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Understanding triglyceride glucose-body mass index: implications for diabetes and cardiovascular disease management

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This article focuses on the Triglyceride-Glucose Body Mass Index (TyG-BMI) in diabetes and its associated cardiovascular complications. It elaborates on the basic concepts, current clinical practices, technological advancements, controversies, challenges, and future directions related to TyG-BMI. By integrating the findings from numerous studies, we aimed to provide a comprehensive understanding of the role of TyG-BMI in diabetes and cardiovascular disease research, diagnosis, and treatment, highlighting its significance and potential for improving the management of diabetic cardiovascular health.

KEYWORDS

triglyceride glucose-body mass index, diabetes, cardiovascular disease, insulin resistance, mortality

1 Introduction

Diabetes mellitus (DM), particularly type 2 diabetes, is one of the most common chronic diseases worldwide (1). The most common complication of diabetes is cardiovascular disease, the leading cause of morbidity and mortality (2). Many biomarkers have been developed to assess the risk of incident diabetic complications; however, few have been validated in subsequent analyses or applied in clinical practice (3). Thus, there is great interest in exploring clinical biomarkers that can accurately predict the risk of diabetes-related diseases and mortality.

Numerous studies have demonstrated the association between the Triglyceride-Glucose (TyG) index and the risk of type 2 DM. For example, in a prospective study of 1923 women and 3016 men from the Vascular Metabolic CUN cohort, the hazard ratio (HR) for incident diabetes per one-standard-deviation increment in the TyG index was 1.54 [95% confidence interval (CI): 1.40–1.68], indicating that an increase in the TyG index significantly increases the risk of developing diabetes across different metabolic health categories (4). A 4-year retrospective study involving 2900 adults without diabetes found

that individuals with a high TyG index had an elevated risk of diabetes compared with those with a low TyG index. For TyG index quartiles, the HRs for quartiles 3 and 4 were 4.06 ($p = 0.033$) and 5.65 ($p = 0.006$), respectively, suggesting its predictive value for incident diabetes (5).

Some studies have explored the application of the TyG index combined with anthropometric measures; notably, the Triglyceride–Glucose Body Mass Index (TyG–BMI) has been developed. In a cross-sectional study involving Nigerian adults, TyG–BMI showed good performance in identifying metabolic syndrome (MS). The area under the curve (AUC) for TyG–BMI in detecting MS was 0.838 (95% CI: 0.802–0.870), indicating its potential as a screening tool for MS (6). The relationship between the TyG index and BMI has also been investigated in relation to other diseases. A study on the association between the TyG index and carotid atherosclerosis in patients with non-alcoholic fatty liver disease (NAFLD) found an increased risk for carotid atherosclerosis with an elevated TyG index value. The HR (95% CI) for carotid atherosclerosis risk in the higher TyG index group was significant, with the low TyG index group as the reference. These findings indicate the combined impact of an

elevated TyG index and the presence of NAFLD—often related to BMI—on cardiovascular risk (7).

2 TyG-BMI: definition

TyG-BMI has emerged as an important metric for understanding metabolic and cardiovascular health (Figure 1). Insulin resistance (IR) is a key factor underlying many metabolic disorders and TyG-BMI is closely associated with IR (8). In this study involving 511 Taiwanese individuals, various parameters were analyzed to determine their efficiency as independent risk factors for IR. TyG-BMI, calculated as $\ln [\text{plasma triglyceride (mg/dL)} \times \text{fasting blood glucose (mg/dL)} / 2] \times \text{BMI}$, is strongly associated with homeostasis model assessment of insulin resistance (HOMA-IR), with 16.6% of the variability in HOMA-IR explained by TyG-BMI (8). These findings indicate that TyG-BMI can serve as a simple and effective surrogate marker for early identification of IR.

The relationship between TyG-BMI and other metabolic factors is complex. For instance, in a cross-sectional study of 184

