ORIGINAL PAPER
KIDNEY DISEASE
RJCCN

Association Between Lipid-related Parameters and the Carotid Intima-media Thickness, Relating to Type 2 Diabetes Mellitus

Alireza Khajavi,[1] Zahra Mirzaasgari,[2] Omolbanin Asadi Ghadikolaei,[3] Atefeh Amouzegar,[4] Laily Najafi[5]

[1]School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences (ORCID: 0000-0001-5238-792X), Tehran, Iran
[2]Department of Neurology, Firoozgar Hospital, School of Medicine, Iran University of Medical Sciences (ORCID: 0000-0002-4046-8471), Tehran, Iran
[3]Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences (IUMS) (ORCID: 0000-0002-4882-9972), Tehran, Iran
[4]Associate Professor of Nephrology Firoozgar Clinical Research Development Center(FCRDC), School of medicine, Iran University of Medical Sciences (ORCID: 0000-0003-3090-1662), Tehran, Iran
[5]Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences (IUMS) (ORCID: 0000-0002-1968-0427), Tehran, Iran

Keywords. association, lipid-related parameters, carotid intima-media thickness, type 2 diabetes mellitus

Introduction. Higher carotid intima-media thickness (CIMT), indicates a greater burden of subclinical atherosclerosis (AS) and cardiovascular disease (CVD). The AS is related to insulin resistance and lipid oxidation. Detection of reliable and affordable surrogate markers and metabolic components for assessing the CVD risk is world-shaking. This study aimed to inspect the relationship between lipid-related parameters and CIMT, considering the impact of type 2 diabetes mellitus (T2DM).

Methods. This cross-sectional study was conducted on a total of 244 participants (113 men and 131 women), including 118 diagnosed with diabetes (DM) and 126 without diabetes (non-DM). Duplex ultrasonography parameters, demographic, physical, biochemical assessments, and lipid-related parameters were measured. Correlation and linear regression analyses assessed the relationship between the lipid-related parameters and CIMT.

Results. The DM patients' levels of triglyceride-glucose (TyG) index were significantly higher than the non-DM ones, however, the two groups demonstrated no statistically significant difference in CIMT levels. CIMT was correlated with low-density lipoprotein ($r = 0.33$, $P = .033$) in the DM group and with age ($r = 0.41$, $P < .001$) in the non-DM group. The multivariate linear regression model demonstrated age, TyG-BMI, and LDL/HDL ratio as the significant associates of CIMT, with age having the largest standardized regression coefficient of 0.311 ($P < .001$).

Conclusions. The current study revealed direct associations of CIMT with age, TyG-BMI, and LDL/HDL ratio, taking into account the DM/non-DM binary among the study participants.

RJCCN 2025; 1: 9-17
www.rjccn.org
DOI: 10.60186/RJCCN.12

INTRODUCTION

Atherosclerosis (AS) is a chronic vascular disease characterized by the accumulation of fatty streaks in arterial walls, with possible progression into plaque formation (atheroma), plaque rupture, and eventually thrombotic occlusion of the vessels.[1] Accordingly, this process may cause mortality and morbidity, such as ischemic heart disease, stroke, and peripheral arterial disease, which, in turn, impose significant burdens on the health of

Please cite this article as: Khajavi A, Mirzaasgari Z, Asadi Ghadikolaei O, Amouzegar A, Najafi L. Association Between Lipid-related Parameters and the Carotid Intima-media Thickness, Relating to Type 2 Diabetes Mellitus. RJCCN 2025; 1(1): 9-17

community members.[2] Thus, it is crucial for the early identification of high-risk people and the timely control of AS progression.[3] It is known that some risk factors, including hypertension (HTN) and diabetes mellitus (DM), can accelerate the progression of AS at different levels,[4] as well as endothelial dysfunction.[5] Hence, HTN and DM are now considered essential parameters in the risk prediction of cardiovascular disease (CVD).[6] In this context, it was also demonstrated that insulin resistance (IR) plays a staple role in the development of DM, HTN, and AS,[1,7] and it is a well-known predictor of a wide range of CVDs.[8] Given these facts, several studies have examined the predictive ability of different insulin resistance markers to achieve an accurate and non-invasive tool for the early detection of AS, particularly in high-risk groups.[9]

In recent years, some reliable and affordable surrogate markers for IR have been introduced, such as the triglyceride glucose (TyG) index, the TyG-modified indices (the TyG-body mass index (TyG-BMI) and TyG-waist circumference (TyG-WC)), triglyceride/ high-density lipoprotein cholesterol (TG/HDL) ratio, total cholesterol/ HDL (TC/HDL) ratio, low-density lipoprotein cholesterol/HDL (LDL/HDL) ratio and TG minus HDL.[10-13] Some of the mentioned parameters could predict IR more accurately than the homeostasis model assessment-estimated insulin resistance (HOMA-IR).[14,15]

