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Possible correlation between Triglyceride/HDL ratio and subclinical myocardial damage in patients with cardiovascular risk factors

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ABSTRACT

Aims: The triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio is considered a predictor of cardiovascular (CV) disease. The aim of the study was to evaluate the TG/HDL-C ratio as CV risk factor and its possible correlation with subclinical myocardial damage.

Methods: We enrolled 545 patients, all of whom underwent oral glucose tolerance test (OGTT). The TG/HDL-C ratio was calculated as the arithmetic ratio between triglyceride and HDL cholesterol concentrations.

Results: Patients were stratified into four quartiles based on TG/HDL-C values. From the first to the fourth quartile, there was a progressive deterioration in glucose metabolism, as evidenced by significant increases in fasting plasma glucose (FPG), 2-hour glucose, fasting plasma insulin (FPI), 2-hour insulin (all $p < 0.001$), along with a reduction in insulin sensitivity. Left ventricular global systolic function, assessed via global longitudinal strain (GLS), showed progressive deterioration across quartiles ($p < 0.001$). Logistic regression analysis revealed that each one-unit increase in the TG/HDL-C ratio was associated with a 61 % higher likelihood of having a pathological GLS (crude odds ratio: 1.61).

Conclusion: In conclusion, patients with elevated TG/HDL-C ratios exhibit subclinical myocardial dysfunction even in the absence of clinical symptoms. The TG/HDL-C ratio may represent a simple marker for early identification of CV risk.

1. Introduction

Cardiovascular disease (CVD) is one of the leading causes of premature death worldwide. In 2019, it was responsible for an estimated 18.6 million deaths and accounted for 34.4 million years of life lost globally [1,2]. These data highlight the importance of identifying risk factors that can predict the likelihood of developing CVD, thereby enabling early preventive strategies. It is well established that abnormal plasma concentrations of lipoproteins and lipids are major risk factors for CVD. Triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) play a significant role in both the pathogenesis and prognosis of cardiovascular conditions such as heart failure, atrial fibrillation, and hypertension [3]. Recent studies have emphasized the potential of the triglyceride-to-HDL cholesterol ratio (TG/HDL-C) as a predictor of CVD risk. Several reports in the literature have shown that an elevated TG/HDL-C ratio is associated with increased mortality in patients with

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aortic dissection, coronary artery disease, and type 2 diabetes mellitus (T2DM) [4]. Furthermore, the TG/HDL-C ratio has been proposed as an atherogenic index and a useful lipid marker associated with insulin resistance [5].

In recent years, growing evidence has supported the hypothesis that insulin resistance is a primary determinant of dyslipidemia in individuals with impaired glucose metabolism [6]. Accordingly, the cardiovascular risk linked to an elevated TG/HDL-C ratio may be better understood in the context of insulin resistance. Thus, the TG/HDL-C ratio could serve as a pragmatic tool for identifying individuals at higher risk of CVD due to insulin resistance and its related metabolic disturbances [7], and may also be employed as a surrogate marker for insulin resistance.

To improve the clinical prognosis of CVD, it is essential to identify early morphological and functional cardiac changes—even before overt reductions in left ventricular (LV) performance become clinically evident. The assessment of myocardial deformation represents a major advancement in echocardiography, as it provides insights into myocardial function beyond conventional echocardiographic parameters [8]. Speckle tracking echocardiography (STE) is a second-level imaging technique that allows semi-automated quantification of global and regional myocardial deformation during both systole and diastole, enabling early detection of declining cardiac efficiency [9]. The gold standard for evaluating myocardial deformation is global longitudinal strain (GLS), which has demonstrated prognostic value for cardiovascular events, even in individuals without a prior history of cardiovascular complications [8].

Based on this evidence, the aim of the present study was to investigate the potential relationship between the TG/HDL-C ratio and GLS in patients with cardiovascular risk factors.

2. Materials and methods

2.1. Study population

We enrolled 545 newly diagnosed hypertensive Caucasian patients (mean age 58.8 ± 12.1 years) participating in the CATAnzaroMEtabolicRIsk factors (CATAMERI) study [10]. All subjects underwent physical examination and review of their medical history.