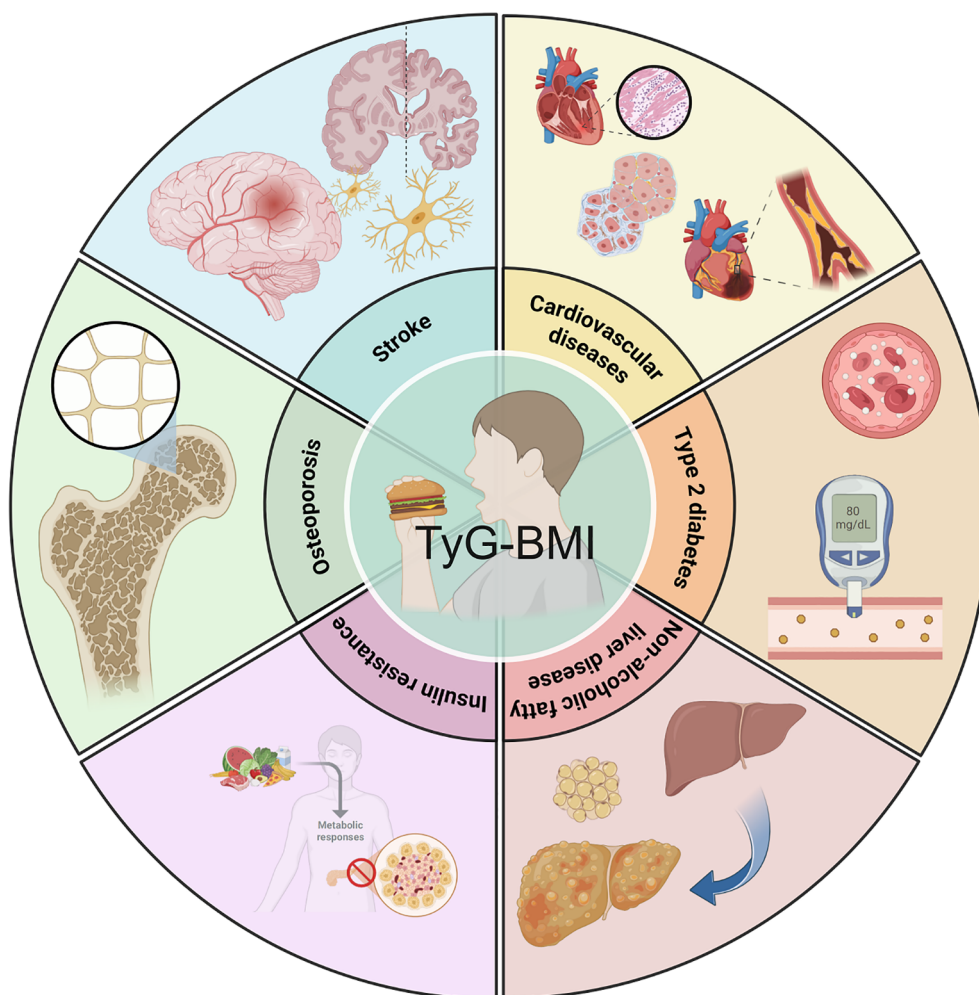


FIGURE 1

Clinical relevance of TyG-BMI. TyG-BMI is closely associated with type 2 diabetes mellitus, non-alcoholic fatty liver disease, insulin resistance, osteoporosis, stroke, cardiovascular disease, and other metabolic diseases.

overweight/obese individuals without diabetes, TyG-BMI, along with other related parameters, TyG-waist circumference (TyG-WC), was found to be significantly associated with nonalcoholic fatty liver disease (NAFLD) and liver fibrosis (9). The study computed TyG, TyG-BMI, and TyG-WC and determined liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) using transient elastography. Correlation analyses showed that CAP and LSM were significantly associated with WC, BMI, TyG, TyG-BMI, and TyG-WC, suggesting that TyG-BMI is a part of a network of metabolic markers related to adipose tissue and liver health.

3 Epidemiological insights

Epidemiological studies have provided valuable insights into the role of TyG-BMI as a cardiovascular risk factor (10–16). In a large-scale analysis of 35,455 participants aged 35–75 years with high risk of cardiovascular disease (CVD) risk, TyG-BMI was associated with an increased risk of all-cause and cardiovascular death (17). The study calculated TyG-BMI as $\ln$ [fasting triglyceride (mg/dL) $\times$ fasting blood glucose (mg/dL)/2] and followed the participants for a median of 3.4 years. Multivariate Cox proportional hazard models showed that participants with a TyG-BMI ≥ 9.83 had a higher risk of all-cause death (Hazard ratio [HR] 1.86, 95% Confidence intervals [CI] 1.37–2.51, $P < 0.001$) and cardiovascular death (HR 2.41, 95%CI 1.47–3.96, $P = 0.001$) compared to those with a TyG-BMI < 9.83 .

Furthermore, in a study of 11,016 US adults from the NHANES 2011–2020 dataset, higher TyG-BMI values were significantly associated with an increased prevalence of CVD (16). Weighted generalized linear models demonstrated a positive association, with individuals in the highest tertile of TyG-BMI having a 38% higher CVD prevalence compared to those in the lowest quartile (OR = 1.380; 95% CI = 1.080, 1.763). These findings suggest that TyG-BMI can be an important epidemiological marker for identifying individuals at high risk of CVD.