Given that both hypertriglyceridemia and impaired glucose metabolism are commonly related to IR and AS,[16] growing attention is now attracted to assessing the association of the TyG index with AS.[11,17] The studies demonstrated that higher TyG-BMI index, TG/HDL, TC/HDL, LDL/HDL ratios, and TG-HDL are associated with increased IR, metabolic dysregulation, and CVD.[11-13]

Carotid intima-media thickness (CIMT) is a widely used imaging marker for the diagnosis of preclinical carotid AS,[18] which was shown to have predictive value for future cardio/cerebrovascular events as well.[19] Previous studies explored the positive relationship between some of the mentioned parameters and CIMT in different populations from the point of view such as of age, weight, and comorbidities,[20-26] however, some controversial results are present.[17,27]

Moreover, to our knowledge, previously published research has not precisely compared the associations of lipid-related parameters totally and CIMT in individuals with and without diabetes mellitus.[28,29] Consequently, the current research examined the mentioned relationship.

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study was conducted at the Endocrine Research Center, Iran University of Medical Sciences, and Firoozgar General Hospital, Tehran, Iran; from 2019 to 2021. The eligible participants were enrolled via convenience sampling, DM patients from the endocrine clinic, and non-DM patients from the neurologic clinic. The site of sampling was a referral center located in a metropolitan district of the middle socioeconomic status, which to some extent secures the generalizability of the findings.

The inclusion criteria were as follows: (DM group) T2DM, and the age range of 20 to 70 years old for both groups. The exclusion criteria for both groups were: smoking; substance abuse; pregnancy; taking corticosteroids, immunosuppressive medications, omega-3, lipid-lowering agents, and contraceptives; renal transplantation; systemic conditions (autoimmune diseases, chronic renal disease, chronic or acute infection); CV surgery; malignancy; and albuminuria (urine albumin to creatinine ratio > 30 mg/g). Diabetes mellitus was diagnosed according to criteria recommended by the American Diabetes Association (ADA).[19]

The research protocol was approved by the ethics committee of the Iran University of Medical Sciences (No: IR.IUMS.REC.1401.820), and all participants signed and provided written permission.

Clinical Measurements and Definitions

Data on demographic characteristics, clinical assessments, past medical history, and medications were collected via a standard questionnaire by a trained physician, who conducted a face-to-face interview at the initial appointment.

A calibrated stadiometer & digital scale (Seca GmbH& Co. KG. Germany) were used to measure standing height and weight, respectively. BMI was demonstrated as the weight (kg) divided by the square of the height (m^2). Participants' blood pressures were measured by a mercury sphygmomanometer (Riester, Exacta 1350, Germany) in the standard position (sitting position after a 10-minute rest).

The blood samples were collected in the tubes containing the clot activator after an overnight fast of at least 8 hours. The separated serum was then analyzed for evaluating the biochemistry panel, including fasting blood glucose (FBG), creatinine, and lipid profile. The samples were analyzed using the Enzymatic Calorimeter technique (Biorex).

The TyG index and modified TyG index were calculated using the following formulae:

TyG index: Ln [TG (mg/dl) × FBG (mg/dl) /2][30] and TyG-BMI (TyG index × BMI). In addition, the other lipid-related parameters are as follows: TG/HDL-C ratio (TG divided by HDL-C), TC/HDL-C ratio (TC divided by HDL-C), LDL-C/HDL-C ratio (LDL-C divided by HDL-C), and TG minus HDL-C.

Additionally, e-GFR was determined by applying diet modification in renal disease (MDRD) formula.[31]

Assessment of Carotid Intima-media Thickness (CIMT)

An expert neurologist with certified neurosonology experience performed the carotid ultrasonography assessments. The mentioned neurologist was blinded to all participants' characteristics and laboratory results.

A high-resolution duplex ultrasound system (B-Mode) with an 8-Hz linear probe (Sonosite M Turbo, Fuji Film, Japan) measured CIMT. The CIMT was estimated by measuring the thickness of the innermost two layers of intima-media 10 mm before the bifurcation of the common carotid artery (CCA), where no atherosclerotic plaque was present. The left and right CIMT average was calculated and used in all analyses. Mean CIMT over the 75th percentile for age, race, and gender was considered a CV events risk factor, according to the American Echocardiographic Association criteria.[32]

Statistical Analysis

Demographic and clinical characteristics of participants in the study groups are described as proportions, means (standard deviation (SD)), or medians (interquartile range (IQR)). Between-group comparisons were conducted using an independent sample t-test and Mann-Whitney test for data with and without normal distribution. Categorical variables were compared using the χ^2 test. A Spearman's correlation analysis was performed to examine the correlations of CIMT with different clinical parameters.