Exclusion criteria were positive history for chronic respiratory or malignant disease, endocrinological pathologies, malabsorption diseases, CV complications or events, alcohol and/or drug abuse, drug therapies capable of affecting glucose metabolism.

All subjects recruited in the study participation underwent anthropometric evaluation, with measurement of height, weight and body mass index (BMI).

The ethics committee approved the protocol and informed written consent was obtained from all participants (code protocol number 2012.63). All investigations were performed in accordance with the principles of the Helsinki Declaration.

2.2. Blood pressure measurement

The assessment of clinical Blood Pressure (BP) was conducted according to current guidelines. Measurements of BP were acquired in the left arm of patients in sitting position using a semi-automatic sphygmomanometer (OMRON, M7 Intelli IT) after 5 min of rest. BP values were the average of three measurements. The evaluation was repeated on three different occasions at least 2 weeks apart. Patients with a clinic SBP > 140 mmHg and/or DBP > 90 mmHg were defined as hypertensive. Pulse pressure (PP) values were acquired as the difference between systolic and diastolic BP [11].

2.3. Laboratory determinations

All laboratory tests were performed after an overnight fast of at least 12 h. The Oral Glucose Tolerance Test (OGTT) was performed by administering 75 g of glucose dissolved in 300 ml of water and collecting samples at 0, 30, 60, 90, and 120 min to determine plasma glucose and insulin levels. T2DM was defined according to the American Diabetes Association (ADA) criteria [12].

Plasma glucose was quantified by the glucose oxidation method (Beckman Glucose Analyzer II; Beckman Instruments Milan, Italy) and plasma insulin concentration by chemiluminescence (Roche Diagnostics). Insulin sensitivity was assessed by the Matsuda index, which was calculated using the following formula:

[10,000 / $\sqrt{}$ glucose minute 0 x insulin minute 0) (mean blood glucose (OGTT) x mean insulin OGTT)] [13].

Serum Creatinine was measured by the Jaffé method. Glomerular filtration rate was measured according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula [14]. Blood uric acid levels were measured using the URICASE/POD method on an automated analyzer (Boehringer Mannheim, Mannheim, Germany) [15].

TG and total, LDL, and HDL cholesterol concentrations were measured by enzymatic methods (Roche Diagnostics, Mannheim, Germany).

TG/HDL-C ratio values were assessed by the arithmetic ratio between plasma TG and HDL concentrations [1].

2.4. Echocardiographic measurements

Comprehensive 2D and Doppler echocardiography were obtained using an ultrasound machine (Vivid E95, GE Healthcare, Horten, Norway) and performed according to the American Society of Echocardiography (ASE) guidelines [16]. Echocardiographic readings were made in random order by the investigator, who had no knowledge of patient's clinical data.

Left ventricular mass (LVM) was measured using the formula proposed by Devereux et al. and corrected for body surface area (BSA), to derive the LV mass index (LVMI) [17]. LV end-diastolic and end-systolic volumes and LV ejection fraction (LVEF) were calculated using biplane disk-summation algorithm [17], and the indexed by BSA. The values of all parameters were obtained as the average value of three consecutive cardiac cycles.

A 2D speckle tracking analysis was retrospectively performed using vendor-specific 2D speckle tracking software (EchoPAC PC, version 113.0.5, GE Healthcare, Horten, Norway). Manual tracings of the endocardial border during end-systole in three apical views was performed to evaluate GLS [18].

2.5. Statistical methods

Variables with a normal distribution were summarised as mean and standard deviation (SD), while non-normally distributed data as median and interquartile range and binary and categorical variables as absolute frequencies and percentages.

The aim of this study was to investigate the relationship between GLS and the TG/HDL-C- ratio.

Descriptive statistics were performed on the total sample and stratified by TG/HDL ratio quartiles (1st quartile (≤ 1.77 mg/dL); 2^{sd} quartile (>1.77–2.60 mg/dL); 3rd quartile (>2.60–3.75 mg/dL) and 4th quartile (>3.75 mg/dL). Differences across TG/HDL-C ratio quartiles were evaluated using analysis of variance (ANOVA) for normally distributed variables, the Kruskal-Wallis test for non-normally distributed variables, and the chi-square (χ^2) test for categorical variables. The Spearman correlation coefficient was used to assess the association between the TG/HDL-C ratio (as continuous variables) and the remaining risk factors. Results are reported as rho and p-values.

