International Journal of Multiphysics
Volume 18, No. 3, 2024
ISSN: 1750-9548

Coronary Artery Calcification and Triglyceride-Glucose Index

Reda Abd Elmoniem Kamel [1], Ezzat Mostafa Mohamed [1], Ibrahim M Salem [1], Huda Fathy Mohammad Ebian[3], Ibrahim Mohamed Mahmoud Elsayed Abdoun [1], Ahmed Noaman Elsayed [1], Hanzada Mohamed Helmi Elmaghrabi [2]

[1] Internal Medicine Department, Faculty of Medicine, Zagazig University, Egypt

[2] Internal Medicine Department, Faculty of Medicine, Port said University, Egypt

[3] Clinical pathology Department, Faculty of Medicine, Zagazig University, Egypt

[*]Corresponding Author: Ibrahim Mohamed Mahmoud Elsayed Abdoun

E-mail: ibra7im3bdoun@gmail.com

Abstract:

Coronary artery calcification (CAC) represents a key marker of subclinical atherosclerosis and is widely used for cardiovascular risk stratification. As a non-invasive, quantifiable indicator assessed by computed tomography, the CAC score reflects the cumulative burden of atherosclerotic plaque and strongly predicts coronary events beyond traditional cardiovascular risk factors. Individuals with elevated CAC scores have significantly higher risks of myocardial infarction, coronary revascularization, and cardiovascular mortality. In recent years, metabolic indices have gained attention as simple yet powerful tools for predicting cardiometabolic risk. The triglyceride-glucose (TyG) index calculated from fasting triglyceride and glucose levels has emerged as a reliable surrogate marker of insulin resistance. It is strongly associated with endothelial dysfunction, arterial stiffness, and the development of atherosclerosis. Several studies suggest that higher TyG index values correlate with increased coronary artery disease (CAD) severity, adverse plaque characteristics, and higher CAC burden. Understanding the relationship between TyG index and CAC is clinically important because both indices are inexpensive, widely accessible, and easily reproducible in routine practice. Investigating their association may support early identification of high-risk individuals, optimize preventive strategies, and improve cardiovascular outcomes.

Keywords: Coronary artery calcification; CAC score; Triglyceride-glucose index; TyG index; Insulin resistance; Atherosclerosis; Coronary artery disease; Cardiometabolic risk.

Coronary Artery Calcification

1. Introduction

Coronary artery calcification was previously thought to be a benign process, and the calcified lesion increases in accordance with aging. Subsequently, studies determined that medial calcification is associated with arterial stiffness, which increases risk for adverse cardiovascular events. The extent of coronary artery calcification (CAC) strongly correlated with the degree of atherosclerosis and the rate of future cardiac events, and the high prevalence of CAC in coronary heart disease (CHD) patients makes percutaneous coronary intervention (PCI) difficult to perform**(1).**

2. Epidemiology and risk factors

The prevalence of CAC is age- and gender-dependent, occurring in over 90% of men and 67% of women older than 70 years of age. Additionally, people who have higher body mass index, higher blood pressure, abnormal lipids (higher low density lipoprotein or triglycerides, lower high density lipoprotein, or use of lipid-lowering medication), glucose disorders (impaired fasting glucose, untreated or treated diabetes mellitus), a familial history of CAC, chronic kidney disease (CKD), higher fibrinogen level and higher C-reactive protein level are more susceptible to CAC**(2).**

Two recognized types of CAC are intimal or superficial and medial artery calcification. Atherosclerotic calcification mainly occurs in the intima. Inflammatory mediators and elevated lipid content within atherosclerotic lesions induce osteogenic differentiation of vascular smooth muscle cells (VSMC). Conversely, CAC in the media is associated with advanced age, diabetes, and CKD. **(3).**

Several studies have confirmed that advanced age, diabetes mellitus, dyslipidemia, hypertension, male gender, cigarette smoking and renal disease are risk factors of intimal calcification. On the other hand, renal dysfunction (mostly reduction of glomerular filtration rate), hypercalcemia, hyperphosphatemia, parathyroid hormone abnormalities and duration of dialysis are connected to medial calcification. **(4).**