Moreover, the associations of CIMT with lipid-related parameters were explored using univariate and multivariate linear regression analyses. The significance level was set at .05. The statistical analyses were performed using the statistical software Stata (ver. 13).

RESULTS

Data included 244 participants (113 men and 131 women) with a mean (SD) of age equal to 46.4 (10.4) years, consisting of 126 individuals without and 118 with T2DM (median (IQR) duration of DM = 7 (5 to 10) years). As presented in Table 1, the two groups of participants were comparable in terms of gender, BMI, serum TG, and HDL-C. Also, there was no significant difference between CIMT evaluated in the two groups. However, individuals with T2DM were older and had significantly higher BP, FBG, and TyG indexes and lower e-GFR, TC, LDL-C, LDL/HDL, and TC/HDL than those without diabetes (all P values < .05).

Next, the Spearman correlations were computed between CIMT and the variables assessed in Table 1, stratified for the diabetes status, and applying the Bonferroni multiple testing adjustment. Accordingly, in the DM group, LDL showed an association of 0.33 (P value = .033), and in the non-DM group, age, SBP, and TyG-BMI owned correlations of 0.41, 0.30, and 0.30 (P values of < .001, .085, .076; respectively).

Furthermore, considering the variables of P values lower than .1 in Table 1 and the Spearman correlations of P values lower than .1, the univariate regression models were fitted on CIMT as the response variable and adjusted for the diabetes status. The covariates included age, SBP, DBP, FBG, Total cholesterol, LDL-C, TyG, TyG-BMI, LDL/HDL, TC/HDL, and e-GFR. The findings reported in Table 2 indicated all covariates to be significantly

Table 1. Characteristics of the Study Participants, Compared in Terms of Diabetes Status

	Non-diabetic group (n = 126)	Diabetic group (n = 118)	*P*
Age, y (mean (SD))	42.7 (9.8)	50.3 (9.6)	< .001[a]
Gender (female, n (%))	69 (54.8%)	62 (52.5%)	.730[b]
BMI, kg/m^2 (mean (SD))	26.2 (4.3)	26.6 (3.9)	.459[a]
SBP, mmHg (median (IQR))	120 (110 to 120)	120 (120 to 130)	< .001[c]
DBP, mmHg ((median (IQR))	80 (70 to 80)	80 (70 to 80)	.004[c]
FBG, mmol/l (median (IQR))	96 (92 to 103)	115 (103 to 138)	< .001[c]
TG, mmol/l (median (IQR))	95 (75 to 148)	105 (89 to 124)	.288[c]
TC, mmol/l (median (IQR))	149 (123 to 182)	132 (122 to 146)	.001[c]
LDL-C, mmol/l (median (IQR))	95 (80 to 118)	70 (58 to 83)	< .001[c]
HDL-C, mmol/l (median (IQR))	43 (41 to 48)	44 (41 to 48)	.567[c]
TyG, median (IQR)	8.4 (8.2 to 8.9)	8.8 (8.5 to 9)	< .001[c]
TG/HDL, median (IQR)	2.3 (1.8 to 3.5)	2.4 (2 to 2.9)	.616[c]
TG-HDL, median (IQR)	51.5 (32 to 106)	60 (44 to 82)	.396[c]
TyG-BMI, median (IQR)	223.2 (196.4 to 250.6)	230.1 (211.8 to 254)	.069[c]
LDL/HDL, median (IQR)	2.3 (1.7 to 2.8)	1.5 (1.3 to 1.9)	< .001[c]
TC/HDL, median (IQR)	3.5 (2.8 to 4.3)	3 (2.7 to 3.4)	< .001[c]
e-GFR, mL/min/ 1.73m^2 (median (IQR))	103.5 (82.9 to 130)	88.5 (74.4 to 106.3)	.001[c]
CIMT, mm (mean (SD))	0.41 (0.11)	0.40 (0.13)	.506[a]

Abbreviations: SD, standard deviation; IQR, interquartile range; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TG, triglyceride; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TyG, triglyceride glucose index; e-GFR, estimated glomerular filtration rate; CIMT, carotid intima-media thickness.
a, t-test; b, χ^2 test; c, Mann-Whitney test.