The GLS variable was dichotomised, with values greater than or equal to −20 (absolute values, more positive) indicating a pathological condition.

To assess the association between binary GLS status and the TG/

HDL-C ratio, logistic regression analysis was employed. In multivariable logistic models, covariates were selected as potential confounders if they were associated with TG/HDL and binary GLS (both with $p < 0.10$).

Data were expressed as odds ratios (OR), 95 % confidence intervals (CI) and p value. Data analyses were performed in STATA statistical package (version 16.1 for Windows, TX United States).

3. Results

The entire study population (n = 545 patients, mean age 58.8 ± 12.1 years) was divided into quartiles based on increasing values of the TG/HDL-C ratio. The median TG/HDL-C ratio in the total sample was 2.60, with an interquartile range (IQR) of 1.77–3.75.

Table 1 presents the demographic and clinical characteristics of the study cohort. Among the 545 enrolled patients, 58 % were male, 33 % were current smokers, 43 % had normal glucose tolerance (NGT), 19 % had newly diagnosed type 2 diabetes mellitus (T2DM), and the remaining 38 % were classified as prediabetic. A positive family history of cardiovascular disease was reported in 33 % of patients. Furthermore, 43 % of participants were hypertensive, and 49 % were classified as obese (BMI ≥ 30 kg/m^2).

Across the TG/HDL-C quartiles (from Q1 to Q4), a progressive deterioration in glucose metabolism was observed, reflected by increasing levels of fasting plasma glucose (FPG), 2-hour post-load glucose, fasting plasma insulin (FPI), 2-hour post-load insulin, and glycated hemoglobin (HbA1c) (all $p < 0.001$). As expected, there was a corresponding decline in insulin sensitivity, as indicated by a significant reduction in the Matsuda index ($p < 0.001$).

3.1. Echocardiographic parameters

Table 2 summarizes the morphological and functional echocardiographic parameters of the entire study population, stratified by TG/HDL-C quartiles.

From the first to the fourth quartile, there was a significant increase in LVMI ($p < 0.001$). Left ventricular global systolic function, as assessed by LVEF, did not differ significantly among the quartiles, remaining within the normal range. However, a progressive decline in GLS was noted across quartiles (median GLS: –19.0 %; IQR: –21.3 to –17.0; $p < 0.001$) (Fig. 1). Notably, a pathological GLS was observed in 58 % of patients.

Regarding right ventricular function, a significant reduction in the TAPSE/PASP ratio was observed with increasing TG/HDL-C ratio ($p = 0.002$). Diastolic function also showed a gradual deterioration, with the E/A ratio decreasing from the first to the fourth quartile ($p < 0.001$). Additionally, the E/e′ ratio increased significantly across quartiles ($p < 0.001$), indicating elevated left ventricular filling pressures.

3.2. Logistic regression analysis

Table 3 presents unadjusted logistic regression models examining associations between study variables and dichotomized GLS (normal vs pathological) as the dependent variable. Potential confounding variables included glycemic status, obesity, CKD-EPI-estimated glomerular filtration rate, C-reactive protein (CRP), Matsuda index, LVMI, TAPSE/PASP, and E/e′ ratio. Glucose, insulin, and HbA1c were excluded from the adjusted model due to collinearity with the Matsuda index.

Table 4 reports the odds ratios (ORs) and corresponding 95 % confidence intervals (CIs) for the association between the TG/HDL-C ratio and pathological GLS, derived from both unadjusted and adjusted logistic regression models, with age and sex included as covariates.

The unadjusted OR was 1.61, indicating that each one-unit increase in the TG/HDL-C ratio (1 mg/dL) was associated with a 61 % higher likelihood of having a pathological GLS ($p = 0.001$). This suggests that

Table 1
Clinical, anthropometric, biochemical, and hemodynamic characteristics of the study population according to the TG/HDL-C index quartiles.