3. Pathogenesis

CAC results in reduced vascular compliance, abnormal vasomotor responses, and impaired myocardial perfusion. The pathogenesis of CAC and bone formation share common pathways, and risk factors have been identified which contributed to the initiation and progression of CAC. Although a majority of the studies demonstrated that calcium intake had no significant adverse or beneficial effect on vascular calcification and cardiovascular endpoints, dietary calcium intake above the median of 805 mg/d was associated with an increased risk of myocardial infarction (MI). However, one should not cease consumption of calcium supplements at recommended levels when adequate dietary calcium intake cannot be achieved. **(2).**

Vascular calcification is an active and regulated process. Several theories on the mechanisms of vascular calcification have been put forward, including distributed Ca/Pi imbalance (hyperphosphatemia, hypercalcemia), induction of bone formation (vascular bone and cartilage-like cells), presence of apoptotic bodies, circulating nucleational complexes and loss of inhibitions (e.g., pyrophosphate, matrix glycoprotein, oxypropionitrile, Fetuin/alpha2-HS, glycoprotein) . In fact, VSMC plays an integral role in this process by undergoing trans-differentiation to osteoblast-like cells, elaborating calcifying matrix vesicles and secreting factors that diminish the activity of osteoclast-like cells with mineral resorbing capacity. The receptor activator of nuclear factor-kappaB ligand/osteoprotegerin pathway has emerged as a potential link between osteoporosis and CAC. However, the entire mechanism of CAC progression has not been fully elucidated. (**3).**

Recent advances have identified microRNAs (miRs) as key regulators of CAC by directing the complex genetic reprogramming of smooth muscle cells (VSM) and the functional responses of other related cell types relevant for vascular calcification. The transcription factor, osterix, was identified as a miR-125b target, and inhibition of miR-125 was associated with increased Runx2 and osterix expression, as well as increased alkaline phosphatase activity and SMC calcification. **(5).**

4. Clinical manifestations

While CAC itself might not have specific clinical manifestation, this asymptomatic phenomenon was often associated with severe consequences. In recent study that included 4,609 consecutive asymptomatic individuals referred by primary physicians for serial CAC measurement with electron beam computerized tomography and after a mean follow up of 3.1 years, the progression of CAC was significantly associated with mortality regardless of the method used to assess progression ($P < 0.0001$) **(2).**

In another study in which 5007 outpatients enrolled and suspected to have CHD and underwent cardiac computerized tomographic angiography (CTA) and followed up for a mean period of 1,081 days, found that 363 (8.2%) patients had experienced major adverse cardiovascular events (MACE) and the cumulative probability of 3-year MACE increased across CT strata for coronary artery calcification score (CACS) (CACS 0, 2.1%; CACS 1–100, 12.9%; CACS 101–400, 16.3%; and CACS > 400, 33.8%; log-rank P < 0.001). **(6)**.

CAC is not only independently associated with CHD of asymptomatic subjects, but also carries prognostic importance in patients with known CHD, and has demonstrated in multiple intravascular ultrasound studies that the average number of calcium deposits within an arc of < 90 degrees per patient was significantly higher in patients with acute MI than with stable angina. Conversely, calcium deposits were significantly longer in patients with stable angina, in contrast to the typical pattern of spotty calcification in acute MI. **(7).**

5. Diagnostic methods

5.1. Computed tomography coronary angiography (CTCA)

Coronary artery calcium is primarily evaluated by noncontrast, electrocardiographic (ECG)-gated cardiac electron beam computed tomography (EBCT) or multislice detector computed tomography (MDCT). A coronary calcium score is associated with plaque burden; it is not a marker of plaque vulnerability. Nonetheless, it gives an insight into the patient’s level of cardiovascular disease risk and helps guide interventions or prevent coronary artery disease. **(8)**

The detection of CAC via CT was made possible in the 1980s after EBCT's development; EBCT's significantly superior speed allows the detection of CAC despite heart motion. MDCT allows even faster image acquisition. MDCT is used more commonly than EBCT due to increased accuracy and image quality. Newer cardiac CT angiography (CTA) developments can also reveal characteristics such as plaque volume and density. **(9)**

The evaluation of CAC scoring via CT offers a fast, reproducible, and relatively inexpensive modality to determine the extent and presence of coronary calcification. CT does not require intravenous access or specific patient preparation. Scans are typically obtained with prospective electrocardiogram triggering during diastole. After imaging is acquired, the extent of calcification is quantified using the Agatston score.

