Hypertriglyceridemia: From an Innocent Bystander to an Independent Cardiovascular Risk Factor in Young Prehypertensive Subjects

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This article was submitted to RAD CASA - Medical Sciences as the original article

Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 12 May 2025
Accepted: 29 May 2025
Published: 25 June 2025

Citation:
Josipović J, Jelaković A, Valent Morić B, Prelević V, Mirošević G, Bulj N, Pećin I, Matijaca H, Ivanko I, Gabrić ID, Reiner Ž, Jelaković B. Hypertriglyceridemia: from an innocent bystander to an independent cardiovascular risk factor in young prehypertensive subjects 567=70-71 (2025): 18-26
DOI: 10.21857/m8vqrt3gp9

Abstract

Introduction: Prehypertension is increasingly recognized as a state associated with adverse cardiometabolic profiles, even in apparently healthy individuals. Although triglycerides (TG) have been implicated in cardiovascular disease (CVD), their role in low-risk prehypertensive populations remains underexplored.

Aim: To compare the cardiorenometabolic characteristics and cardiovascular risk (CVR) of prehypertensive (PHT) individuals with normotensive (NT) and hypertensive (HT) counterparts, with a focus on the independent contribution of TG.

Materials and Methods: A cross-sectional study included 323 untreated adults aged 18–45. Participants underwent anthropometric assessments, standardized blood pressure measurements, fasting blood sampling, spot urine collection, and transthoracic echocardiography. CVR was estimated using the Framingham 10-Year General Cardiovascular Risk Score.

Results: Compared to the NT group, PHT individuals had significantly higher BMI, waist circumference, HOMA-IR, LDL-cholesterol, TG, uric acid, and left ventricular mass index (LVMI) ($p<0.05$). No differences were observed in renal function markers. A stepwise increase in CVR across BP categories was evident (7.9% NT vs. 24.6% PHT vs. 48.1% HT; $p<0.05$). Multivariate logistic regression identified TG as an independent predictor of CVR in the PHT group (Exp(β)=1.88, 95% CI 1.08–3.28, p=0.03).

Conclusion: Hypertriglyceridemia is an early and independent marker of cardiovascular risk in young, prehypertensive individuals. Early identification may improve risk stratification and guide preventive strategies.

Keywords: Prehypertension; Blood Pressure; Hypertension; Hypertriglyceridemia; Risk Factors

Sažetak

Hipertrigliceridemija; Od nevinog promatrača do neovisnog faktora kardiovaskularnog rizika kod mladih predhipertenzivnih osoba

Uvod: Prehipertenzija se sve više prepoznaje kao stanje povezano s nepovoljnim kardiometaboličkim profilima, čak i kod naizgled zdravih osoba. Iako su trigliceridi (TG) povezani s kardiovaskularnim bolestima (KVB), njihova uloga u populacijama s niskim rizikom od prehipertenzije ostaje nedovoljno istražena.
Cilj: Usporediti kardiorenometaboličke karakteristike i kardiovaskularni rizik (KVR) prehipertenzivnih (PHT) osoba s normotenzivnim (NT) i hipertenzivnim (HT) osobama, s naglaskom na neovisni doprinos TG.
Materijali i metode: Presječna studija obuhvatila je 323 neliječene odrasle osobe u dobi od 18 do 45 godina. Sudionici su podvrgnuti antropometrijskim procjenama, standardiziranim mjerenjima krvnog tlaka, uzimanju uzoraka krvi natašte, prikupljanju urina na trenutak i transtorakalnoj ehokardiografiji. KVR je procijenjen pomoću Framingham 10-godišnjeg općeg kardiovaskularnog rizika.
Rezultati: U usporedbi s NT skupinom, osobe s PHT-om imale su značajno veći BMI, opseg struka, HOMA-IR, LDL-kolesterol, TG, mokraćnu kiselinu i indeks mase lijeve klijetke (LVMI) ($p<0,05$). Nisu uočene razlike u markerima bubrežne funkcije. Postupni porast CVR-a u svim kategorijama krvnog tlaka bio je evidentan (7,9% NT u odnosu na 24,6% PHT u odnosu na 48,1% HT; $p<0,05$). Multivarijantna logistička regresija identificirala je TG kao neovisni prediktor CVR-a u PHT skupini (Exp(β)=1,88, 95% CI 1,08–3,28, $p=0,03$).
Zaključak: Hipertrigliceridemija je rani i neovisni marker kardiovaskularnog rizika kod mladih osoba s prehipertenzijom. Rana identifikacija može poboljšati stratifikaciju rizika i usmjeriti preventivne strategije.

