 9.97	53.21 ± 9.16	53.88 ± 9.73	54.03 ± 10.07	54.92 ± 10.88	0.518
LAAPD (mm), Mean ± SD	43.39 ± 8.36	43.88 ± 8.73	44.55 ± 8.10	42.62 ± 8.60	42.51 ± 7.88	0.09
IVSD (mm), Mean ± SD	9.95 ± 1.74	9.73 ± 1.43	10.01 ± 1.76	10.10 ± 1.93	9.97 ± 1.81	0.284
QRSd (ms), Mean ± SD	108.62 ± 23.58	107.56 ± 23.69	111.18 ± 24.86	106.90 ± 24.04	108.85 ± 21.61	0.4
Comorbidities						
DM, n (%)	137 (22.35)	20 (12.99)	34 (22.37)	40 (26.14)	43 (27.92)	**0.008***
Hypertension, n (%)	232 (37.79)	52 (33.77)	53 (34.64)	65 (42.48)	62 (40.26)	0.316
CAD, n (%)	230 (37.46)	54 (35.06)	51 (33.33)	55 (35.95)	70 (45.45)	0.12
PCI, n (%)	70 (11.40)	15 (9.74)	12 (7.84)	20 (13.07)	23 (14.94)	0.198

Table 1 (continued)

Variables	Total (*n* = 614)	Quartile 1 (*n* = 154)	Quartile 2 (*n* = 153)	Quartile 3 (*n* = 153)	Quartile 4 (*n* = 154)	*P*-value
Valvular diseases, n (%)	222 (36.16)	68 (44.16)	53 (34.64)	54 (35.29)	47 (30.52)	0.086
AF, n (%)	261 (42.51)	69 (44.81)	71 (46.41)	64 (41.83)	57 (37.01)	0.36
CKD, n (%)	177 (28.83)	31 (20.13)	46 (30.07)	52 (33.99)	48 (31.17)	**0.042***
COPD, n (%)	102 (16.61)	48 (31.17)	17 (11.11)	23 (15.03)	14 (9.09)	**< 0.001***
Medical therapy						
ACEI/ARB/ARNI, n (%)	501 (82.13)	131 (86.18)	121 (79.61)	126 (82.89)	123 (79.87)	0.398
Beta blocker, n (%)	464 (76.07)	111 (73.03)	105 (69.08)	124 (81.58)	124 (80.52)	**0.028***
Diuretics, n (%)	490 (80.33)	126 (82.89)	122 (80.26)	120 (78.95)	122 (79.22)	0.817
SGLT2 inhibitors, n (%)	172 (28.20)	30 (19.74)	37 (24.34)	49 (32.24)	56 (36.36)	**0.005***
Lipid lowering therapies, n (%)	283 (46.09)	71 (46.10)	62 (40.52)	70 (45.75)	80 (51.95)	0.257
Outcomes						
MACE, n (%)	156 (25.41)	18 (11.64)	41 (26.28)	34 (21.79)	63 (40.38)	**< 0.001***
CV Rehospitalization, n (%)	138 (22.48)	17 (11.04)	39 (25.49)	31 (20.26)	51 (33.12)	**< 0.001***
CV death, n (%)	18 (2.93)	1 (0.65)	2 (1.31)	3 (1.96)	12 (7.79)	**0.001***

Continuous variables are expressed as mean ± standard deviation, or as medians and interquartile ranges; Categorical variables are expressed as frequency (percentage).

* $P<0.05$. SD: standard deviation, M: Median, Q_1: 1st Quartile, Q_3: 3rd Quartile.

NYHA: New York Heart Association; LVEF: left ventricle ejection fraction; HFpEF: HF with Preserved Ejection Fraction; HFmrEF: HF with Mid-Range Ejection Fraction; HFrEF: HF with Reduced Ejection Fraction; BMI: body mass index; RBC: red blood cell; Hb: hemoglobin; CRP: C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; eGFR: estimated glomerular filtration rate; CK-MB: creatine kinase isoenzymes; FPG: fasting plasma glucose; HbA1c: hemoglobin A1c; LVEDD: left ventricular end diastolic dimension; LAAPD: left atrium anteroposterior diameter; IVSD: interventricular septum diameter; QRSd: QRS duration; DM: diabetes mellitus; CAD: coronary artery disease; PCI: percutaneous coronary intervention; AF: atrial fibrillation; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; MACE: major adverse cardiovascular event; CV: cardiovascular; ACEI/ARB/ARNI: angiotensin-converting enzyme inhibitor/angiotensin receptor blocker/ angiotensin receptor II blocker - neprilysin inhibitor; SGLT2i: sodium-glucose cotransporter-2 inhibitors.