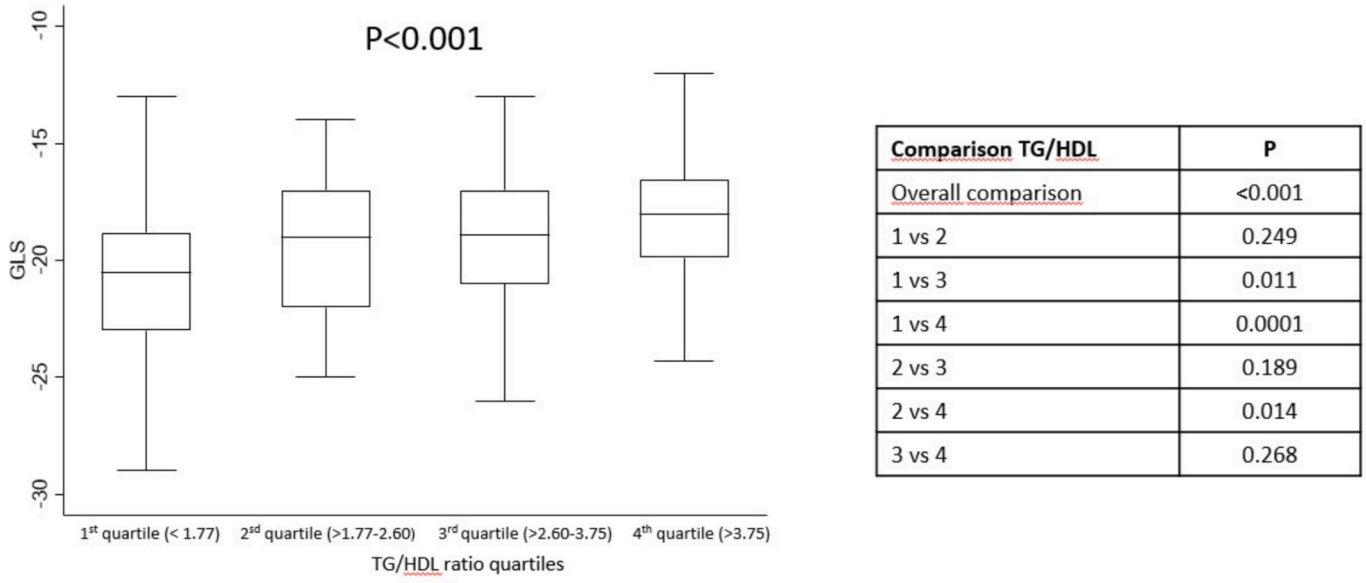
Variables	All (n = 545)	1st quartile (≤1.77 mg/dL) (n = 137)	2sd quartile (>1.77–2.60 mg/dL) (n = 136)	3rd quartile (>2.60–3.75 mg/dL) (n = 137)	4th quartile (>3.75 mg/dL) (n = 135)	P	Correlation with TG/HDL (rho and p)
Age, yrs	58.8 ± 12.1	57.3 ± 13.2	60.8 ± 12.2	59.7 ± 12.2	57.5 ± 10.4	0.047	−0.004(0.918)
Male gender, %	58	42	51	69	67	<0.001	0.197 (<0.001)
Glycemic profile, %						<0.001	0.678 (<0.001)
NGT, %	43	85	63	18	5		
Diabetes, %	19	1	7	18	52		
Pre-diabetes, %	38	13	30	64	43		
Smoking, %	33	26	35	27	42	0.017	0.091 (0.035)
Hypertension, %	43	40	43	45	44	0.840	0.03 (0.49)
Family history of CVD, %	33	32	37	28	33	0.530	−0.004 (0.929)
Obesity, %	49	36	51	50	59	0.002	0.14 (0.002)
BMI, Kg/m^2	30.4 ± 5.6	29.6 ± 6.8	30.6 ± 5.1	30.7 ± 5.3	30.9 ± 4.7	0.220	0.11 (0.009)
SBP, *mmHg*	132.6 ± 14.4	131.3 ± 13.3	133.3 ± 14.8	134.3 ± 15.9	131.5 ± 13.5	0.257	0.02 (0.631)
DBP, *mmHg*	79.1 ± 10.3	78.0 ± 10.6	79.7 ± 10.8	80.2 ± 9.8	78.6 ± 9.8	0.286	0.04 (0.384)
PP, *mmHg*	53.5 ± 11.9	53.3 ± 12.3	53.6 ± 11.6	54.1 ± 12.3	53.00 ± 11.3	0.869	0.02 (0.633)
Total cholesterol, *mg/dl*	189.4 ± 42.8	187.5 ± 38.3	185.2 ± 41.5	182.4 ± 42.8	202.7 ± 46.0	<0.001	0.13 (0.003)
LDL, *mg/dl*	114.2 ± 37.4	112.5 ± 31.9	112.5 ± 36.6	108.1 ± 39.9	123.6 ± 39.1	0.005	0.11 (0.013)
e-GFR, *ml*/min/*1.73* m^2	88.0 ± 17.7	90.8 ± 19.2	85.6 ± 17.7	88.3 ± 16.2	87.2 ± 17.3	0.105	−0.09 (0.036)
Hs-PCR, *mg/L*	3.0 (1.3–4.3)	2.5 (1.2—4)	3.0 (1.2—4.3)	3 (1.5–4.5)	3.3 (1.8–4.3)	0.044	0.16 (<0.001)
FPG, *mg/dl*	97.3 ± 12.8	83.6 ± 6.6	93.2 ± 4.9	101.2 ± 6.0	111.6 ± 11.3	<0.001	0.85 (<0.001)
2-h glucose, *mg/dl*	140 (120–188)	121 (99—135)	134 (115–164)	160 (129–187)	200 (170–214)	<0.001	0.58 (<0.001)
FPI, *μU/ml*	15 (11–21)	10.8 (8.7–14)	14.6 (11.3–19)	16.7 (12.3–21.2)	19 (14.6–23)	<0.001	0.43 (<0.001)
2-h insulin, *μU/ml*	95.7 (65.5–135.7)	68.23 (54.4–89.0)	83.2 (59.8–109.2)	113.6 (89.5–145)	131.5 (95.2–156)	<0.001	0.42 (<0.001)
Matsuda index	43.6 (32.9–68.4)	75.5 (55.8–95.7)	51.7 (40.2–68.9)	37.8 (32.4–45.3)	32.5 (26.3–37.7)	<0.001	−0.64 (<0.001)
HbA1C %	5.8 (5.5–6.3)	5.7 (5.5–5.9)	5.9 (5.5–6.3)	5.9 (5.6–6.5)	6.0 (5.6–6.6)	<0.001	0.18 (<0.001)
Uric acid, *mg/dl*	5.6 ± 1.3	5.4 ± 1.3	5.7 ± 1.5	5.7 ± 1.2	5.8 ± 1.2	0.210	0.11 (0.012)