4 TyG-BMI, insulin resistance and hyperinsulinemia

IR is a complex pathophysiological state in which cells exhibit a reduced response to insulin, leading to elevated blood glucose levels (18). The relationship between TyG-BMI and IR is multifaceted. Obesity, often reflected in a high BMI, is closely associated with IR. Additionally, the distribution and function of adipose tissue play a role; visceral adiposity, which can be related to TyG-BMI, is associated with IR. Moreover, the visceral adiposity index (VAI) and lipid accumulation product (LAP)—indices related to TyG-BMI—are effective surrogate markers for IR and are predictors of MS and DM (19).

In a study of 511 Taiwanese individuals, TyG-BMI was strongly associated with HOMA-IR, with 16.6% of the variability in HOMA-IR explained by TyG-BMI. Receiver operating characteristic (ROC)

curve analysis indicated that TyG-BMI had the largest AUC (0.801), suggesting its effectiveness as a surrogate marker for the early identification of IR (20). In a Korean study, the adjusted odds ratio for predicting IR was 12.82 (95% CI: 10.89–15.10) in TyG-BMI quartile 4 compared with quartile 1. The AUC-ROC for TyG-BMI was 0.748, suggesting its superiority over other parameters for IR prediction in the Korean adult population (21).

IR is significantly associated with cardiovascular events and is considered an independent risk factor for CVD (22–24). Multiple studies have shown that IR is closely associated with various cardiovascular risk factors, including hypertriglyceridemia, low high-density lipoprotein cholesterol levels, hypertension, obesity, and elevated plasminogen activator inhibitor-1 levels (25). The combined action of these factors accelerates the development of atherosclerosis and increases the risk of cardiovascular events (26).

IR and hyperinsulinemia play distinct roles in cardiovascular diseases, and their combined effects increase the risk of cardiovascular diseases. IR itself can trigger a series of cardiovascular problems. IR impairs the function of vascular endothelial cells, reduces the production of nitric oxide (NO), increases oxidative stress, leads to decreased vasodilatation ability, and promotes atherosclerosis (27). Furthermore, IR is associated with a chronic low-grade inflammatory state, with elevated levels of inflammatory factors such as interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF α), further exacerbating atherosclerosis (28). Moreover, IR often accompanies dyslipidemia, such as elevated triglycerides and decreased high-density lipoprotein cholesterol (HDL-C), which are risk factors for cardiovascular diseases (29). Long-term hyperinsulinemia can also have adverse effects on the cardiovascular system. Hyperinsulinemia increases renal sodium reabsorption, activates the sympathetic nervous system, and leads to elevated blood pressure (30). Insulin promotes the proliferation of vascular smooth muscle cells, and long-term hyperinsulinemia accelerates the progression of atherosclerosis (31). Hyperinsulinemia may affect the coagulation system, increasing the risk of thrombosis (32). Therefore, IR and hyperinsulinemia each play their own roles in cardiovascular diseases while also influencing each other. Early intervention for IR and hyperinsulinemia is crucial for the prevention and control of cardiovascular diseases.

5 Current clinical application

Currently, various diagnostic techniques are used for cardiovascular diseases and TyG-BMI can potentially complement these methods. For example, coronary artery disease is often diagnosed using invasive angiography and computed tomographic angiography. However, these methods have limitations, such as exposure to invasive complications, ionizing radiation, and iodinated contrast agents (33).

Noninvasive methods, such as cardiac magnetic resonance imaging (CMR) angiography, are being explored as alternatives. In addition, TyG-BMI measurements can provide valuable information about the underlying metabolic state of the patient.

In a study of patients with ischemia and nonobstructive coronary arteries (INOCA), TyG-BMI was found to be an independent predictor of the slow coronary flow phenomenon (SCFP) (34). This study enrolled 1,625 patients with INOCA and divided them into the SCFP and control groups based on thrombolysis in myocardial infarction (TIMI) frame counts. TyG-BMI was significantly higher in the SCFP group and showed a better predictive value than BMI or triglyceride glucose alone, suggesting that it could be used as an additional diagnostic marker in such patients.

Therapeutic strategies targeting TyG-BMIs are emerging as an important aspect of cardiovascular disease management. Because TyG-BMI is closely associated with insulin resistance, interventions that improve insulin sensitivity may also affect TyG-BMI. Lifestyle modifications such as diet and exercise are fundamental in this regard. A study on the effects of digital health obesity treatment interventions in medically vulnerable primary care patients showed that interventions aimed at weight loss and improving metabolic parameters could potentially influence TyG-BMI-related factors (35).