Quartile 4 were associated with significantly higher risks of MACE, HF rehospitalization, and CV death (Log-rank $P<0.001$, $P<0.001$ and $P=0.025$, respectively; Additional file 1: Fig. S1); In contrast, higher HDL-C levels were only associated with reduced HF rehospitalization risk (Log-rank $P=0.021$), with no significant associations found for MACE or CV death (Log-rank $P=0.058$ and $P=0.170$, respectively; Additional file 2: Fig. S2).

Nonlinear relationship between the TG/HDL-C ratio and MACE risk

Figure 3 demonstrates the nonlinear relationship between the TG/HDL-C ratio and MACE risk in patients with new-onset HF, as analyzed using a Cox proportional hazards regression model with RCS analysis. After adjusting for multiple comprehensive factors (gender, DM, age, weight, BMI, FBG, HbA1C and LVEF), the findings confirmed a nonlinear association between the TG/HDL-C ratio and MACE incidence (P for nonlinear = 0.026), with a cut-off point at 1.08. Based on this, a two-piecewise Cox proportional hazards regression model was applied to determine the HRs and CIs on either side of the inflection point (Table 2). Below the inflection point (TG/HDL-C ratio < 1.08), the HR was 1.38 (95% CI: 1.19–1.59), indicating a moderate increase in MACE risk with rising TG/HDL-C ratios; Above the inflection point (TG/HDL-C ≥ 1.08), the HR increased sharply to 7.27 (95% CI: 1.56–33.89), highlighting a steep rise in adverse events in patients with elevated TG/HDL-C ratios.

Association between the TG/HDL-C ratio and other factors

To explore the association between the TG/HDL-C ratio and various clinical and metabolic factors that play important roles in HF development, a Pearson correlation test was performed. The results identified significant correlations between the TG/HDL-C ratio and FPG, BMI and HbA1c in HF patients, with correlation coefficients of $R=0.196$, 0.176 and 0.107, respectively (all $P<0.001$, Fig. 4). However, traditional HF markers such as LVEF and NT-proBNP did not show significant correlations with the TG/HDL-C ratio in the overall population (Additional file 4: Table S4). Notably, in patients with HFpEF, TG/HDL-C ratio showed a weak positive correlation with NT-proBNP ($r=0.135$, $P=0.026$), while no significant correlations were observed in HFrEF or HFmrEF patients (Additional file 5: Table S5).

Correlation between the TG/HDL-C ratio and MACE risk

Since the baseline characteristics and based on established clinical relevance, we performed univariate and multivariate Cox proportional hazards regression analyses to explore the association between the TG/HDL-C ratio and MACE, and the results are presented in (Additional file 3: Fig. S3) and Table 3. When treated as a continuous variable, each 1-unit increase in the TG/