The Agatston score is obtained by multiplying the area of calcification by the corresponding density factor (1-4) in Hounsfield units (HU) as follows:

- 130-199 HU: 1
- 200-299 HU: 2
- 300-399 HU: 3
- 400+ HU: 4

For example, for a calcification area measuring 7 mm^2 and a HU of 400, the Agatston score is $7 \times 4 = 28$. The score is obtained using a slice thickness of 2.5 mm to 3 mm. The Agatston score is the most validated method of CAC quantification. The total CAC is calculated by summing individual calcification speck scores. Other methods of CAC quantification include calcium volume score, visual assessment, calcium density score, calcium mass score, and segment involvement score. **(4).**

Currently, the American College of Cardiology/American Heart Association gives class IIa indication for coronary CTA in asymptomatic patients with intermediate-risk (10%-20%) of cardiac events over 10 years based on the Framingham risk score, as well as for asymptomatic individuals 40 years and older with diabetes. CAC measurement is generally not recommended for patients at low (<10%) or high (>20%) 10-year risk of cardiac events based on the Framingham risk score. (**10).**

The following definitions are used to quantify coronary artery calcium score and coronary plaque burden:

- 0: No identifiable disease
- 1 to 99: Mild disease
- 100 to 399: Moderate disease
- Greater than 400: Severe Disease

Although CAC can help predict the presence or absence of coronary artery stenosis, it is generally a better marker for the extent of coronary atherosclerosis rather than the degree of stenosis. In early atherosclerosis, the arteries have compensatory enlargement to accommodate the plaque. Therefore, although extensive plaque burden may be present, there may not be any clinically relevant stenosis. Severe coronary calcification (Agatston score >1000) is associated with advanced obstructive coronary disease **(11).**

CAC may also be found incidentally on CT performed for other indications. The presence and extent of CAC should be reported on all noncontrast chest CTs. Nongated scans usually do not have a slice thickness of 2.5 mm to 3 mm, and hence, formal Agatston scoring may not be possible. However, a significant correlation between the gated Agatston and nongated ordinal scores is evidenced **.** The effective radiation exposure with EBCT is approximately 0.7 mSv to 1.0 mSv in men and 0.9 mSv to 1.3 mSv in women. MDCT has a slightly higher radiation dose of 1.0 mSv to 1.5 mSv in men and 1.1 mSv to 1.9 mSv in women. The average annual background radiation in the United States is 3.0 mSv to 3.6 mSv. A zero Agatston score is the most powerful negative predictive risk factor in asymptomatic patients compared to a within reference-range level of hs-CRP or lack of carotid plaque**. (12)**

Coronary angiography: Compared with intravascular ultrasound (IVUS) and CT, coronary angiography has a low-moderate sensitivity and high specificity for CAC. The angiographic classification of CAC is primarily based on visual assessment during coronary angiography. Mild calcification is typically spotted as faint, localized, or linear opacities within the vessel wall and is visible only during the cardiac cycle's later phases. Moderate calcification appears as dense, linear opacities during systole and diastole before contrast injection. Severe calcification is observed without cardiac motion before contrast injection; it appears as dense, radiopaque calcium deposits visible in both systole and diastole and may extend around the entire circumference of the vessel ("tram-track" appearance). CTCA is the main noninvasive tool to detect calcified lesion. In CTCA, CACS is widely used to quantify CAC. and is one of the most commonly used methods to evaluate coronary atherosclerotic burden. Agatston scores were divided into three groups: a CACS between 0–100, 101–400, and more than 400. And CACS > 400 has significant prognostic implications in specific patient groups. **(2).**

5.2. Intravascular ultrasound

Intravascular ultrasound was determined to be the gold standard of CAC because of its high sensitivity (90%) and specificity (100%). According to the range of calcified lesion, CAC was classified into 4 classes through detection by intravascular ultrasound: Class I, 0°–90° calcification; Class II, 91°–180° calcification; Class III, 181°–270° calcification; and Class IV > 270° calcification. **(13).**