NGT= Normal glucose tolerance; CVD= Cardiovascular disease; BMI = Body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; Hs-PCR = high-sensitivity C-reactive protein; e-GFR = estimated glomerular filtration rate; LDL = low density lipoproteins;FPG = fasting plasma glucose; FPI = Fasting plasma insulin; HbA1C = glycated haemoglobin.

Table 2
Morpho-functional echocardiographic parameters of the study population according to the TG/HDL index quartiles.

Variables	All (n = 545)	1st quartile (< 1.77) (n = 137)	2sd quartile (>1.77–2.60) (n = 136)	3rd quartile (>2.60–3.75) (n = 137)	4th quartile (>3.75) (n = 135)	p	Correlation with TG/HDL (rho and p)
LVMI,g/m^2	125.63 ± 27.3	117.5 ± 27.78	124.0 ± 27.0	128.1 ± 26.3	133.4 ± 25.9	<0.001	0.243 (<0.001)
LVEF%	60.0 (58.0–63.0)	60.0 (58.0–63.0)	60.0 (58.0–63.0)	60.0 (58.0–62.0)	60.0 (57.0–62.0)	0.322	−0.073 (0.087)
GLS%	−19.0 (from 21.3- to 17.0)	−20.5 (from 23-to 18.8)	−19.0 (from 22.0 – to 17.0)	−18.9 (from 21.0 – to 17.0)	−18 (from 19.9 −to 16.6)	<0.001	0.367 (<0.001)
Binary GLS (>=20 % patological)	58 %	41 %	54 %	61 %	76 %	<0.001	0.306 (<0.001)
TAPSE/PAPS, *mm/mmHg*	0.79 ± 0.24	0.84 ± 0.23	0.79 ± 0.25	0.80 ± 0.25	0.73 ± 0.22	0.002	−0.176 (<0.001)
E/A	0.8 (0.7—1.1)	0.91 (0.8—1.2)	0.8 (0.7—1.1)	0.8 (0.7 – 1.1)	0.8 (0.7—0.9)	<0.001	−0.204 (<0.001)
E/e'	12.0 (9.0–13.5)	10.0 (8.0–13.0)	11.0 (8.9–13.0)	11.0 (9.0–13.6)	13.0 (10.0–14.0)	<0.001	0.243 (<0.001)
LAVI, *ml/mq*	32.3 ± 8.0	30.9 ± 78.5	32.4 ± 6.3	31.7 ± 8.1	34.1 ± 8.6	0.010	0.139 (0.002)