Ključne riječi: Prehipertenzija; Krvni tlak; Hipertenzija; Hipertrigliceridemija; Čimbenici rizika

Introduction

Prehypertension (PHT) has long been associated with an increased risk of developing hypertension (HT), cardiovascular diseases (CVD), and premature mortality, even before it was formally defined in the JNC-7 guidelines as a distinct blood pressure (BP) category (1–4). Data from the Framingham Heart Study showed that individuals with high–normal BP had significantly elevated risk of CVD compared to those with optimal BP, with hazard ratios of 2.5 in women and 1.6 in men, both adjusted for standard CV risk factors (2). A large meta-analysis involving nearly one million participants confirmed a linear association between BP and CV mortality, with risk doubling for every 20 mmHg rise in systolic BP and 10 mmHg rise in diastolic BP, beginning at levels as low as 115/75 mmHg (3). Definitions of PHT vary across guidelines. The JNC-7 classification encompasses systolic BP of 120–139 mmHg or diastolic BP of 80–89 mmHg, whereas the 2007 ESC/ESH and later European guidelines divide this range into "normal" (120–129/80–84 mmHg) and "high–normal" (130–139/85–89 mmHg) categories. In contrast, the 2017 ACC/AHA guidelines now consider BP values within the 130–139/80–89 mmHg range as stage 1 hypertension (4–9). These inconsistencies reflect the lack of consensus on defining "normal" BP and the benefits of early, intensive management. Numerous studies in both Western and Asian populations have demonstrated that PHT is linked with adverse cardiometabolic profiles, even among individuals who are otherwise healthy (10–12). The concept of PHT was introduced to identify individuals with above-average CV risk in whom preventive measures could delay or prevent the development of full-blown HT and related complications (13).
This study aimed to assess the clinical and metabolic profiles with the focus on hypertiglycerdiemia of young, untreated PHT individuals in to normotensive (NT) and untreated HT participants, focusing on their association of BP with CVD risk.

Materials and Methods

Subjects A total of 326 participants aged 18–45 years of both sexes were included in this cross-sectional study. Of these, 175 were selected from the hypertension, nephrology and cardiology outpatient clinics of University Hospital Centre Sestre milosrdnice or were voluntary employees of the same institution, based on anamnesis indicating either previously measured normal, high-normal BP or newly diagnosed, untreated HT. The remaining 151 participants were selected from the cohort of the research project "Endemic Nephropathy in Croatia – Epidemiology, Diagnostics, and Etiopathogenesis" (project code: 108-0000000-0329), funded by the Ministry of Health of the Republic of Croatia, based on satisfactory inclusion criteria. The study was conducted at the Department of Internal Medicine of University Hospital Centre Sestre milosrdnice and in the field

within Brodsko-posavska County. Data collection was conducted between April 2016 and April 2018. Participants were excluded if they met any of the following criteria: age below 18 years, BP values outside the defined range (BP >160/100 mmHg), diabetes mellitus, cardiac arrhythmias, heart failure (NYHA class I), coronary artery disease, chronic kidney disease (eGFR CKD-EPI <60 mL/min/1.73 m²), limb amputation, acute inflammation, use of antihypertensive medication, nonsteroidal anti-inflammatory drugs, steroids, oral contraceptives, pregnancy and breastfeeding, and lack of signed informed consent. All participants were interviewed using a pre-structured questionnaire covering family and personal medical history, medication use, and smoking habits. The study complied with the Declaration of Helsinki and local institutional guidelines. Ethical approval was obtained from relevant committees, and all participants provided written informed consent.