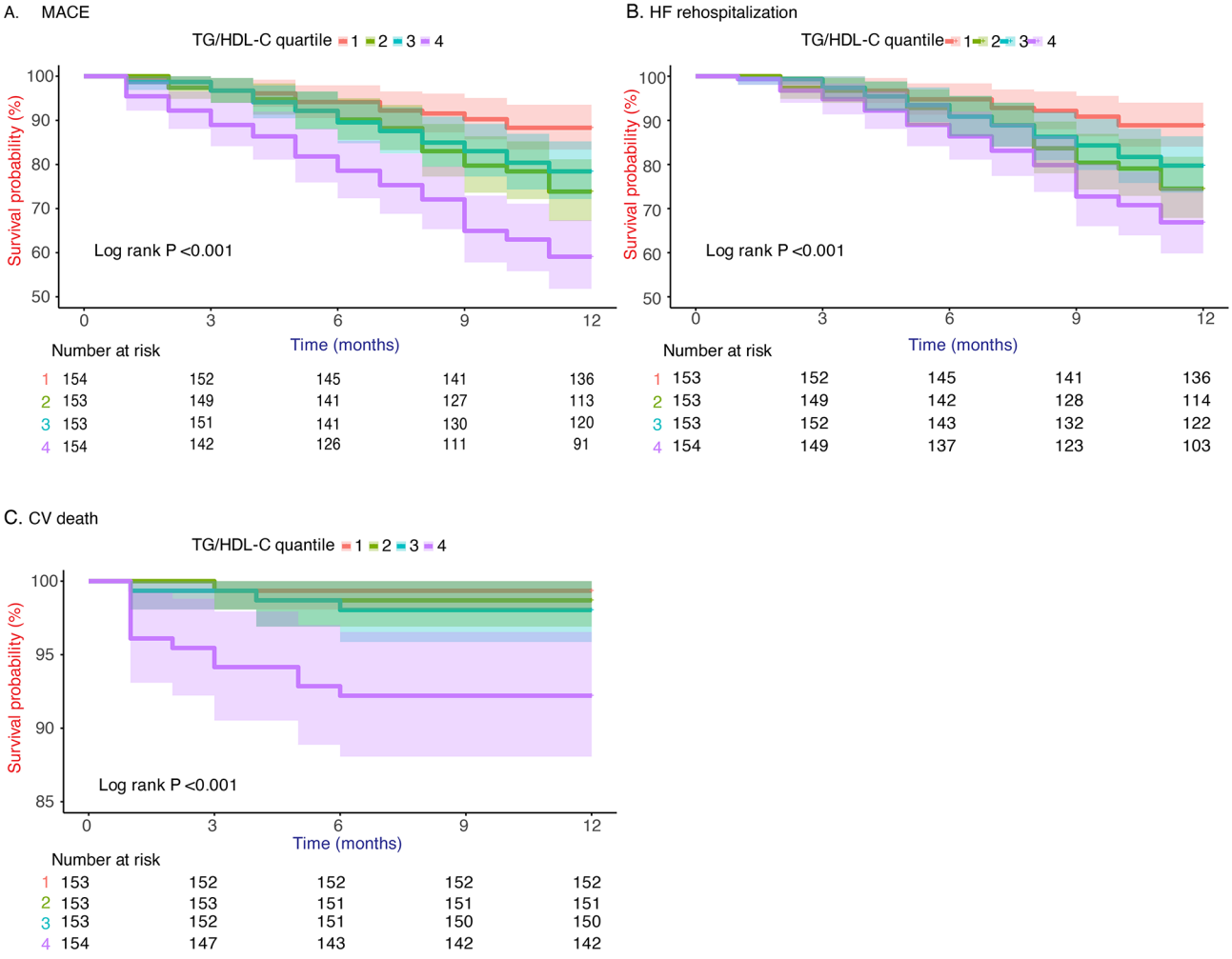

Fig. 2 Kaplan–Meier analyses for different endpoints among the TG/HDL-C ratio quartiles. **A**: MACE. **B**: CV death. **C**: HF rehospitalization. CV, cardiovascular; HF, heart failure

HDL-C ratio was associated with a 31% higher risk of adverse events in Model 1 (HR = 1.31, 95% CI: 1.20–1.44, $P < 0.001$). After adjusting for multiple factors, including Gender, Age, BMI, FDG, RBC, Hb, NT-proBNP, TC, LDL, eGFR, FPG, HbA1c, LVEF, DM, Hypertension, CAD, CKD, COPD, Smoke, ACEI/ARB/ARNI, Beta blocker, Diuretics and SGLT2 inhibitors, the risk increased to 44% in Model 4 (HR = 1.44, 95% CI: 1.29–1.60, $P < 0.001$). When considering the TG/HDL-C ratio was analyzed as a categorical variable, the risk of MACE was significantly higher in the upper quartiles (Quartile 2, Quartile 3 and Quartile 4) compared to the Quartile 1 group (all $P < 0.05$). In Model 4, Quartile 2 had an HR of 2.44 (95% CI: 1.34–4.46, $P = 0.004$), Quartile 3 had an HR of 2.78 (95% CI: 1.49–5.16, $P = 0.001$), and Quartile 4 had an HR of 5.78 (95% CI: 3.08–10.08, $P < 0.001$). These findings underscore the clinical utility of the TG/HDL-C ratio for risk stratification in patients with new-onset HF, identifying those at significantly higher risk for adverse events within 12 months.

Sensitivity analysis

To validate the relationship between the TG/HDL-C ratio and MACE risk incidence, multiple sensitivity analyses were conducted (Table 4). In the subgroup of patients with a BMI < 24 kg/m²(Model I), adjusting for factors such as age, FDG, RBC, Hb, neutrophils (Neu), CRP, NT-proBNP, TC, LDL, eGFR, FBG, HbA1c, LVEF, diabetes mellitus (DM), hypertension, CKD, COPD, smoking status, ACEI/ARB/ARNI, beta blockers, diuretics, and SGLT2 inhibitors, the TG/HDL-C ratio was significantly associated with MACE (HR = 1.51, 95% CI: 1.04–2.20, $P = 0.028$). Similar associations were observed in patients without diabetes (Model II) and in those not receiving SGLT2 inhibitors (Model III), with HRs of 1.58 (95% CI: 1.26–1.99, $P < 0.001$) and 1.53 (95% CI: 1.19–1.97, $P < 0.001$), respectively. Furthermore, when analyzed as a