LVMI = Left ventricular Mass Index; LVEF = Left Ventricular Ejection Fraction; GLS = Global longitudinal strain; TAPSE/PAPS = Tricuspid annular plane systolic excursion/ systolic pulmonary arterial pressure; LAVI = left atrial volume index; E = Wave E; A = Wave A.



Comparison TG/HDL	P
Overall comparison	<0.001
1 vs 2	0.249
1 vs 3	0.011
1 vs 4	0.0001
2 vs 3	0.189
2 vs 4	0.014
3 vs 4	0.268

Fig. 1. Global longitudinal strain (%) according to the TG/HDL index quartiles. Each box represents the interquartile range (IQR), spanning from the first quartile (Q1, 25th percentile) to the third quartile (Q3, 75th percentile). The horizontal line inside the box indicates the median (50th percentile). Whiskers extend to the smallest and largest values within 1.5 × IQR from the lower and upper quartiles, respectively.

the TG/HDL-C ratio is an independent risk factor for impaired myocardial deformation. Importantly, this association remained statistically significant even after adjustment for potential confounders (Table 4).

4. Discussion

In the present study, we investigated the potential correlation between the TG/HDL-C ratio and subclinical myocardial damage, as assessed by STE, in patients with CV risk factors. Recent studies have demonstrated that the TG/HDL-C ratio is strongly associated with CV risk and may help identify a subgroup of apparently healthy individuals with an unfavourable cardiometabolic profile and an increased risk of developing CVD. Our findings, based on a large cohort of 545 patients stratified into quartiles by increasing TG/HDL-C ratio, revealed a progressive deterioration of the metabolic profile in parallel with worsening lipid parameters. Specifically, patients in the fourth quartile exhibited significantly higher FPG and FPI levels compared to those in the first and second quartiles. Additionally, we observed a progressive increase in HbA1c levels across quartiles. A corresponding reduction in insulin sensitivity was also noted, as reflected by decreasing Matsuda index values [19].

These results are consistent with previous research. Caselli et al. demonstrated a significant positive correlation between TG/HDL-C ratio and the HOMA index, a marker of insulin resistance [20]. Similarly, Kim et al. found that an elevated TG/HDL-C ratio was associated with insulin resistance even in individuals without metabolic syndrome [21].

With regard to subclinical myocardial damage, our data showed a clear deterioration in myocardial deformation, as measured by GLS, with increasing TG/HDL-C ratio. GLS—considered the gold standard for assessing myocardial strain—was significantly impaired in the higher TG/HDL-C quartiles. Notably, patients in the Q3 and Q4 quartiles demonstrated worse GLS values, suggesting early myocardial dysfunction. Logistic regression analysis further supported this association, revealing that each one-unit increase in TG/HDL-C ratio was associated with a 61 % increase in the likelihood of having a pathological GLS.

Previous studies have linked the TG/HDL-C ratio with increased risk of myocardial infarction, ischemic heart disease, and arterial stiffness, even in apparently healthy individuals [22].

Several potential mechanisms may underlie the observed subclinical

Table 3
Univariate association of study variables with dichotomic GLS as dependent variable.