Clinical and Laboratory Assessments All measurements were performed in the morning between 08:00 and 09:30 after an overnight fast. Anthropometric data were collected using standardized protocols. Blood pressure was measured in the sitting position using an automated Omron M6 device, with a cuff appropriate to arm size, following a 5-minute rest. BP was recorded in mmHg and measured three times to minimize bias (6). Fasting venous blood samples (10.5 mL) and spot urine samples were collected from all participants. The complete blood count was determined via laser scattering technology (analyzer XN 1000, Sysmex); the biochemistry panel was obtained after 10 minutes of blood centrifugation. The fasting blood glucose was assessed via UV photometry with hexokinase (Architect analyzer), triglycerides via photometry with glycerol phosphate oxidase (GPOPAP), HDL-cholesterol via the homogeneous enzyme-immunoinhibitory method, LDL-cholesterol via the homogeneous method (CHE, CHOD-DSBmT), and C-reactive protein via the immunoturbidimetric method with latex particles. The serum urate levels were assessed via the spectrophotometric uricase enzyme-based method, serum insulin levels via electrochemiluminescent immunoassay (ECLIA, Cobas e 411, Roche), serum and urinary creatinine levels via photometry with alkaline picrate (Architect analyzer, Abbott), serum and urine electrolytes via the indirect potentiometric method, and urine alpha-1-microglobulin via continuous photometry with alkaline picrate and latex immunonephelometric (Nephelometer analyzer, BNII, Siemens). Uromodulin (UM) was measured from urinary samples stored at -60°C using an enzyme-linked immunosorbent assay (Bio-Vendor, Cobas Roche) and standardized to urinary creatinine [indexed UM (iUM)]. The glomerular filtration rate (eGFR) was estimated using the CKD-EPI creatinine equation: {eGFR, ml/min/1.73 m2=141 x min (SCr/κ, 1)α x max(SCr/κ, 1)-1.209 x 0.993Age x 1.018 [if female] x 1.159 [if Black]} (14). Insulin resistance and pancreatic beta cell function were assessed using the HOMA method, i.e., HOMA-IR (Homeostasis Model Assessment for Insulin Resistance): [HOMA-IR = fasting plasma insulin x fasting plasma glucose)/22.5] and HOMA-β (Homeostasis Model Assessment of β-Cell Function) [HOMA ß (%ß) = HOMA-IR – (20 x fasting plasma insulin) / (fasting plasma glucose – 3.5)] (15). Transthoracic echocardiograms were performed in 143 participants by a single experienced operator. Left ventricular mass (LVM) was calculated and indexed in accordance with established echocardiographic methods (16).

Cardiovascular Risk Stratification Cardiovascular risk was assessed using the Framingham 10-Year Risk Score for General Cardiovascular Disease (FRS). Participants were categorized into low-risk (<5%) and elevated-risk (≥5%) groups (17).

Statistical Analysis Descriptive statistics were used to summarize the data. Continuous variables were reported as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on normality. Categorical data were expressed as absolute and relative frequencies. Group differences in categorical variables were assessed using Chi-square or Fisher's exact tests. Continuous variables between two groups were analyzed using the Mann–Whitney U test; comparisons across three or more groups employed ANOVA (with Bonferroni or Scheffé post hoc tests) or the Kruskal–Wallis test (with Conover post hoc analysis). Correlations between numeric variables were examined using Spearman's rank correlation coefficient (ρ). Stepwise multivariate linear regression and logistic regression were applied to identify independent associations of interest. All statistical tests were two-tailed, with significance set at $\alpha = 0.05$. Analyses were conducted using MedCalc Statistical Software version 18.2.1 (MedCalc Software bvba, Ostend, Belgium; www.medcalc.org; 2018) and IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Baseline clinical and laboratory characteristics are summarized in table 1. Although not statistically significant, NT and PHT participants were slightly younger than those in the HT group. Gender distribution varied significantly ($p<0.001$). The PHT group had intermediate BMI ($p=0.009$) and waist circumference ($p=0.001$) values between NT and HT participants. Significant differences were observed in serum uric acid and fasting blood glucose, ($p<0.001$), HbA1c ($p=0.01$), insulin ($p=0.002$), HOMA-IR ($p=0.001$), total cholesterol ($p=0.04$), and triglycerides ($p<0.001$) levels across the three BP groups. However, glucose and HbA1c did not differ significantly between NT and PHT groups, while triglycerides and uric acid levels were elevated in both PHT and HT groups compared to NT. Kidney function markers (eGFR, ACR, and tubular markers), showed no significant differences. Sodium/potassium ratio and estimated salt intake were above recommended levels but did not differ across groups. A non-significant positive trend of increased urinary uromodulin with rising BP was observed.