5.3. Coronary computed tomography angiography (CCTA):

While invasive coronary angiography remains the diagnostic gold standard, CCTA steadily gains ground as a non-invasive, low-risk alternative. It circumvents the hazards associated with invasive procedures and expedites assessments for patients at intermediate risk of CAD. Given the minute dimensions and dynamic nature of epicardial coronary arteries, CCTA relies on precise spatial and temporal resolutions. Spatial resolution determines the smallest distinguishable distance between two points, while temporal resolution dictates how rapidly images of moving structures can be captured. With the advent of 64-slice multi-detector CT (64-MDCT) systems and contemporary technologies, CCTA now boasts the necessary spatial and temporal resolution to visualize even the most distal coronary artery segments. **(14).**

Triglyceride-Glucose Index

Plasma triglycerides are transported in chylomicrons and very-low-density lipoproteins (VLDLs), collectively referred to as Triglyceride-Rich Lipoprotein (TGRLs). Although TGRLs are generally too large to cross the endothelium, they can significantly affect certain aspects of atherosclerotic lesion development. TGRLs contain high levels of cholesterol and undergo remodeling during intravascular lipolysis. This process produces free fatty acids and monoglycerides, which can increase the concentration of cytotoxic free fatty acids, particularly saturated fatty acids. TGRLs and their remnants can lead to endothelial dysfunction, activate the coagulation cascade, and enhance platelet aggregation .The TyG index is a composite measure that assesses IR by analyzing fasting triglyceride (TG) and fasting glucose (FG) levels. The index was computed using the formula TyG index = logarithm (triglycerides (mmol/l) × glucose level (mg/dl)/2). (**15).**

Insulin resistance (IR) is a metabolic condition in which insulin levels are elevated due to insensitivity to insulin and associated with elevated triglyceride levels. Hypertriglyceridemia leads to increased transport of free fatty acids to the liver, which increases liver sugar production. The Triglyceride-glucose index (TyG index) was first proposed in 2008, and the formula for calculating the TyG index is TyG index = Ln [fasting triglyceride (mg/dl) × fasting glucose (mg/dl) /2]. It is a composite indicator consist of fasting triglyceride (TG) and fasting plasma glucose (FPG) levels, With high sensitivity and specificity, the TyG index can serve as an alternative biomarker for IR due to its simple calculation and few constraints on time or cost(**16).**

TyG index has a linear dose-response association with IR risk. TyG index was significantly correlated with the incidence of multiple diseases. The TyG threshold predicts an increased risk of death in a large, homogeneous general population. Therefore, summarizing and analyzing the connection among the TyG index and different diseases is of positive significance for clinical treatment and basic experimental research. (**17).**

Relationship between TyG index and different diseases

Prediabetes

Data from the International Diabetes Federation (IDF) indicate a year-on-year rise in the prevalence of diabetes, highlighting the importance of delaying the progression from prediabetes to diabetes. Study reveals that the TyG index can forecast prediabetes with impaired glucose tolerance; regardless of glucose metabolism status, the TyG index can identify the risk of early and late β cell dysfunction **(18).**

. A multicenter randomized controlled trial (RCT) involving eight countries, focusing on lifestyle interventions for prediabetes, indicated that personalized approaches based on TyG could prevent the progression to T2DM, thereby aiding in the differentiation of prediabetes/diabetes patients. The aforementioned researchers have elucidated the influential role of the TyG index in the context of prediabetes. Furthermore, it may serve as a strategic intervention to mitigate the progression to T2DM, thereby playing a crucial role in the management and treatment of prediabetes. **(19).**

Diabetes mellitus

Type 2 diabetes constitutes a substantial proportion of the total incidence of diabetes mellitus. Each incremental unit in the TyG index is correlated with nearly a tenfold increase in the risk of T2DM, with a direct correlation between the TyG index and T2DM risk and the most valuable biomarker. Extensive population-based studies have underscored the predictive ability of the TyG index in assessing T2DM risk. A longitudinal study spanning 12 years on non-obese adults has confirmed the TyG index's involvement in T2DM pathogenesis (**20).**