Age, yrs	1.007 (0.993–1.021, p = 0.325)
Male gender, %	1.048 (0.743–1.478, p = 0.79)
Glycemic profile, %	1.876 (1.474–2.388, p < 0.001)
Smoking, %	1.223 (0.849–1.763, p = 0.28)
Hypertension, %	1.083 (0.768–1.527, p = 0.65)
Family history of CVD, %	0.97 (0.676–1.394, p = 0.871)
Obesity, %	1.363 (0.969–1.917, p = 0.075)
BMI, *Kg/m2*	1.02 (0.989–1.053, p = 0.202)
SBP, *mmHg*	1.006 (0.994–1.018, p = 0.338)
DBP, *mmHg*	1.003 (0.987–1.02, p = 0.707)
PP, *mmHg*	1.006 (0.992–1.021, p = 0.402)
Total cholesterol, *mg/dl*	0.999 (0.995–1.003, p = 0.482)
LDL, *mg/dl*	0.999 (0.995–1.004, p = 0.776)
e-GFR *ml*/min/*1.73 m2*	0.982 (0.972–0.992, p < 0.001)
Hs-PCR, *mg/L*	1.238 (1.134–1.352, p < 0.001)
FPG, *mg/dl*	1.036 (1.021–1.051, p < 0.001)
2-h glucose, *mg/dl*	1.01 (1.006–1.014, p < 0.001)
FPI, *μU/ml*	1.023 (1.002–1.044, p = 0.028)
2-h insulin, *μU/ml*	1.005 (1.002–1.009, p = 0.001)
Matsuda index	0.977 (0.97–0.983, p < 0.001)
HbA1C %	1.257 (0.983–1.608, p = 0.068)
Uric acid, *mg/dl*	1.096 (0.96–1.25, p = 0.175)
LVMI, g/m^2	1.020 (1.013–1.027, p < 0.001)
LVEF%	1.009 (0.966–1.055, p = 0.68)
TAPSE/PAPS, *mm/mmHg*	0.538 (0.263–1.1, p = 0.09)
E/A	0.817 (0.514–1.301, p = 0.395)
E/e'	1.083 (1.022–1.147, p = 0.007)
LAVI, *ml/mq*	1.009 (0.987–1.032, p = 0.411)

BMI = Body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; PP = pulse pressure; Hs-PCR = high-sensitivity C-reactive protein; e-GFR = estimated glomerular filtration rate; LDL = low density lipoproteins; FPG = fasting plasma glucose; FPI = Fasting plasma insulin; HbA1C = glycated haemoglobin; LVMI = Left ventricular Mass Index; LVEF = Left Ventricular Ejection Fraction; TAPSE/PAPS = Tricuspid annular plane systolic excursion/ systolic pulmonary arterial pressure; LAVI = left atrial volume index; E = Wave E; A = Wave A.

Table 4
Crude and adjusted logistic regression models of TG/HDL-C ratio with dichotomic GLS as dependent variable.

	Crude model	Adjusted model
TG/HDL-C, *mg/dL*	1.61 (1.398—1.854, p < 0.001)	1.381 (1.15—1.658, p = 0.001)
Age, yrs		1.001 (0.983—1.019, p = 0.943)
Male gender, %		0.914 (0.587—1.423, p = 0.689)
Glycemic profile		0.841 (0.592—1.195, p = 0.333)
Obesity, %		1.128 (0.757—1.682, p = 0.553)
e-GFR *ml*/min/*1.73 m2*		0.986 (0.973—0.999, p = 0.035)
Hs-PCR, *mg/L*		1.215 (1.104—1.336, p < 0.001)
Matsuda index		0.987 (0.978—0.997, p = 0.008)
LVMI, g/m^2		1.015 (1.008—1.023, p < 0.001)
TAPSE/PAPS, *mm/mmHg*		0.796 (0.353—1.795, p = 0.582)
E/e'		1.000 (0.934—1.07, p = 0.992)

Hs-PCR = high-sensitivity C-reactive protein; e-GFR = estimated glomerular filtration rate; LVMI = Left ventricular Mass Index; TAPSE/PAPS = Tricuspid annular plane systolic excursion/ systolic pulmonary arterial pressure; E = Wave E.