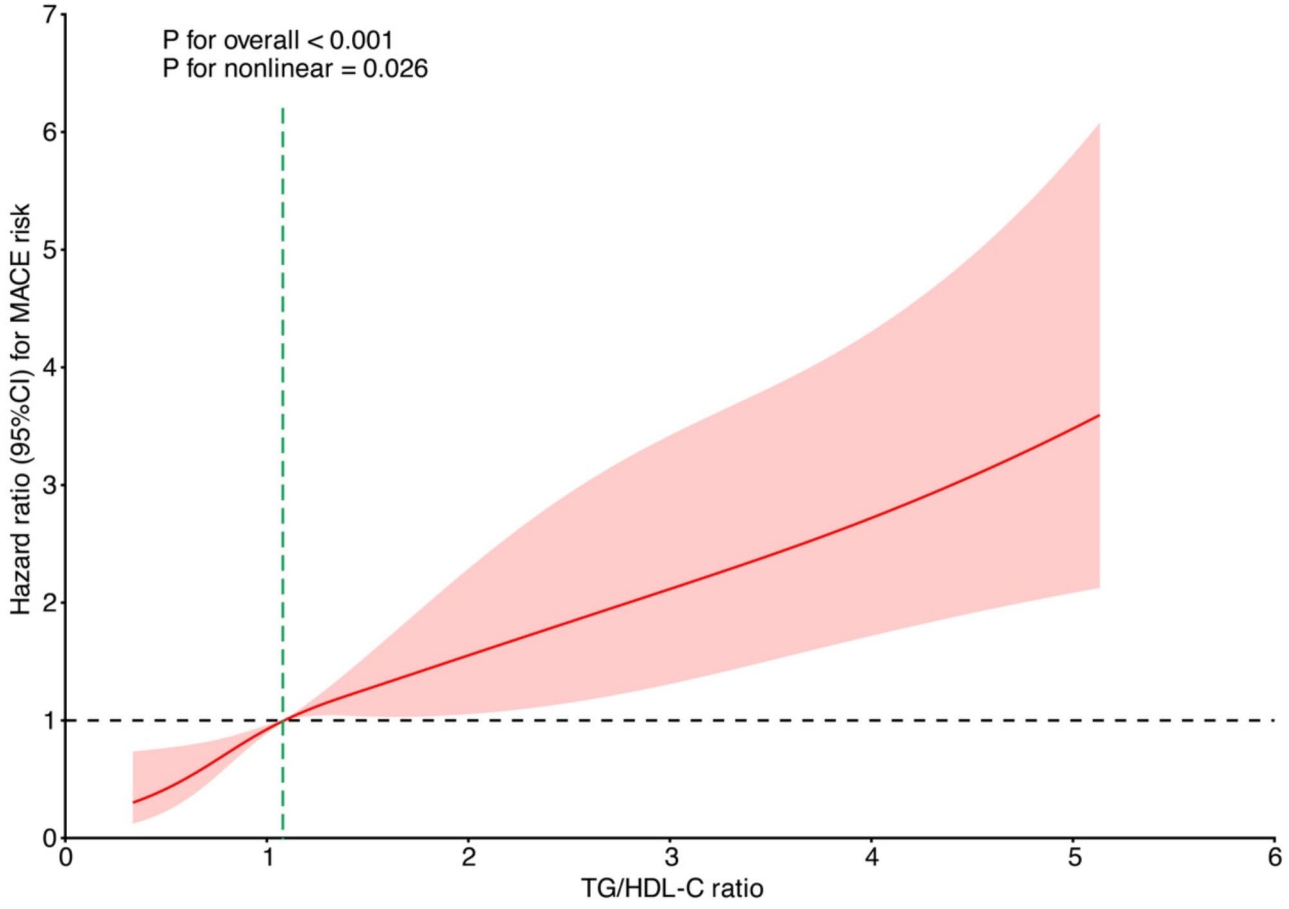

Fig. 3 Nonlinear correlation between the TG/HDL-C ratio and MACE risk

Table 2 Results of the two-piecewise linear regression model

Outcome: MACE	HR (95%CI)	*P*-value
Fitting model by standard linear regression	1.44 (1.29, 1.60)	< 0.001
Inflection points of the TG/HDL-C ratio	1.08	
< 1.08	1.38 (1.19, 1.59)	< 0.001
≥ 1.08	7.27 (1.56, 33.89)	0.012
P for log-likelihood ratio test		0.026

categorical variable, the TG/HDL-C ratio demonstrated a consistent positive association with MACE across all subgroups (all $P<0.05$). These sensitivity analyses reinforce the robustness and reliability of our findings, highlighting the independent prognostic value of the TG/HDL-C ratio across different clinical contexts.