Table 2. Univariate Regression Analyses of Carotid Intima-media Thickness

Variables	Coefficients	95% CI	*P*	Standardized Coefficients
Age, y	0.0039	0.0025, 0.0052	< .001	0.333
SBP, mmHg	0.0010	-0.0002, 0.0022	.101	0.108
DBP, mmHg	-0.0002	-0.0016, 0.0013	.839	-0.014
FBG, mmol/L	0.0010	0.0003, 0.0017	.005	0.208
TC, mmol/L	0.0007	0.0003, 0.0011	.002	0.207
LDL-C, mmol/L	0.0013	0.0008, 0.0018	< .001	0.320
TyG	0.0518	0.0248, 0.0788	< .001	0.216
TyG-BMI	0.0007	0.0003, 0.0011	< .001	0.229
LDL/HDL	0.0443	0.0223, 0.0664	< .001	0.272
TC/HDL	0.0215	0.0055, 0.0374	.009	0.168
e-GFR, mL/min/ 1.73m^2	-0.0005	-0.0009, 0.0000	.063	-0.126

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; TyG, triglyceride glucose index; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; e-GFR, estimated glomerular filtration rate.

Table 3. Multivariate Regression Analyses of Carotid Intima-media Thickness

Variables	Coefficients	95% CI	*P*	Standardized Coefficients
Age, y	0.0036	0.0023, 0.0049	< .001	0.311
TyG-BMI	0.0005	0.0002, 0.0009	.005	0.172
LDL/HDL	0.0466	0.0215, 0.0716	< .001	0.285
TC/HDL	-0.0069	-0.0261, 0.0123	.478	-0.054

Abbreviations: TyG, triglyceride glucose index; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol.

associated with CIMT, except for SBP, DBP, and e-GFR. Moreover, age and LDL-C had the highest standardized regression coefficients. Regarding the significant covariates and the interrelations between them, the multivariate regression model was fitted, including the covariates of age, TyG-BMI, LDL/HDL, and TC/HDL, leading to the findings reported in Table 3. In this model, age, TyG-BMI, and LDL/HDL remained significant correlates of CIMT and the largest standardized coefficient belonged to age.

DISCUSSION

This study examined the association of the lipid-related parameters totally with CIMT as an accepted marker for AS in a sample of the Iranian population with T2DM compared to that in non-diabetic people.

Our results highlighted a direct correlation between CIMT and age, TyG-BMI, and LDL/HDL ratio, evaluated in the diabetic and non-diabetic groups.

It is known that IR can accelerate AS progression through metabolic abnormalities, such as hyperglycemia and dyslipidemia.[33] Given both abnormalities,[16] growing attention is now attracted to assessing the association of the TyG index with AS.[11,17] Recently, the TyG-modified indices, TG/HDL, TC/HDL, LDL/HDL ratios, and TG minus HDL[10-13] have been highlighted as reliable surrogate markers for IR, and their high values are associated with increased IR, metabolic dysregulation, and CVD.[11-13]

In addition, existing evidence confirms the positive association of the mentioned parameters with obesity and atherogenic dyslipidemia[14] and other CVD risk factors such as T2DM, HTN, and metabolic syndrome.[34-40] TG/HDL ratio and TyG index are defined as a useful predictor of glycemic control in normal-weight and overweight patients with T2DM respectively.[41] Furthermore, the TyG index, modified TyG indices and TG/HDL ratio have been suggested as reliable markers for predicting each aspect of CVD in different populations.[12,13,42-44] The TC/HDL ratio is considered a probable biomarker for screening early peripheral arterial disease.[45] To some extent, controversies are present, a J-shaped relationship was detected between baseline TG/HDL and T2DM risk in Japanese.[34]

CIMT as a predictive marker for the diagnosis of preclinical carotid AS and cardio/cerebrovascular events,[18,19] is positively related to the TyG index;[17] however, some controversial results are presented. For instance, it was revealed that a higher TyG index is linked to carotid AS measured by CIMT in patients with ischemic stroke,[3] this association is consistent with the role of IR in promoting AS and CVD. In another study on 2560 Korean subjects without a previous coronary artery disease and stroke history, the TyG index was associated with CIMT and arterial stiffness.[46] Furthermore, Lu *et al.* detected a direct association between the TyG index and abnormal CIMT in non-diabetic females after adjustment for AS traditional risk factors.[7]

Also, Jia *et al.* detected a U-shaped relationship between the TyG index and elevated CIMT in non-obese Chinese people.[17] However, the TyG index was not significantly correlated with a high CIMT in another study conducted on the Chinese population.[27]