myocardial damage in patients with elevated TG/HDL-C levels. Insulin resistance plays a key role in the pathogenesis of CVD and is a major contributor to dyslipidaemia in individuals with impaired glucose metabolism [6]. Insulin stimulates fatty acid and triacylglycerol synthesis, enhances the uptake of triglycerides from circulation, and suppresses fatty acid oxidation in skeletal muscle and liver [23]. The dyslipidaemia characteristic of insulin resistance and type 2 diabetes—termed diabetic dyslipidaemia—is marked by elevated plasma triglycerides, reduced HDL cholesterol, increased LDL cholesterol, and postprandial lipemia [24].

These metabolic abnormalities can damage the myocardium both directly, through altered cardiac energy metabolism, and indirectly via several secondary pathways, including the polyol pathway, advanced glycation end product (AGE) formation, and hexosamine pathway activation [25]. These mechanisms promote oxidative stress, which contributes significantly to myocardial injury [25]. Therefore, the subclinical myocardial damage observed in individuals with a high TG/HDL-C ratio may be mediated, at least in part, by impaired insulin sensitivity.

5. Conclusion

In conclusion, the TG/HDL-C ratio may serve as a valuable surrogate marker for insulin resistance and a potential indicator of CV risk.

This study demonstrated that patients with CV risk factors and elevated TG/HDL-C ratios exhibit signs of subclinical myocardial damage, as assessed by STE, even in the absence of a reduction in LVEF. This finding suggests that early detection of morphological and functional cardiac changes is possible before clinically evident impairments in systolic function occur, potentially leading to improved patient prognosis through earlier intervention. Nevertheless, further research is needed to establish standardized cut-off values for the TG/HDL-C ratio to be reliably used as a CV risk marker in clinical practice. Despite numerous recent studies on the TG/HDL ratio, there is still no standardised cut-off point. Moreover, previous studies regarding cut-off values of the TG/HDL-C ratio reported that the TG/HDL-C ratio cut/off varies not only according to sex but also according to ethnicity.

Importantly, the identification of elevated TG/HDL-C ratios is not intended to replace the diagnostic criteria for metabolic syndrome. Rather, it should be regarded as a simple and practical tool to aid in the rapid identification of individuals at increased risk for cardiometabolic diseases.

CRediT authorship contribution statement

Velia Cassano: Writing – original draft, Data curation, Conceptualization. **Graziella D'Arrigo:** Writing – original draft, Formal analysis. **Mercedes Gori:** Writing – original draft, Formal analysis. **Giovanni Tripepi:** Formal analysis. **Giuseppe Armentaro:** Writing – review & editing. **Carlo A. Pastura:** Data curation. **Giandomenico Severini:** Data curation. **Mariarosangela Scarcelli:** Data curation. **Daniele Dallimonti Perini:** Writing – review & editing. **Sofia Miceli:** Data curation. **Raffaele Maio:** Writing – review & editing. **Vanessa T. Fiorentino:** Writing – review & editing. **Elena Succurro:** Writing – review & editing. **Marta L. Hribal:** Writing – review & editing. **Giorgio Sesti:** Writing – review & editing. **Francesco Andreozzi:** Writing – review & editing. **Angela Sciacqua:** Writing – review & editing, Supervision, Conceptualization.

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.

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None.

Author contributions

V.C., A.S. : conception and design of the study; V.C., CA.P., G.S., M.S., S.M., acquisition of data; G.D., M.G, G.T.: statistical analysis and interpretation of data; V.C. G.D. M.G.: writing original draft; A.S.: supervision; A.S., V.C., R.M., G.A., M.L.H., S.M., E.S., D.D.P., T.V.F., F.A., G.S.: revising the article critically for important intellectual content; all authors approved the final version to be submitted.

Institutional review board statement

Informed consent was obtained from all subjects involved in the study. The study was conducted in accordance with the Declaration of Helsinki, and approved by Institutional Ethics Committee of Thelocal Ethical Committee (ComitatoEtico Azienda Ospedaliera "Mater Domini") (code protocol number 2012.63 and date of approval 23.10.2012).

Informed consent statement

All investigations were performed in accordance with the principles of the Helsinki Declaration.

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