Discussion

This study examined the relationship between the TG/HDL-C ratio and clinical outcomes in patients with new-onset HF. Our findings demonstrate that a higher TG/HDL-C ratio is strongly associated with an increased risk of MACE within 12 months, including HF rehospitalization and CV death. The TG/HDL-C ratio emerged as an independent predictor of MACE, both as a continuous and categorical variable, even after adjusting for confounders. These results highlight its value as a reliable and practical prognostic marker for risk stratification in this population.

IR, a hallmark of metabolic syndrome, plays a central role in this process by disrupting glucose and lipid metabolism, heightened inflammatory responses, and oxidative stress [21, 22]. These factors exacerbate myocardial remodeling and accelerate HF progression. Although the hyperinsulinemia-euglycemic clamp (HEC) is considered the gold standard for measuring IR, its complexity and cost limit use [23]. The homeostasis model assessment of insulin resistance (HOMA-IR) index provides a practical alternative, though it is unsuitable for individuals using exogenous insulin or with β-cell dysfunction [24]. To address these limitations, markers such as the triglyceride-glucose index (TyG), triglyceride-glucose body mass index (TyG-BMI), TG/HDL-C ratio, and metabolic score for insulin resistance (METS-IR) have gained traction as reliable, cost-effective, and straightforward surrogates for assessing IR [25–29].

Most prior studies have examined the TG/HDL-C ratio in coronary artery disease and metabolic syndrome