Liu; demonstrated a direct association between TyG-WC and CIMT, reflecting a higher burden of subclinical carotid AS especially in middle-aged and older adults with normal weight.[21]

In addition, the other studies described positive associations between TG/HDL, TC/HDL, and LDL/HDL ratios with CIMT, AS, and carotid plaques in different populations,[22-26] and also these correlations are confirmed in the diabetes population complicated by chronic kidney disease on peritoneal dialysis.[20]

No previous published study has examined the relationship between lipid-related parameters and CIMT in individuals with T2DM compared to non-DM people. However, our findings partially align with the results of only one available preliminary report investigating the predictive ability of TyG concerning carotid atherosclerosis in individuals with T2DM without any control group.[47] Similarly, in another study by Gothwal *et al.*, the TyG index significantly correlated with CIMT in non-DM people.[48]

The mechanism by which the mentioned parameters contribute to the development of AS is not fully demonstrated; however, it has been proposed that at the onset of IR, an increase of fatty acids in the liver, activates the pro-inflammatory pathways and consequently causes AS development and also increase the risk of coronary heart disease.[49-51] In addition, the elevated levels of fatty acids in pancreatic islets alter the metabolism of glucose and damage the beta cells.[52] Another suggested mechanism is that high glucose levels, which increase reactive oxygen radicals, exert injury to beta cells[25,53] and cause endothelial dysfunction.[20]

Our data also confirmed the direct effects of dyslipidemia and FBG on CIMT reported in previous studies.[54,55] No correlation between BP and CIMT was detected from our data, possibly due to the aggressive hypertension treatment consistent with Oguntola et. al.[24]

In the present manuscript, the references listed are based on studies of the Asian population (e.g., Chinese and Korean). In contrast, the results collected and presented here are based on results collected from the Iranian people, who are genetically closer to the Caucasian population. The differences between results may be due to the differences in the diet and lifestyles of the different populations.

Given the cheapness and simplicity of calculation, the TyG-BMI, and LDL/HDL may be regarded as a plausible and available indicator of subclinical carotid atherosclerosis. Although statin therapy is for the reduction of LDL-C level, a residual risk of carotid AS remains, so a combination therapy to control other lipid parameters, in addition to reducing the LDL-C level can be beneficial.[56] Accordingly, lifestyle modification (nutrition and exercise) and medical treatments are recommended for the primary prevention of CVD. So, these associations highlight the importance of assessing both metabolic and anthropometric factors in diabetic individuals for CVD risk stratification and management.

LIMITATIONS

Some limitations must be taken into account in this investigation. Firstly, recruiting the participants in the study was faced with the challenge of convincing them to go under the color-doppler sonography procedure. Besides, the lack of HbA1C measurements prevented us from achieving a more accurate estimate of the glycemic control status in the diabetic participants. In addition, the lack of medication analysis and categorization, limited us to prove the effect of insulin therapy beyond oral antidiabetic drugs or combination therapy on lipid profile. So the injectable therapies such as insulin could be a confounder variable.

CONCLUSIONS

In conclusion, the present study revealed direct relationships of carotid intima-media thickness with age, triglyceride glucose-body mass index, and low-density lipoprotein to high-density lipoprotein ratio, based on a sample composed of diabetic and nondiabetic patients. More comprehensive research with larger sample sizes and larger pools of covariates is required to authenticate these findings.

ACKNOWLEDGEMENTS

The authors thank the staff who helped us complete the project, especially Dr. Fariba Alaei-Shahmiri. In addition, we appreciate all the people who contributed to this study.

FUNDING

This study was funded and supported by the Iran University of Medical Sciences (IUMS), Grant No. 1401-3-116-24548.

DECLARATIONS

Ethical Approval

This project was accepted by the ethical committee of Iran University of Medical Sciences; ethical code: IR.IUMS.REC.1401.820. The study was conducted after obtaining ethical approval from the ethical committee of the Iran University of Medical Sciences (Ref. No: IR.IUMS.REC.1397.1118). Written informed consent was obtained from all subjects. The authors attest that the participants knew the study's purpose, risks, and benefits. Anonymity was maintained throughout the study period. All activities and methods for the study were carried out considering research ethics guidelines for Iran. All procedures performed in human participant studies followed the institutional and/or national research committee's ethical standards, the 1964 Helsinki Declaration, and its later amendments or comparable ethical standards.

Date of approval: 08/01/2023

Conflict of Interest

All the authors have no competing interests.