Table 1. Baseline data of participants according to the JNC-7 blood pressure categories

Parameter	NT (n=103)	PHT (n=140)	HT (n=80)	P
SBP (mmHg)	108.3 (7.1)	126.9 (80.8)	143.9 (94.2)	<0.001*, †
DBP (mmHg)	70.9 (6.2)	80.8 (6.5)	94.2 (8.2)	<0.001*, †
Sex, m, [n (%)]	74 (71.8)	61 (42.7)	30 (37.5)	<0.001‡
Age (years)	36 (30–42)	37 (29–44)	39 (33–45)	0.07
BMI (kg/m²)	25.6 (22.5–28.7)	26.6 (23.8–30)	28.6 (24.7–32.6)	0.009§
WC (cm)	90 (79–100)	92 (84–102)	99.5 (89–110)	0.001§
Uric acid (µmol/L)	252 (211–307)	297 (244.5–370)	328 (274–412.8)	<0.001†
Glucose (mmol/L)	4.9 (4.5–5.2)	5.0 (4.6–5.3)	5.3 (4.8–5.6)	<0.001§
HbA1c (%)	5.1 (4.9–5.4)	5.1 (4.9–5.1)	5.2 (5.0–5.4)	0.01‖
Insulin (mIU/L)	9.3 (6.6–14.6)	13.4 (8.6–17.7)	14.9 (10–25.9)	0.002
HOMA-IR	1.9 (1.4–2.7)	2.9 (1.7–4.1)	3.5 (2.1–5.6)	0.001¶
Total cholesterol (mmol/L)	4.9 (4.3–5.6)	5.2 (4.6–5.7)	5.2 (4.6–5.9)	0.04†
HDL-cholesterol (mmol/L)	1.3 (1.1–1.6)	1.3 (1.1–1.7)	1.3 (1.0–1.6)	0.35
LDL-cholesterol (mmol/L)	3.0 (2.4–3.6)	3.1 (2.6–3.7)	3.1 (2.6–3.9)	0.32
Triglycerides (mmol/L)	0.9 (0.7–1.4)	1.0 (0.7–1.5)	1.4 (0.9–2.0)	<0.001†
Serum potassium (mmol/L)	4.3 (4.2–4.63)	4.4 (4.1–4.7)	4.3 (4.1–4.5)	0.09
Serum sodium (mmol/L)	140 (139–141)	140 (139–142)	140 (139–141)	0.48
Serum creatinine (µmol/L)	68 (63–76)	75 (65–86)	74 (65–86.3)	0.001¶
CKD-EPI eGFR (ml/min/1.73 m²)	107 (96.3–115)	105 (91–113)	104.5 (94–110)	0.32
ACR urine (mg/g creatinine)	4.14 (2.64–6.05)	4.1 (2.3–6.6)	4.7 (2.8–8.3)	0.54
A1mCR urine (mg/g creatinine)	5.6 (3.3–7.7)	4.3 (3.2–6.7)	5.1 (3.6–8.4)	0.07
Na/K ratio, urine	3.3 (2.5–4.5)	3.3 (2.4–5.2)	3.1 (2.4–4.1)	0.71
Uromodulin (mg/g creatinine)	43 (27–66)	42.9 (25.5–65.3)	40.6 (24.1–60.4)	0.73
C-reactive protein (mg/L)	1.8 (0.9–2.8)	1.2 (0.6–2.4)	2.0 (0.9–4.1)	0.05