In terms of pharmacological interventions, drugs that target lipid and glucose metabolism may also affect TyG-BMI. For example, a study on the association between TyG-BMI and the incidence of cardiovascular disease in middle-aged and older Chinese adults suggested that effective management of metabolic risk factors could potentially modify TyG-BMI and reduce CVD risk (36). However, further research is needed to determine the specific drugs and treatment regimens that can most effectively target TyG-BMI and improve cardiovascular outcomes.

Several cardiovascular risk assessment tools are available in clinical practice, and understanding their performance with TyG-BMI is crucial (37). However, these tools may not fully capture the risk associated with insulin resistance, which is represented by TyG-BMI. In a study comparing different risk assessment models in patients with and without rheumatoid arthritis, it was found that the addition of certain biomarkers could improve the predictive accuracy of the models (38). Similarly, incorporating TyG-BMI into existing cardiovascular risk assessment tools may enhance their ability to identify individuals at high risk for cardiovascular diseases. For example, in a study of patients with type H hypertension, TyG-BMI was significantly associated with the severity of coronary artery disease and could potentially be used to refine risk assessments in this patient population (39).

Traditional cardiovascular risk assessment tools typically focus on a single factor, whereas TyG-BMI considered both metabolic and anthropometric factors, thereby improving the predictive accuracy (40). This comprehensive assessment is superior to using BMI or the TyG index alone, as CVD risk is complex and influenced by multiple factors (41). TyG-BMI can help identify early CVD risk factors that traditional risk assessment methods may overlook. For example, adding the TyG index to traditional risk models can improve the model's ability to distinguish CVD cases (42).

Although TyG-BMI has value in assessing metabolic risk, some limitations remain (43, 44). In summary, while TyG-BMI can serve as an indicator of metabolic risk, it cannot be the sole basis for guiding treatment and preventive drug use. In clinical practice, the

overall risk status of patients should be comprehensively considered, and personalized intervention strategies should be developed based on other biomarkers and clinical judgment.

6 Controversies and challenges

Despite growing evidence of an association between TyG-BMI and various cardiovascular and metabolic conditions, its clinical utility remains debated. Some studies have questioned the specificity of TyG-BMI as a biomarker (8). Additionally, the cut-off values for TyG-BMI in predicting different diseases may vary across populations studied, which adds to the complexity of its clinical application. Further research is needed to standardize these cutoff values and determine the optimal use of TyG-BMI in different clinical settings.

The integration of TyG-BMI into the clinical practice presents several challenges. One of the main challenges is a lack of awareness among healthcare providers. Many clinicians are not familiar with the concept of TyG-BMI and its potential clinical implications (9).

In addition, there is a need for more standardized measurements and reporting of TyG BMI. Although there is a primary calculation method, TyG-BMI may also have other variations that may be relevant to specific study populations or experimental designs. Different studies may adjust the calculation formula of TyG-BMI according to the needs of the research subjects or experimental design (40). Moreover, the interpretation of TyG-BMI values in the context of other clinical parameters must be better defined. For example, in a study investigating the use of TyG-BMI in predicting the slow coronary flow phenomenon in patients with INOCA, while TyG-BMI was found to be a significant predictor, more research is needed to determine how it should be integrated with other diagnostic and prognostic factors in clinical decision-making (34).

7 Future directions

Emerging therapies targeting TyG-BMI are likely to focus on improving insulin sensitivity and modulating lipid and glucose metabolism. One potential approach is the development of drugs that specifically target pathways related to TyG-BMI components. For instance, drugs that reduce triglyceride levels while improving glucose metabolism may have beneficial effects on TyG-BMI. In a study of the association between TyG-BMI and new-onset diabetes, a nonlinear relationship was found, suggesting that interventions aimed at different TyG-BMI levels may be required (45).

TyG-BMI has the potential to play a significant role in personalized medicine for CVH. Personalized treatment plans can be developed by integrating TyG-BMI with other genetic, genomic, and clinical data. For example, in a study on patient similarity-based predictive modeling for cardiovascular diseases, the use of multimodal data, including genetic and clinical information, was explored (46).

Adding TyG-BMI to this data pool could enhance the accuracy of predicting an individual's risk and treatment response. Additionally, the development of targeted therapies based on TyG-BMI and associated metabolic profiles could be a future direction. This could involve the use of precision medicine approaches, such as pharmacogenetics, to optimize the treatment of cardiovascular diseases in patients with abnormal TyG-BMI.

Author contributions

SZ: Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. RG: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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