Authors' Contributions

LN, AA, AKH, OAGH and ZM did the

interventions, reviewed medical aspects, and participated in preparing the manuscript. LN, AA, AKH, OAGH and ZM drafted the manuscript. LN, AKH, OAGH and AA supervised the project and revised the manuscript critically. LN and AKH analyzed the manuscript. All authors read and approved the final version of the manuscript.

Abbreviations

ADA, American Diabetes Association; AS, Atherosclerosis; BMI, Body Mass Index; BP, Blood Pressure; CCA, Common Carotid Artery; CIMT, Carotid Intima-media Thickness; CV, Cardiovascular; CVD, Cardiovascular Disease; DBP, Diastolic Blood Pressure; DM, Diabetes Mellitus; e-GFR, Estimated Glomerular Filtration Rate; FBG, Fasting Blood Glucose; FRS, Framingham Risk Score; HbA1C, Hemoglobin A1C; HDL-C, High-density Lipoprotein Cholesterol; HOMA-IR, Homeostasis Model Assessment-estimated Insulin Resistance; HTN, Hypertension; IR, Insulin Resistance; LDL-C, Low-density Lipoprotein Cholesterol; MDRD, Modification of Diet in Renal Disease; SBP, Systolic Blood Pressure; TC, Total Cholestrol; T2DM, Type 2 Diabetes Mellitus; TG, Triglyceride; TyG, Triglyceride Glucose Index

The place where the study was performed

1. Endocrine Research Center, Institute of Endocrinology & Metabolism, Iran University of Medical Sciences (IUMS), Tehran, Iran
2. Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran

REFERENCES

1. Alizargar J, Bai C-H. Comparison of carotid ultrasound indices and the triglyceride glucose index in hypertensive and normotensive community-dwelling individuals: a case control study for evaluating atherosclerosis. Medicina. 2018;54(5):71.
2. Herrington W, Lacey B, Sherliker P, Armitage J, Lewington S. Epidemiology of atherosclerosis and the potential to reduce the global burden of atherothrombotic disease. Circulation research. 2016;118(4):535-46.
3. Miao M, Zhou G, Bao A, et al. Triglyceride-glucose index and common carotid artery intima-media thickness in patients with ischemic stroke. Cardiovascular Diabetology. 2022;21(1):1-10.
4. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The lancet. 2012;380(9859):2224-60.
5. Zaheer M, Chrysostomou P, Papademetriou V. Hypertension and atherosclerosis: pathophysiology, mechanisms and benefits of BP control. Hypertension and Cardiovascular Disease. Springer; 2016. p. 201-16.
6. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. The Lancet Global health. 2019;7(10):e1332-e45.
7. Lu Y-W, Chang C-C, Chou R-H, et al. Gender difference in the association between TyG index and subclinical atherosclerosis: results from the I-Lan Longitudinal Aging Study. Cardiovascular diabetology. 2021;20(1):1-10.
8. Guo W, Zhu W, Wu J, et al. Triglyceride glucose index is associated with arterial stiffness and 10-year cardiovascular disease risk in a Chinese population. Frontiers in cardiovascular medicine. 2021;8:585776.
9. Kannan L, Chernoff A. Insulin Resistance and Atherosclerosis: Is it Time to Measure HOMA-IR to Predict Coronary Artery Disease? North American journal of medical sciences. 2013;5(10):615-6.
10. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. The Journal of Clinical Endocrinology & Metabolism. 2010;95(7):3347-51.
11. Du T, Yuan G, Zhang M, Zhou X, Sun X, Yu X. Clinical usefulness of lipid ratios, visceral adiposity indicators, and the triglycerides and glucose index as risk markers of insulin resistance. Cardiovascular diabetology. 2014;13:1-10.
12. Kosmas CE, Rodriguez Polanco S, Bousvarou MD, et al. The triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio as a risk marker for metabolic syndrome and cardiovascular disease. Diagnostics. 2023;13(5):929.
13. Song K, Lee HW, Choi HS, et al. Comparison of the modified TyG indices and other parameters to predict non-alcoholic fatty liver disease in youth. Biology. 2022;11(5):685.
14. Khan SH, Sobia F, Niazi NK, Manzoor SM, Fazal N, Ahmad F. Metabolic clustering of risk factors: evaluation of Triglyceride-glucose index (TyG index) for evaluation of insulin resistance. Diabetology & metabolic syndrome. 2018;10(1):1-8.
15. Vasques ACJ, Novaes FS, de Oliveira MdS, et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. Diabetes research and clinical practice. 2011;93(3):e98-e100.
16. Low Wang CC, Hess CN, Hiatt WR, Goldfine AB. Clinical update: cardiovascular disease in diabetes mellitus: atherosclerotic cardiovascular disease and heart failure in type 2 diabetes mellitus–mechanisms, management, and clinical considerations. Circulation. 2016;133(24):2459-502.
17. Jia X, Zhu Y, Qi Y, et al. Association between triglyceride glucose index and carotid intima-media thickness in obese and nonobese adults. Journal of diabetes. 2022;14(9):596-605.