Statistical test used for P values: Kruskal–Wallis test [median (25%-75%)]; * ANOVA; ‡ χ^2 test; post hoc Conover, as appropriate.
† Significant differences between NT vs. PHT, NT vs. HT, and PHT vs. HT
§ Significant differences between NT vs. HT and PHT vs. HT
‖ Significant differences between PHT vs. HT
¶ Significant differences between NT vs. PHT and NT vs. HT

Abbreviations:
NT – normotensive; PHT – prehypertensive; HT – hypertensive.
SBP – systolic blood pressure; DBP – diastolic blood pressure.
BMI – body mass index; WC – waist circumference.
HbA1c – glycated hemoglobin A1c; HOMA-IR – Homeostasis Model Assessment for Insulin Resistance.
HDL – high-density lipoprotein; LDL – low-density lipoprotein.
eGFR – estimated glomerular filtration rate; CKD-EPI – Chronic Kidney Disease Epidemiology Collaboration.
ACR – albumin/creatinine ratio in spot urine.
A1mCR – alpha-1-microglobulin/creatinine ratio in spot urine.
Na/K ratio – sodium/potassium ratio in spot urine.

Table 2. Echocardiographic data of participants according to the JNC-7 BP categories.

Parameter	NT (n=41)	PHT (n=52)	HT (n=50)	P
LA (mm)	32.5 (30.3 - 36)	33 (30 - 36)	36.5 (32.8 - 39)	0.007*
LAVI (ml/m2)	20.8 (16.8 – 23.6)	19.1 (16.5 – 22.7)	21.2 (17.4 - 26)	0.25
LV (mm)	47 (44 – 50.5)	49 (45 - 51)	46.5 (43 - 52)	0.43
IVS (mm)	10 (8 - 10)	10 (9 - 11)	10 (9 - 12)	0.02†
LVPW (mm)	9 (8 – 10.5)	10 (9 - 11)	11 (10 - 12)	<0.001‡
LVM (g)	142.1 (122.3 – 180.9)	163.72 (146.4 -193.8)	190.4 (145.9 – 228.3)	0.001‡
LVMI (g/m2)	77.5 (67.6-88.3)	84.3 (73.3-95.9)	87.7 (74.3-107.4)	0.01†
RWT (cm)	0.4 (0.4 – 0.4)	0.4 (0.4-0.5)	0.5 (0.4 – 0.6)	<0.00*
E/A	1.3 (1 – 1.5)	1.3 (1 – 1.5)	1.3 (1 – 1.5)	0.89
E/e′	7 (5.6 – 8.7)	7.4 (6.3 - 9)	8.2 (6.8 – 9.4)	0.03†
SV (ml)	67.5 (58.5 – 82.8)	74 (63.5 - 86)	74 (61 – 95.5)	0.24
EFLV (%)	66 (62 - 70)	64 (60 - 69)	67 (62 – 68.3)	0.34

Statistical test used for the P value: Kruskal–Wallis, [median (25%-75%) and interquartile range]; post hoc Conover, as appropriate.
*Significant differences between NT vs.HT and PHT vs.HT
†Significant differences between NT vs.HT
‡Significant differences between NT vs. PHT, NT vs.HT, and PHT vs.HT

Abbreviations:
NT, normotensive; PHT, prehypertensive; HT, hypertensive.
LA, left atrium; LAVI, indexed left atrium volume; LV, left ventricle.
IVS, interventricular septum; LVPW, left ventricular posterior wall; LVM, left ventricular mass.
LVMI, left ventricular mass indexed; RWT, relative wall thickness.
E/A, the ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave).
E/e', the ratio of early filling velocity on transmittal Doppler (E) with the early relaxation velocity on tissue Doppler (E′).
SV, stroke volume; EFLV, left ventricular ejection fraction.