Early identification and monitoring of the TyG index are pivotal in managing T2DM comprehensively, aiding in clinical decision-making and patient care. Given the gradual onset of hyperglycemia and the low diagnosis rate of T2DM, early screening of the TyG index can partially address this diagnostic challenge. Research indicates a strong interconnection between elevated TyG index levels before pregnancy, during the first trimester, and throughout pregnancy, and the increased risk of GDM (**21).**

Cardiovascular disease

Cardiovascular disease (CVD) represents the foremost cause of mortality on a global scale. According to a report from the World Health Organization, fatalities attributed to cardiovascular diseases constitute a significant health risk to human populations. The TyG index's capability to pinpoint individuals at heightened risk of cardiovascular events. Notably, baseline TyG index levels have been linked to an elevated cardiovascular risk. Moreover, an escalation in the TyG index has shown a close linkage with an increased susceptibility to cardiovascular diseases (**22),** enabling the prediction of CVD risk within populations. This increase in TyG index has also been correlated with amplified risks of all-cause mortality and cardiovascular death among individuals at high CVD risk, as well as a positive correlation with 28-day and 90-day mortality rates in CVD patients. Furthermore, individuals exhibiting higher baseline TyG index levels and a trajectory of sustained or progressive increase in early adulthood have displayed significantly heightened rates of CVD events and all-cause mortality in later life. So, under equivalent total cumulative exposure, the risk of CVD and all-cause mortality stemming from early TyG index accumulation surpasses that of late accumulation, underscoring the significance of early TyG index management. The TyG index can serve as a straightforward supplementary indicator for CVD screening and the early identification of vascular disease severity. It is imperative to leverage the TyG index's potential in the context of CVD to mitigate mortality rates and enhance patient prognosis. (**23).**

Hypertension

Hypertension constitutes a significant global health concern. Its prevalent nature presents substantial challenges to healthcare systems and carries considerable socio-economic ramifications on a global scale. A significant correlation between elevated TyG index levels and the incidence of hypertension, with a linear positive correlation observed between the TyG index and the risk of developing hypertension and the TyG index has been independently linked to branch artery and aortic diastolic blood pressure (BP).The TyG index plays a crucial role in identifying and managing prehypertension and hypertension, influencing various stages, phenotypes, and progression of the condition. In the initial stages of pregnancy, the TyG index demonstrates a significant correlation with the incidence of hypertensive disorders of pregnancy (HDP) as well as negative pregnancy outcomes Analysis of patients with grade 1–3 hypertension reveals a stronger correlation in patients with grade 1–2 hypertension compared to those with grade 3 hypertension . The TyG index of hypertensive patients exhibits an L-shaped relationship with all-cause mortality (**24**).

Metabolic syndrome

A growing prevalence of adults is being identified as meeting the diagnostic criteria for metabolic syndrome (MetS). Recent research indicates a concerning increase in the incidence of MetS among younger populations, implying that these conditions are no longer confined to adults and the elderly. The TyG index exhibits a direct association with multiple metabolic risk factors, thereby serving as an important instrument for the identification of populations at elevated risk for metabolic disorders. Research suggests that the TyG index is a more reliable predictor of MetS compared to HOMA-IR and other metabolic indicators **.** MetS constitutes a multifaceted array of metabolic disorders that serve as risk factors for numerous diseases. Emphasizing the strong association between the TyG index and MetS may facilitate the mitigation of both the incidence and progression of this syndrome. (**25).**

Hyperuricemia

There exists a direct association between hyperuricemia (HUA) and various medical conditions, including hypertension, diabetes, severe obesity, hyperlipidemia, renal failure, and other related disorders. The TyG index demonstrated a notable correlation with HUA, exceeding the obesity index in its efficacy for identifying HUA. Moreover, an increase in baseline TyG levels and associated indicators has been associated with a heightened risk of HUA. TyG and its derivative indicators have demonstrated potential as sensitive biomarkers for the prediction of HUA. While the overall prognosis for HUA is generally favorable, a subset of patients may still experience complications; thus, early detection and prompt intervention utilizing the TyG index are crucial. **(26).**