18. Cobble M, Bale B. Carotid intima-media thickness: knowledge and application to everyday practice. Postgraduate medicine. 2010;122(1):10-8.
19. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: the Rotterdam Study. Circulation. 1997;96(5):1432-7.
20. Nannapaneni SS, Nimmanapalli HD, Lakshmi A, Vishnubotla SK. Markers of Oxidative Stress, Inflammation, and Endothelial Dysfunction in Diabetic and Nondiabetic Patients with Chronic Kidney Disease on Peritoneal Dialysis. Saudi Journal of Kidney Diseases and Transplantation. 2022;33(3):361-72.
21. Liu Z, Deng B, Huang Q, et al. Comparison of seven surrogate insulin resistance indexes for predicting the prevalence of carotid atherosclerosis in normal-weight individuals. Frontiers in Public Health. 2023;11:1241523.
22. Tecer D, Sunar I, Ozdemirel AE, et al. Usefullnes of atherogenic indices and Ca-LDL level to predict subclinical atherosclerosis in patients with psoriatic arthritis? Advances in Rheumatology. 2019;59:49.
23. Li Z, Cheng Q, Liu Y, et al. LDL-C/HDL-C and carotid plaques in patients with coronary heart disease: A Chinese cohort study. 2021.
24. Oguntola SO, Hassan MO, Duarte R, et al. Atherosclerotic vascular disease and its correlates in stable black South African kidney transplant recipients. International Journal of Nephrology and Renovascular Disease. 2018:187-93.
25. Cüre E, İçli A, Uslu AU, et al. Atherogenic index of plasma may be strong predictor of subclinical atherosclerosis in patients with Behçet disease. 2017.
26. Unal E, Akın A, Yıldırım R, Demir V, Yildiz İ, Haspolat YK. Association of subclinical hypothyroidism with dyslipidemia and increased carotid intima-media thickness in children. Journal of clinical research in pediatric endocrinology. 2017;9(2):144.
27. Zhao S, Yu S, Chi C, et al. Association between macro- and microvascular damage and the triglyceride glucose index in community-dwelling elderly individuals: the Northern Shanghai Study. Cardiovascular diabetology. 2019;18(1):1-8.
28. Li H, Lin J, ying Liu Y, Liu Y, Wan Q. Association between triglyceride glucose index and carotid atherosclerosis in patients with type 2 diabetes mellitus: a cross-sectional study. 2021.
29. Gothwal SK, Goyal K, Barjatya H, et al. Estimating the correlation between TYG and CIMT in non-diabetic adult patients. Obesity Medicine. 2022;35:100460.
30. Ma X, Dong L, Shao Q, et al. Triglyceride glucose index for predicting cardiovascular outcomes after percutaneous coronary intervention in patients with type 2 diabetes mellitus and acute coronary syndrome. Cardiovascular diabetology. 2020;19(1):1-14.
31. Levey AS, Coresh J, Greene T, et al. Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. Clinical chemistry. 2007;53(4):766-72.
32. Johri AM, Nambi V, Naqvi TZ, et al. Recommendations for the assessment of carotid arterial plaque by ultrasound for the characterization of atherosclerosis and evaluation of cardiovascular risk: from the American Society of Echocardiography. Journal of the American Society of Echocardiography. 2020;33(8):917-33.
33. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovascular diabetology. 2018;17(1):1-14.
34. Wang H, Wang C, Xuan X, et al. Association between triglyceride to high-density lipoprotein cholesterol ratio and type 2 diabetes risk in Japanese. Scientific Reports. 2023;13(1):3719.
35. Zheng D, Li H, Ai F, et al. Association between the triglyceride to high-density lipoprotein cholesterol ratio and the risk of type 2 diabetes mellitus among Chinese elderly: the Beijing Longitudinal Study of Aging. BMJ Open Diabetes Research and Care. 2020;8(1):e000811.
36. Wang X, Liu J, Cheng Z, Zhong Y, Chen X, Song W. Triglyceride glucose-body mass index and the risk of diabetes: a general population-based cohort study. Lipids in health and disease. 2021;20(1):1-10.
37. Jian S, Su-Mei N, Xue C, Jie Z, Xue-Sen W. Association and interaction between triglyceride–glucose index and obesity on risk of hypertension in middle-aged and elderly adults. Clinical and Experimental Hypertension. 2017;39(8):732-9.
38. Angoorani P, Heshmat R, Ejtahed H-S, et al. Validity of triglyceride–glucose index as an indicator for metabolic syndrome in children and adolescents: the CASPIAN-V study. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity. 2018;23(6):877-83.
39. Low S, Khoo KCJ, Irwan B, et al. The role of triglyceride glucose index in development of Type 2 diabetes mellitus. Diabetes research and clinical practice. 2018;143:43-9.
40. Zhang M, Wang B, Liu Y, et al. Cumulative increased risk of incident type 2 diabetes mellitus with increasing triglyceride glucose index in normal-weight people: the Rural Chinese Cohort Study. Cardiovascular diabetology. 2017;16(1):1-11.
41. Babic N, Valjevac A, Zaciragic A, Avdagic N, Zukic S, Hasic S. The triglyceride/HDL ratio and triglyceride glucose index as predictors of glycemic control in patients with diabetes mellitus type 2. Medical archives. 2019;73(3):163.
42. Wang M, Wang C. Triglyceride–glucose (TYG) index for acute myocardial infarction patients with or without metabolic fatty liver (MAFLD): A retrospective study. Atherosclerosis. 2022;355:109.
43. Hong S, Han K, Park C-Y. The triglyceride glucose index is a simple and low-cost marker associated with atherosclerotic cardiovascular disease: a population-based study. BMC medicine. 2020;18(1):1-8.
44. Wang A, Wang G, Liu Q, et al. Triglyceride-glucose index and the risk of stroke and its subtypes in the general population: an 11-year follow-up. Cardiovascular diabetology. 2021;20(1):1-9.
45. Zhan Y, Yu J, Ding R, Sun Y, Hu D. Triglyceride to high density lipoprotein cholesterol ratio, total cholesterol to high density lipoprotein cholesterol ratio and low ankle brachial index in an elderly population. Vasa. 2014;43(3):189-97.