Echocardiographic data (table 2) revealed progressive increases in IVS, LVPW, LVM, RWT, LVMI, and E/e′ ratio across BP categories (all $p<0.05$). Notably, PHT participants exhibited early signs of cardiac remodeling without significant differences from HT individuals in several parameters. Framingham risk scoring showed a stepwise increase in the proportion of high-risk individuals across BP groups (7.9% NT, 24.6% PHT, 48.1% HT; $p<0.05$). In multivariate logistic regression, triglycerides emerged as the only independent predictor of elevated CV riskin the PHT group ($Exp(\beta) = 1.88$, 95% CI: 1.08–3.28; $p = 0.03$). ROC analysis yielded an AUC of 0.706 for triglycerides, with a cutoff of >1.3 mmol/L indicating elevated CV risk.

Table 3. Final model of significant predictors of CVR in the PHT group.

Parameter	ß	Standard error	Wald	p	Odds ratio (Exp ß)	95% CI za Exp ß
Triglycerides (mmol/L)	0.63	0.28	4.96	**0.03**	1.88	1.08 do 3.28
Constant	-2.8	0.73	15.0	**<0.001**		

ß, regression coefficient; CI, confidence interval

Table 4. ROC curve parameters for CVR in the PHT group.

Parameters	AUC	95% CI	Sensitivity	Specificity	Cut-off	Youden index	P
Triglycerides (mmol/L)	0.706	0.622-0.781	58.8	74.8	> 1.3	0.34	**<0.001**

AUC, area under the curve

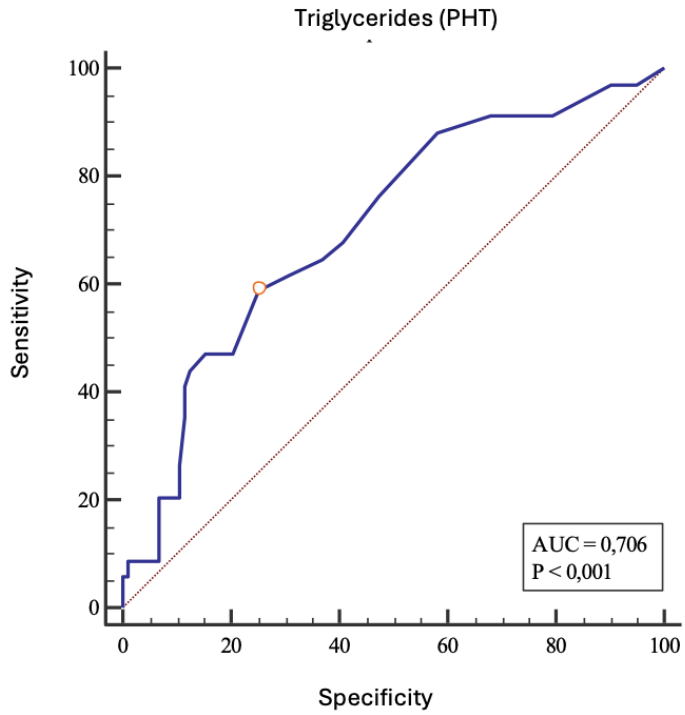

Figure 1. ROC analysis of sensitivity, specificity, and cut-off value for triglycerides regarding CVR in the PHT group.