Thyroid disease

The study involved the determination of serum thyrotropin (TSH) and free thyroxine (FT4) levels in the participants. Research findings suggest that the TyG index is a dependable measure for assessing the relationship between thyroid function. It was noted that the TyG index demonstrated a substantial negative correlation with levels of FT4, while showing a positive correlation with TSH levels and anti-thyroglobulin antibodies (TgAb). This indicates a significant association between the TyG index and thyroid function (**27).**

Among individuals with normal thyroid function, the log-transformed TSH (LnTSH) was notably linked to the TyG index in females. Furthermore, both hyperthyroidism and hypothyroidism demonstrated associations with the TyG index (**28)** .

Stroke

Stroke has emerged as a predominant cause of mortality and disability. As a major chronic noncommunicable disease, it presents a substantial risk to public health and demonstrates a troubling increasing trend. One study conducted on extensive populations have demonstrated that elevations in the baseline level and long-term cumulative mean TyG index autonomously forecast stroke and IS, including analyses of the general population, young adults, and middle-aged and elderly individuals. The progression, recurrence, and prognosis of stroke are significantly intertwined with the survival and quality of life of patients. A plethora of studies have underscored that the TyG index IS is linked to an escalated risk of stroke recurrence and fatality (**29).**

Patients who received dual antiplatelet therapy (DAPT) were assessed. The findings indicated that an increase in the TyG index was associated with enhanced platelet reactivity and a higher incidence of high residual on-treatment platelet reactivity (HRPR), serving as an independent risk factor for assessing aspirin HRPR. Given that the sequelae of stroke can result in prolonged cognitive impairment for patients, the early identification and intervention based on the prognostic value of the TyG index are of considerable importance. **(30).**

Kidney disease

Extensive research involving large populations has indicated that an increased TyG index is associated with a greater risk of CKD, which can significantly enhance the predictive capacity of CKD. It is notably correlated with the severity of CKD, serving as a valuable indicator for identifying the risk of CKD progression. The early identification of elevated TyG index and renal hyperfiltration (RHF) may have the potential to prevent the future development of CKD in relatively healthy young adults **(31).**

The likelihood of AKI increases in direct correlation with the elevation of the TyG index, and patients with critical AKI exhibiting higher TyG index levels face an elevated risk of all-cause mortality . Moreover, the TyG index demonstrates a significant independent positive association with the decline in renal function (WRF) among the elderly population. The TyG index serves as a mediating factor in the relationship between overweight and ESRD . A dose-response analysis indicated a positive association between the TyG index and the risk of developing kidney stones, implying its potential applicability as a biomarker for the prediction of kidney stone formation **(32)**.

Cancer

The TyG index demonstrates a significant correlation with the risk of non-small cell lung cancer (NSCLC). The escalation of the TyG index is notably associated with gastric cancer, serving as an independent prognostic factor for gastric cancer and elevating the risk of gastrointestinal system cancer **(33).**

An elevated TyG index is connected to a higher risk of colorectal adenoma occurrence and recurrence, with a stronger association observed with recurrence . The TyG index is correlated with prostate cancer (PCa) risk and a lower PCa survival rate. Research has validated the TyG index's ability to identify high-risk groups for thyroid papillary carcinoma. Notably, an elevated TyG index is linked to an increased incidence of female reproductive tissue tumors and serves as a biomarker for endometrial carcinoma (EC). There is a notable association between the TyG index and the survival outcomes of patients with renal cell carcinoma (RCC)**. (34).**

The incidence of cancer in all systems is increasing year by year, and the mortality rate is extremely high, which brings huge economic and health burden to all mankind. Although the continuous development of chemotherapy, radiotherapy, immunotherapy and targeted therapy can prolong the progression-free survival (PFS) and overall survival (OS) of patients, the early diagnosis and intervention of cancer are still very important, and the TyG index can play a predictive role. **(31).**

References:

1. Lanzer, P., Boehm, M., Sorribas, V., Thiruvengadam, D., et al. (2021). Medial arterial calcification: JACC state-of-the-art review. Journal of the American College of Cardiology.
2. Ji B, Liu XB. (2024) Coronary artery calcification: concepts and clinical applications. Ann Med Surg (Lond). 2024 Apr 3;86(5):2848-2855.
3. Demer LL, Tintut Y(2018). Vascular calcification: pathobiology of a multifaceted disease. Circulation. 2018;117:2938–2948.
4. Onnis C, Virmani R, Kawai K, Nardi V, Lerman A, Cademartiri F, Scicolone R, Boi A, Congiu T, Faa G, Libby P, Saba L. Coronary Artery Calcification: Current Concepts and Clinical Implications. Circulation. 2024 Jan 16;149(3):251-266
5. Nakahara T, Dweck MR, Narula N, Pisapia D, Narula J, Strauss HW. Coronary Artery Calcification: From Mechanism to Molecular Imaging. JACC Cardiovasc Imaging. 2017 May;10(5):582-593.
6. Jinnouchi H, Sato Y, Sakamoto A, Cornelissen A, Mori M, Kawakami R, Gadhoke NV, Kolodgie FD, Virmani R, Finn AV(2020). Calcium deposition within coronary atherosclerotic lesion: Implications for plaque stability. Atherosclerosis. 2020 Aug;306:85-95
7. Lemanowicz A, Białecki M, Leszczyński W, Hawrył M. Coronary age, based on coronary calcium measurement, is increased in patients with morbid obesity. Pol J Radiol. 2018;83:e415-e420
8. Chen Y, Hu Z, Li M, Jia Y, He T, Liu Z, Wei D, Yu Y(2019). Comparison of Nongated Chest CT and Dedicated Calcium Scoring CT for Coronary Calcium Quantification Using a 256-Dector Row CT Scanner. Acad Radiol. 2019 Oct;26(10):e267-e274.
9. Disthabanchong S, Boongird S. Role of different imaging modalities of vascular calcification in predicting outcomes in chronic kidney disease. World J Nephrol. 2017 May 06;6(3):100-110.
10. Mohan J, Shams P, Bhatti K, et al. Coronary Artery Calcification. [Updated 2024 Nov 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519037
11. Nasir K, Cainzos-Achirica M. Role of coronary artery calcium score in the primary prevention of cardiovascular disease. BMJ. 2021 May 04;373:n776.
12. Hecht HS, Cronin P, Blaha MJ, Budoff MJ, Kazerooni EA, Narula J, Yankelevitz D, Abbara S. (2016) SCCT/STR guidelines for coronary artery calcium scoring of noncontrast noncardiac chest CT scans: A report

of the Society of Cardiovascular Computed Tomography and Society of Thoracic Radiology. J Cardiovasc Comput Tomogr. 2017 Jan-Feb;11(1):74-84