46. Won K-B, Park G-M, Lee S-E, et al. Relationship of insulin resistance estimated by triglyceride glucose index to arterial stiffness. Lipids in health and disease. 2018;17(1):1-6.

47. Li H, Lin J, ying Liu Y, Liu Y, Wan Q. Association between triglyceride glucose index and carotid atherosclerosis in patients with type 2 diabetes mellitus: a cross-sectional study. Research Square. 2021.

48. Gothwal SK, Goyal K, Barjatya HC, et al. Estimating the correlation between TYG and CIMT in non-diabetic adult patients. Obesity Medicine. 2022;35:100460.

49. Tenenbaum A, Klempfner R, Fisman EZ. Hypertriglyceridemia: a too long unfairly neglected major cardiovascular risk factor. Cardiovascular diabetology. 2014;13(1):1-10.

50. Xu H, Barnes GT, Yang Q, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. The Journal of clinical investigation. 2003;112(12):1821-30.

51. Sitnik D, Santos IS, Goulart AC, et al. Fasting glucose levels, incident diabetes, subclinical atherosclerosis and cardiovascular events in apparently healthy adults: A 12-year longitudinal study. Diabetes and Vascular Disease Research. 2016;13(6):429-37.

52. Unger RH. Lipotoxicity in the pathogenesis of obesity-dependent NIDDM: genetic and clinical implications. Diabetes. 1995;44(8):863-70.

53. Robertson RP, Harmon J, Tran POT, Poitout V. β-cell glucose toxicity, lipotoxicity, and chronic oxidative stress in type 2 diabetes. Diabetes. 2004;53(suppl_1):S119-S24.

54. Tzou WS, Douglas PS, Srinivasan SR, et al. Distribution and predictors of carotid intima-media thickness in young adults. Preventive cardiology. 2007;10(4):181-9.

55. Kotb NA, Gaber R, Salama M, Nagy HM, Elhendy A. Clinical and biochemical predictors of increased carotid intima-media thickness in overweight and obese adolescents with type 2 diabetes. Diabetes & vascular disease research. 2012;9(1):35-41.

56. Catapano AL, Tokgözoğlu L, e Silva AM, Bruckert E. Atherogenic markers in predicting cardiovascular risk and targeting residual cardiovascular risk. Atherosclerosis Supplements. 2019;39:100001.

Correspondence to:
Laily Najafi, MD
Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences (IUMS)
(ORCID: 0000-0002-1968-0427), Tehran, Iran
E-mail: lailynajafi@yahoo.com

Received August 2025
Revised September 2025
Accepted September 2025