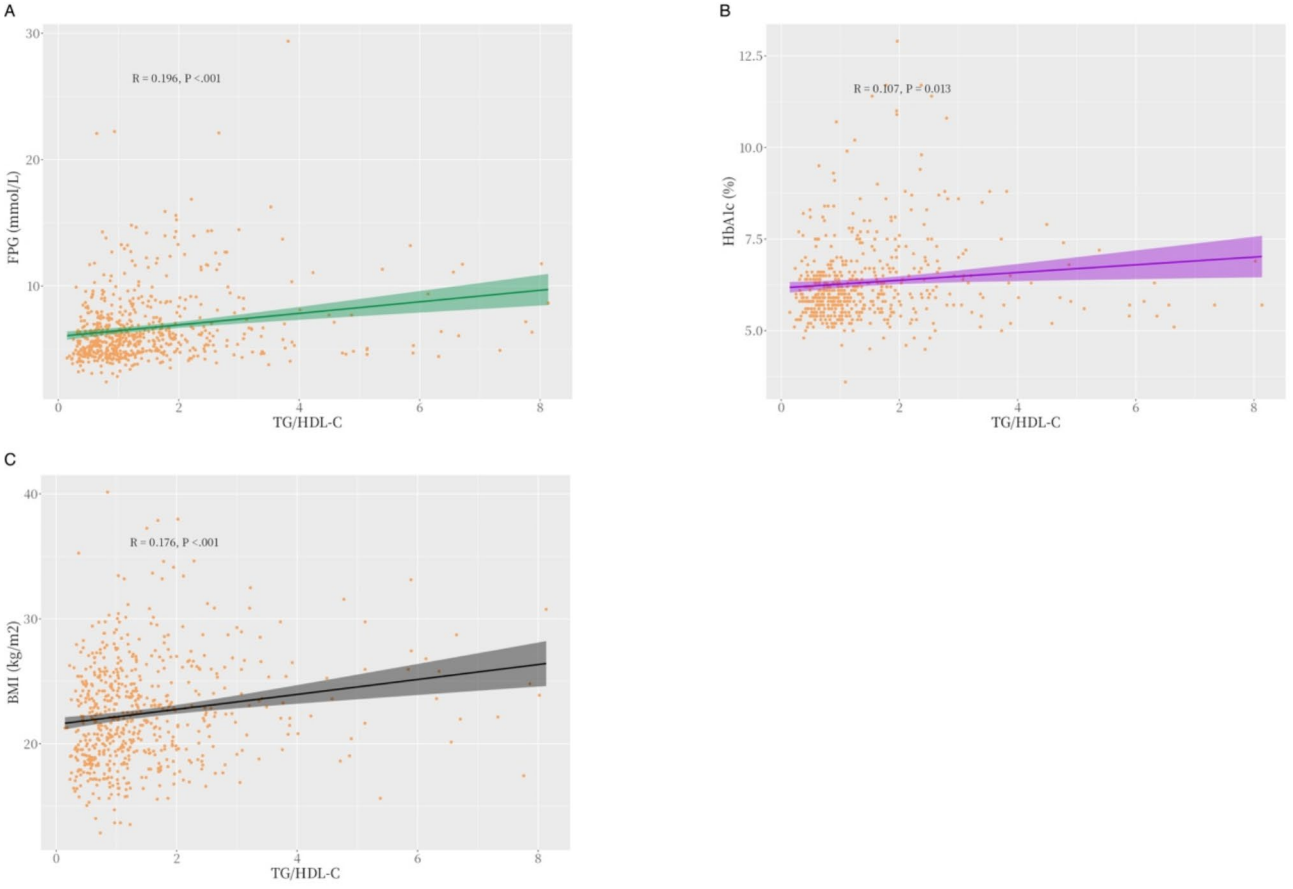

Fig. 4 Correlation between the TG/HDL-C ratio and FPG (**A**), HbA1c (**B**) and BMI (**C**). PG: fasting plasma glucose; HbA1c: hemoglobin A1c; BMI: body mass index

Table 3 Correlation between the TG/HDL-C ratio and MACE risk in different models

Exposure	Model 1		Model 2		Model 3		Model 4	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
#TG/HDL-C ratio	1.31 (1.20, 1.44)	< 0.001	1.39 (1.26, 1.53)	< 0.001	1.41 (1.27, 1.56)	< 0.001	1.44 (1.29, 1.60)	< 0.001
TG/HDL-C ratio quartiles								
Q1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Q2	2.35 (1.35, 4.10)	0.003	2.80 (1.56, 5.03)	< 0.001	2.52 (1.39, 4.57)	0.002	2.44 (1.34, 4.46)	0.004
Q3	1.93 (1.08, 3.42)	0.025	2.48 (1.36, 4.52)	0.003	2.25 (1.22, 4.17)	0.009	2.78 (1.49, 5.16)	0.001
Q4	4.16 (2.46, 7.02)	< 0.001	6.27 (3.57, 11.02)	< 0.001	5.25 (2.95, 9.34)	< 0.001	5.57 (3.08, 10.08)	< 0.001

TG/HDL-C as a continuous variable. HR: Hazard Ratio; CI: Confidence Interval; Q: Quartile.

Model 1: Crude.

Model 2: Adjust Gender, Age.

Model 3: Adjust Gender, Age, BMI, FDG, RBC, Hb, NT-proBNP, TC, LDL, eGFR, LVEF, Hypertension, CAD, CKD, COPD, Smoke.

Model 4: Adjust Gender, Age, BMI, FDG, RBC, Hb, NT-proBNP, TC, LDL, eGFR, FBG, HbA1c, LVEF, DM, Hypertension, CAD, CKD, COPD, Smoke, ACEI/ARB/ARNI, Beta blocker, Diuretics, SGLT2 inhibitors.

[30–32]. For instance, Alifu et al. [30] and Liu et al. [32] reported its association with increased MACE risk in chronic coronary syndrome and community-based cohorts. However, research on the TG/HDL-C ratio is limited, particularly for new-onset HF. Our study addresses this gap and provides new evidence supporting the prognostic relevance of the TG/HDL-C ratio in this vulnerable population.

In our study patients with higher TG/HDL-C ratios experienced significantly higher cumulative MACE rates. For example, 40.38% of patients in Quartile 4 faced MACE, including 33.12% hospitalized for HF and 7.79% who died from CV causes, compared to lower rates in Quartiles 1–3. One molecular link between the TG/HDL-C ratio and IR is apolipoprotein C-I (ApoC-I), a key regulator of TG and HDL-C levels. Reduced ApoC-I

Table 4 Relationship between the TG/HDL-C ratio and the MACE in different sensitivity analyses

Exposure	Model I, HR (95%CI)	*P*	Model II, HR (95%CI)	*P*	Model III, HR (95%CI)	*P*
#TG/HDL-C ratio	1.46 (1.24 ~ 1.71)	< 0.001	1.53 (1.35 ~ 1.74)	< 0.001	1.54 (1.35 ~ 1.75)	< 0.001
TG/HDL-C ratio quartiles						
Q1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
Q2	2.21 (0.96 ~ 5.08)	0.062	2.40 (1.17 ~ 4.93)	0.017	3.00 (1.39 ~ 6.46)	0.005
Q3	3.71 (1.63 ~ 8.45)	0.002	2.68 (1.28 ~ 5.62)	0.009	2.52 (1.14 ~ 5.57)	0.023
Q4	5.80 (2.57 ~ 13.10)	< 0.001	5.81 (2.87 ~ 11.77)	< 0.001	6.56 (3.13 ~ 13.73)	< 0.001

TG/HDL-C as a continuous variable; HR: Hazard Ratio; CI: Confidence Interval; Q: Quartile.