Discussion

Our findings suggest that hypertriglyceridemia is an early and significant metabolic abnormality in young, untreated individuals with PHT. Compared to NT and HT participants, the PHT group demonstrated intermediate but distinctly adverse cardiometabolic profiles. Elevated triglyceride levels, alongside higher HOMA-IR and serum uric acid, were independently associated with increased CV risk even in this low-risk, young adult population. This is a finding that adds to growing evidence but remains underrepresented in the literature (12,18). These observations align with prior studies. Grotto et al. and Chiang et al. found that individuals with PHT exhibited higher levels of fasting blood glucose, triglycerides, and BMI compared to NT group (12,18). Although the HT group in our study showed more severe metabolic derangements, the metabolic shift begins early, supporting the rationale for early detection and targeted prevention strategies. We also found evidence of early cardiac remodeling in the PHT group, including increased left ventricular mass and diastolic dysfunction, while kidney function markers remained similar across BP categories. This suggests that early hypertension-mediated organ damage manifest initially in the heart rather than the kidneys. Previous studies have shown similar cardiac alterations in PHT, such as early changes in left atrial mechanics and geometry, and an association between left ventricular hypertrophy and HT progression (19–21). In contrast, although albuminuria and GFR have been reported in other PHT populations, especially in older cohorts or those with clustered risk factors, we did not observe renal impairment in our younger, healthier participants (22). A stepwise increase in Framingham Risk Score (FRS) was evident across BP groups, with PHT individuals already showing a markedly higher proportion of elevated CV risk. Among all evaluated variables, triglycerides emerged as an independent predictor of elevated FRS in the PHT group. This supports existing genetic, epidemiological, and clinical research indicating that triglyceride-rich lipoproteins (TRLs) and their components, including ApoC3 and ApoE, contribute causally to atherosclerotic CV disease (23-26). Moreover, Mendelian randomization studies and real-world data have confirmed the association between elevated TG levels and increased CV events and all-cause mortality, even in populations with optimal LDL-cholesterol levels (27-31).

Our study has several strengths, including a relatively homogeneous and untreated cohort of young adults with preserved kiney function, and the use of standardized measurement protocols. Nonetheless, it is limited by its cross-sectional design single-center study with unbalanced gender distribution, and reliance on fasting triglyceride levels — despite evidence that nonfasting trigylcerides may better reflect real-world risk (27,29). Additionally, we captured triglyceride levels at a single time point, potentially missing postprandial triglyceride elevations in some individuals.

In conclusion, hypertriglyceridemia should be recognized as an early and independent marker of CV risk in young individuals with PHT. Incorporating triglyceride measurement into routine CV risk assessment may enable timely interventions to prevent the progression to HT and CV disease in this under-recognized group.

Preprint Disclosure:

A version of this manuscript was previously posted on a preprint server, DOI: [insert preprint DOI].

Funding:

This research was supported by the scientific research project *"Endemic Nephropathy in Croatia – Epidemiology, Diagnostics, and Etiopathogenesis"* (project code: 108-0000000-0329), funded by the Ministry of Health of the Republic of Croatia, and by the research grant of the Croatian Hypertension League. The research did not receive a specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest:

The authors declare no conflicts of interest.