13. Bazarbashi N, Kapadia SR, Nicholls SJ, et al. Oral calcium supplements associate with serial coronary calcification: insights from intravascular ultrasound. JACC Cardiovasc Imaging 2021;14:259–268
14. Ramjattan NA, Lala V, Kousa O, et al., (2024). Coronary CT Angiography. [Updated 2024 Jan 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470279/
15. Park B, Lee HS, Lee Y-J(2021). Triglyceride glucose (TyG) index as a predictor of incident type 2 diabetes among nonobese adults: a 12-year longitudinal study of the Korean genome and epidemiology study cohort. Transl Res 2021;228:42–51.
16. Nayak Vineetha K Ramdas, Satheesh Praseeda, Shenoy Mohan T, Kalra Sanjay(2022). Triglyceride glucose (TyG) index: a surrogate biomarker of insulin resistance. J Pak Med Assoc 2022;72:986–8.
17. Yu L, Li Y, Ma R, Guo H, Zhang X, Yan Y, et al(2022). Construction of a personalized insulin resistance risk assessment tool in xinjiang kazakhs based on lipid- and obesity-related indices. RMHP 2022;15:631–41.
18. Chen Z, Wen J(2022). Elevated triglyceride-glucose (TyG) index predicts impaired islet β-cell function: a hospital-based cross-sectional study. Front Endocrinol 2022;13: 973655.
19. Sharafi M, Amiri Z, Pezeshki B, Mohsenpour MA, Eftekhari MH, Afrashteh S, et al(2023). Predictive value of triglycerides to high-density lipoprotein cholesterol and triglyceride glycemic index for diabetes incidence in pre- diabetes patients: a prospective cohort study. J Health Popul Nutr 2023;42:67.
20. Wang Z, Zhao L, He S(2021). Triglyceride–glucose index as predictor for future type 2 diabetes mellitus in a Chinese population in southwest China: a 15-year prospective study. Endocrine 2021;72:124–31
21. Zhang D, Sheng J, Chen L, Jiang Y, Cheng D, Su Y, et al(2023). The role of dietary fiber on preventing gestational diabetes mellitus in an at-risk group of high triglyceride- glucose index women: a randomized controlled trial 2023.
22. Rafiee H, Mohammadifard N, Nouri F, Alavi Tabatabaei G, Najafian J, Sadeghi M, et al(2024). Association of triglyceride glucose index with cardiovascular events: insights from the isfahan cohort study (ICS). Eur J Med Res 2024;29:135.
23. Jiang Y, Chen P, Zhao Y, Cai J, Liang J, Cheng S, et al(2024). Association between triglyceride glucose index and all-cause mortality in patients with cerebrovascular disease: a retrospective study. Diabetol Metab Syndr 2024;16:1.
24. Sun Y-H, Hu N-Q, Huang X-Y, Liu Z-X, Li Q-Y, Li Q- L, et al(2024). Central and peripheral blood pressures in relation to the triglyceride-glucose index in a Chinese population. Cardiovasc Diabetol 2024;23:3.
25. Primo D, Izaola O, De Luis DA(2023). Triglyceride- glucose index cutoff point is an accurate marker for predicting the prevalence of metabolic syndrome in obese caucasian subjects. Ann Nutr Metab 2023;79:238–45.
26. Kahaer M, Zhang B, Chen W, Liang M, He Y, Chen M, et al(2022). Triglyceride glucose index is more closely related to hyperuricemia than obesity indices in the medical checkup population in Xinjiang, China. Front Endocrinol 2022;13:861760.
27. Cheng H, Hu Y, Zhao H, Zhou G, Wang G, Ma C, et al(2023). Exploring the association between triglyceride-glucose index and thyroid function. Eur J Med Res 2023;28: 508.
28. Choi YM, Kim MK, Kwak MK, Kim D, Hong E- G.(2021) Association between thyroid hormones and insulin resistance indices based on the Korean national health and nutrition examination survey. Sci Rep 2021;11:21738.
29. Wang, Li; Cao, Tian-Yu; Li, Jin-Qiao; Ding, Cong-Cong; Li, Jun-Pei; Ying, Hua-Bo; Liu, Li-Shun; Huang, Xiao(2022). “Positive association between triglyceride glucose index and central systolic blood pressure among hypertensive adults.” Journal of Geriatric Cardiology 19, no. 10 (2022): 753–760. doi: 10.11909/j.issn.1671-5411.2022.10.006.

30. Guo Y, Zhao J, Zhang Y, Wu L, Yu Z, He D, et al(2021). Triglyceride glucose index influences platelet reactivity in acute ischemic stroke patients. BMC Neurol 2021; 21:409.
31. Yu C, Shi Y, Wang T, Zhu L, Zhou W, Bao H, et al(2024). Triglyceride–glucose index change and chronic kidney disease progression in a Chinese hypertensive population. Front Endocrinol 2024;15:1342408.
32. Lei L, Liang H, Qu Y, Zhong Q, Zhang Q, Dai L, et al(2022). Association between triglyceride-glucose index and worsening renal function in the elderly. Front Nutr 2022;9:951564.
33. Kwon S, Heo A, Chun S(2023). Triglyceride and glucose index for identifying abnormal insulin sensitivity in women with polycystic ovary syndrome. Obstet Gynecol Sci 2023;66:307–15
34. Shi H, Guo F, Zheng K, Li R, Zhou H(2024). Triglyceride-glucose index (TYG index) and endometrial carcinoma risk: a retrospective cohort study. Intl J Gynecol Obste 2024;164:298–304.