Model I was used for sensitivity analysis in participants with BMI < 24 kg/m2. Adjusted Gender, Age, FDG, RBC, Hb, NT-proBNP, TC, LDL, eGFR, FBG, HbA1c, LVEF, DM, Hypertension, CKD, COPD, Smoke, ACEI/ARB/ARNI, Beta blocker, Diuretics, SGLT2inhibitors

Model II was used for sensitivity analysis in participants without DM. Adjusted Gender, Age, BMI, FDG, RBC, Hb, NT-proBNP, TC, LDL, eGFR, FBG, HbA1c, LVEF, Hypertension, CKD, COPD, Smoke, ACEI/ARB/ARNI, Beta blocker, Diuretics, SGLT2inhibitors.

Model III was used for sensitivity analysis in participants without SGLT2 inhibitors treatment. Adjusted Gender, Age, BMI, FDG, RBC, Hb, NT-proBNP, TC, LDL, eGFR, FBG, HbA1c, LVEF, DM, Hypertension, CKD, COPD, Smoke, ACEI/ARB/ARNI, Beta blocker, Diuretics.

levels are associated with worsening IR, elevated fasting blood glucose, and an increased risk of developing diabetes [33].

A novel finding of this study was the nonlinear relationship between the TG/HDL-C ratio and MACE risk, with an inflection point at 1.08. Below this point, the hazard ratio (HR) for MACE was 1.38 (95% CI: 1.19–1.59), indicating a moderate risk increase; Above the inflection point, the HR increased sharply to 7.27 (95% CI: 1.56–33.89), reflecting a steep escalation in risk. Notably, what changes below the inflection point is the slope of the curve, but that indeed patients with a low TG/HDL ratio have lower risk of MACE. These findings underscore the importance of closely monitoring HF patients with elevated TG/HDL-C ratios during hospitalization and follow-up. This data-driven threshold requires further validation in larger, diverse cohorts, but it highlights the need for closer monitoring and more intensive management in patients with TG/HDL-C ratios exceeding 1.08.

Metabolic dysregulation, characterized by abnormalities in lipid and glucose metabolism, plays a pivotal role in HF progression. This interplay is both causative and complementary, collectively worsening the prognosis of HF [9, 34, 35]. Beyond traditional markers such as NT-proBNP and LVEF, metabolic syndrome components—hypertension, obesity, hyperglycemia, and dyslipidemia—also predict HF outcomes [34, 36, 37]. In this study, patients with new-onset HF in the highest TG/HDL-C ratio group were younger than those in other groups but exhibited a higher prevalence of elevated BMI, FPG, and HbA1c levels ($P < 0.001$). Furthermore, the proportion of DM was significantly greater in the Quartile 4 group compared to the Quartile 1 group[43 (27.92%) vs. 20 (12.99%), $P = 0.008$], identifying a strong association between these metabolic syndrome markers and adverse outcomes in HF patients [38–42]. Additionally, diabetes mellitus was significantly more prevalent in Quartile 4 (27.92%) compared to Quartile 1 (12.99%, $P = 0.008$). The TG/HDL-C ratio showed positive correlations with BMI ($R = 0.176$, $P < 0.001$), FBG ($R = 0.196$, $P < 0.001$), and HbA1c ($R = 0.107$, $P = 0.013$), and a negative correlation with age (R = -0.226, $P < 0.001$). Regarding traditional HF markers, TG/HDL-C ratio did not correlate with NT-proBNP or LVEF in the overall cohort. However, subgroup analysis revealed a weak positive correlation between TG/HDL-C ratio and NT-proBNP in HFpEF patients ($r = 0.135$, $P = 0.026$), while no significant correlations were found in HFrEF or HFmrEF patients. This suggests that TG/HDL-C ratio may reflect myocardial stress more prominently in HFpEF, though further studies are needed to confirm this. To further evaluate the independent prognostic value of TG/HDL-C ratio, our multivariable Cox regression and sensitivity analyses consistently demonstrated that the TG/HDL-C ratio is an independent predictor of MACE, reinforcing its potential utility in routine clinical practice. Beyond traditional risk factors, monitoring TG/HDL-C may help identify high-risk new-onset HF patients who could benefit from more intensive metabolic and cardiovascular management.