References

1. Robinson SC, Brucer M. Range of normal blood pressure: a statistical and clinical study of 11,383 persons. Arch Intern Med 1939; 64:409-44
2. Vasan RS, Larson MG, Leip EP, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. N Engl J Med. 2001: 345(18):1291-7
3. Lewington S, Clarke R, Qizilbash N, et al. Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet.2002;360(9349):1903-13
4. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289:2560-72
5. Mancia G, De Backer G, Dominiczak A, et al. ESH-ESC Task Force on the Management of Arterial Hypertension. 2007 ESH-ESC Practice Guidelines for the Management of Arterial Hypertension: ESH-ESC Task Force on the Management of Arterial Hypertension. J Hypertens. 2007;25(9):1751-62
6. Mancia G, Fagard R, Narkiewicz K, et al. Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013;31(7):1281-357
7. Williams B, Mancia G, Spiering W, et al. ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018; 39(33):3021-3104
8. Mancia G, Kreutz R, Brunström M, et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). J Hypertens. 2023;41(12):1874-2071
9. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2018;138(17):e426-e483
10. Gupta AK, Brashear MM, Johnson WD: Coexisting prehypertension and prediabetes in healthy adults: a pathway for accelerated cardiovascular events. Hypertens Res. 2011; 34 (4): 456-461
11. Gupta AK, McGlone M, Greenway FL, et al. Prehypertension in disease-free adults: a marker for an adverse cardiometabolic risk profile. Hypertens Res. 2010; 33 (9): 905-910
12. Chiang PP, Lamoureux EL, Shankar A. et al. Cardio-metabolic risk factors and prehypertension in persons without diabetes, hypertension, and cardiovascular disease. BMC Public Health 2013; 13; 730
13. Chobanian AV. Prehypertension revisited. Hypertension. 2006;48:812–814
14. Levey AS, Stevens LA. Estimating GFR using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation: more accurate GFR estimates, lower CKD prevalence estimates, and better risk predictions. Am J Kidney Dis 2010; 55:622–7
15. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care 2004;27(6):1487—95
16. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: A report from the American Society of Echocardiography's guidelines and standards committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. Journal of the American Society of Echocardiography 2005; 18: 1440-63
17. D'Agostino RB, Vasan SR; Pencina MJ, et al. General Cardiovascular Risk Profile for Use in Primary Care: The Framingham Heart Study. Circulation. 2008;117: 743-53
18. Grotto I, Grossman E, Huerta M, et al. Prevalence of prehypertension and associated cardiovascular risk profiles among young Israeli adults. Hypertension. 2006;48(2):254-9
19. Bajpai JK, Sahay AP, Agarwal AK, De AK, Garg B, Goel A. Impact of prehypertension on left ventricular structure, function and geometry. J Clin Diagnostic Res 2014; 8:7– 10
20. Aktürk E, Ermis N, Yağmur J, et al. Early left atrial mechanics and volume abnormalities in subjects with prehypertension: A real time three- dimensional echocardiography study. Echocardiography 2012; 29:1211–7
21. De Marco M, De Simone G, Roman MJ, et al. Cardiovascular and metabolic predictors of progression of prehypertension into hypertension: The strong heart study. Hypertension 2009; 54:974–80
22. Kim BJ, Lee HJ, Sung KC, et al. Comparison of Microalbuminuria in 2 Blood Pressure Categories of Prehypertensive Subjects. Circ J 2007; 71:1283–7
23. Ference BA, Ginsberg HN, Graham I, et al. Low-density lipoproteins cause atherosclerotic cardiovascular disease. 1. Evidence from genetic, epidemiologic, and clinical studies. A consensus statement from the European Atherosclerosis Society Consensus Panel. Eur Heart J. 2017;38(32):2459–72.

24. Ginsberg HN, Packard CJ, Chapman MJ, et al. Triglyceride-rich lipoproteins and their remnants: metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies – a consensus statement from the European Atherosclerosis Society. Eur Heart J. 2021;42(47):4791–806
25. Berglund L, Brunzell JD, Goldberg AC, et al. Endocrine Society. Evaluation and treatment of hypertriglyceridemia: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012;2969–2989
26. Toth PP, Granowitz C, Hull M, et al. High triglycerides are associated with increased cardiovascular events, medical costs, and resource use: a real-world administrative claims analysis of statin-treated patients with high residual cardiovascular risk. J Am Heart Assoc. 2018;7(15): e008740.
27. Jørgensen AB, Frikke-Schmidt R, West AS, et al. Genetically elevated non-fasting triglycerides and calculated remnant cholesterol as causal risk factors for myocardial infarction. Eur Heart J. 2013;1826–1833
28. Sarwar N, Sandhu MS, Ricketts SL, et al. Triglyceride Coronary Disease Genetics Consortium and Emerging Risk Factors Collaboration, Triglyceride-mediated pathways and coronary disease: collaborative analysis of 101 studies. Lancet. 2010;1634–1639
29. Thomsen M, Varbo A, Tybjærg-Hansen A, et al. Low nonfasting triglycerides and reduced all-cause mortality: a Mendelian randomization study. Clin Chem. 2014;737–746
30. Arca M, Veronesi C, D'Erasmo L, et al. Association of hypertriglyceridemia with all-cause mortality and atherosclerotic cardiovascular events in a low-risk Italian population: the TG-REAL retrospective cohort analysis. J Am Heart Assoc. 2020;9(19): e015801
31. Langsted A, Freiberg JJ, Tybjaerg-Hansen A, Schnohr P, Jensen GB, Nordestgaard BG. Nonfasting cholesterol and triglycerides and association with risk of myocardial infarction and total mortality: the Copenhagen City Heart Study with 31 years of follow-up. J Intern Med. 2011 270 (1):65-75