Notably, a study by Zhou et al. demonstrated that the TG/HDL-C ratio is associated with both 5-year and 360-day mortality in ICU-admitted HF patients, focusing on all-cause mortality [43]. In contrast, our study concentrated on newly diagnosed HF patients, with MACE—including HF rehospitalization and CV death—as the primary endpoint over 12 months. This distinction underscores the TG/HDL-C ratio's prognostic value in early HF stages, supporting its utility in risk stratification and guiding early intervention strategies.

Conclusions

This study highlights the TG/HDL-C ratio as a new marker that independently predicts the risk of MACE in new-onset HF patients during the first year after discharge. Incorporating this marker into routine risk assessment may help identify high-risk patients for closer monitoring and early intervention. Prospective multicenter studies with longer follow-up and diverse

populations are warranted to validate the prognostic utility of the TG/HDL-C ratio and explore its potential integration into HF risk stratification frameworks.

Limitations

This study has several limitations. First, being a single-center retrospective study with a small, homogeneous sample, its findings may lack generalizability. Multicenter, diverse cohort studies are needed to validate these results. Second, the retrospective design also limits causal inference, and the bidirectional relationship between HF and the TG/HDL-C ratio complicates interpretation. Third, conclusions are based on a one-year follow-up period, leaving uncertainty about whether the TG/HDL-C ratio serves as a long-term risk factor. Extended follow-up studies are needed for further validation. Fourth, TG and HDL-C levels were measured during hospitalization, which may not fully reflect the patients' overall glycemic and lipid metabolic status. Fifth, direct comparisons between the TG/HDL-C ratio and other established lipid and metabolic markers (e.g., LDL-C, apolipoprotein B, and the triglyceride-glucose index) were not performed, limiting the ability to assess its incremental predictive value relative to traditional markers. Sixth, subgroup analyses by HF etiology or severity were not conducted due to limited sample size, leaving the applicability of these findings across HF subtypes uncertain. Future studies with extended follow-up and broader populations are warranted. Finally, this study did not apply competing risk analysis, such as the Fine and Gray model, which could have provided additional insights into the distinct risks of HF rehospitalization and CV death. Future studies with larger cohorts could further explore these risks using appropriate competing risk models and comparative analyses with other lipid and metabolic markers to further clarify the prognostic role of the TG/HDL-C ratio in new-onset HF.

Abbreviations

TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol
TG/HDL-C	Triglyceride to high-density lipoprotein cholesterol
HF	Heart failure
MACE	Major adverse cardiovascular events
CV	Cardiovascular
K–M	Kaplan–Meier
RCS	Restricted cubic splines
CI	Confidence interval
HR	Hazard ratio
NYHA	New York Heart Association
BMI	Body mass index
RBC	Red blood cell
Hb	Hemoglobin
CRP	C-reactive protein
NT-proBNP	N-terminal pro-B-type natriuretic peptide
TC	Total cholesterol
LDL-C	Low-density lipoprotein cholesterol
eGFR	Estimated glomerular filtration rate
CK-MB	Creatine kinase isoenzymes
FPG	Fasting plasma glucose
HbA1c	Hemoglobin A1c
LVEF	Left ventricle ejection fraction
LVEDD	Left ventricular end diastolic dimension
LAAPD	Left atrium anteroposterior diameter
IVSD	Interventricular septum diameter
QRSd	QRS duration
DM	Diabetes mellitus
CAD	Coronary artery disease
PCI	Percutaneous coronary intervention
AF	Atrial fibrillation
CKD	Chronic kidney disease
COPD	Chronic obstructive pulmonary disease
MACE	Major adverse cardiovascular event
CV	Cardiovascular
ACEI/ARB/ARNI	Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker/ angiotensin receptor ll blocker - neprilysin inhibitor
SGLT2i	Sodium-glucose cotransporter-2 inhibitors

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Supplementary Material 6

Supplementary Material 7

Supplementary Material 8

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Author contributions

X.P designed the study. J.W, W.D, R.L, Y.Z, J.Y and X.F acquired the data, analyzed and interpreted the data. Y. Z and X.C performed the statistical analysis. J.W drafted the manuscript. revised the manuscript. All the authors have read and approved the final manuscript.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study adhered to the Helsinki Declaration and was approved by the Ethical Review Board of The First Affiliated Hospital of Nanchang University (Ethical Number: IIT2024402). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study, and all data were anonymized and handled with strict confidentiality.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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