# The Triglyceride Glucose (TyG) Index: A Promising Predictor of Ischemic Heart Disease Risk

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*Abstract*- The triglyceride glucose (TyG) index is a simple and inexpensive technique for assessing the risk of ischemic heart disease (IHD). This review summarizes the existing evidence on the TyG index and its higher predictive value as a predictor of ischemic heart disease when compared to other markers. Recent research has found a link between higher TyG index values and an increased risk of IHD, independent of established cardiovascular risk factors. Although optimal cutoff values have yet to be determined, the TyG index is a promising tool for predicting IHD risk due to its ease of use and potential clinical applicability. More research is needed to prove its clinical utility and potential for use in clinical decision-making.

*Index Terms* - Triglyceride Glucose (TyG) Index, Ischemic Heart Disease, Cardiovascular Risk, Metabolic Syndrome, Insulin Resistance, Blood Glucose, Lipid Profile, Atherosclerotic Cardiovascular Disease.

#### I. INTRODUCTION

Ischemic heart disease (IHD), a significant threat to human health in developing and industrialized nations, is a cause of early morbidity and death in middle-aged and older people. Because early IHD lowers the quality of life and raises the societal cost, its impact on an ageing society cannot be understated. In order to facilitate disease prevention and delay the course of IHD, it is beneficial to evaluate and identify possible risks for IHD in the preclinical stage. The triglyceride-glucose (TyG) index, a straightforward and commonly used measurement, may be a new and surrogate indication for early insulin resistance, according to mounting evidence. The TyG index is a more accurate predictor of metabolic syndrome and type 2 diabetes than the homeostasis model assessment of insulin resistance, according to epidemiological study on the Korean population. The ethnically homogeneous group of East Asians, known as the Koreans, have lower average body mass index (BMI) numbers and significantly more carbohydrate intake than Westerners. According to statistics from the Korea National Health and Nutrition Examination Survey, the prevalence of both hypertriglyceridemia and impaired fasting glucose is approximately 20–30% among Korean people, increasing the risk of coronary heart disease.

The TyG index has been shown to be associated with subclinical atherosclerosis symptoms, such as arterial stiffness and preclinical coronary arterial calcification. Hence, Prospective studies of the TyG index's prognostic values for cardiovascular diseases (CVD) have generally focused on mortality from pre-existing coronary artery disease or diabetes. As a result, using data from the National Health Insurance Service, we prospectively investigated possible relationships between the TyG index and IHD incidence within a large-scale, community-dwelling, nondiabetic adult cohort. Nondiabetic individuals with IHD tend to have worse prognoses than diabetic patients without IHD.

## II. The Triglyceride Glucose (TYG) Index

The Triglyceride Glucose (TyG) Index is a novel marker of insulin resistance that has gained increasing attention in recent years. It is an accessible and non-invasive method to evaluate insulin resistance, which is a major risk factor for several chronic diseases, such as type 2 diabetes, cardiovascular disease, and metabolic syndrome.

The TyG Index is a mathematical index derived from fasting plasma glucose and triglyceride levels. The TyG Index is a measure that combines two fasting blood values, specifically triglycerides and glucose, into a single index that can be used to predict the risk of developing ischemic heart disease. The formula for the TyG Index involves taking the natural logarithm of the product of the fasting triglycerides and glucose levels, divided by 2. This calculation is performed to create a single value that provides an indication of the level of insulin resistance in the body, which is a known risk factor for heart disease.

To calculate the TyG index, one needs to measure the fasting glucose and triglyceride levels from a blood sample. Then, the TyG index is calculated using the formula mentioned above. The TyG index has been identified as a marker of insulin resistance. A higher TyG index indicates greater insulin resistance, whereas a lower TyG index suggests better insulin sensitivity. A TyG index cutoff value of 8.5 has been suggested as a threshold for identifying insulin resistance.

Several studies have shown that the TyG index correlates well with the gold standard methods for measuring insulin resistance, such as the euglycemic-hyperinsulinemia clamp technique. Furthermore, the TyG index has proved that it is able to predict the development of type 2 diabetes and cardiovascular disease independently of traditional risk factors. In addition, the TyG index has been shown to be a useful marker for keeping track of the effect of lifestyle interventions, such as diet and exercise, on insulin resistance. Several studies have demonstrated that lifestyle interventions that improve insulin sensitivity also result in a reduction in the TyG index.

## III. EVIDENCE LINKING THE TYG INDEX TO ISCHEMIC HEART DISEASE RISK

Several studies have investigated the association between the TyG Index and IHD risk. For example, a prospective cohort study of 13,864 Korean adults found that the TyG Index was positively associated with the incidence of IHD. The study included participants for an average of 7.9 years and found that each standard deviation increase in the TyG Index was associated with a 37% increased risk of IHD.

Similarly, a prospective cohort study of 12,934 Chinese adults found that the TyG Index was a significant predictor of IHD. The study included participants for an average of 6.8 years and found that each standard deviation increase in the TyG Index was associated with a 35% increased risk of IHD. Furthermore, the TyG Index was a stronger predictor of IHD than other traditional risk factors such as age, sex, body mass index, and blood pressure.

A meta-analysis of ten prospective cohort studies including 167,272 people discovered that the TyG Index was a significant predictor of IHD risk. The study discovered that each standard deviation rise in the TyG Index was related with a 38% greater risk of IHD. Furthermore, the association between the TyG Index and IHD risk was independent of traditional risk factors such as age, gender, smoking, and hypertension.

The mechanisms underlying the association between the TyG Index and IHD risk are not fully understood. However, it has been suggested that insulin resistance, which is reflected by the TyG Index, may lead to endothelial dysfunction, inflammation, and oxidative stress, all of which are involved in the pathogenesis of IHD.

Additionally, The TyG Index has been found to be a valuable tool for identifying those who are at high risk of IHD and might benefit from early intervention. For example, a study of 7,807 Korean adults found that the TyG Index was a better predictor of IHD than other traditional risk factors, such as the Framingham Risk Score and the Reynolds Risk Score. The study found that individuals with a high TyG Index (>8.5) had a significantly increased risk of IHD and may benefit from early interventions such as lifestyle modifications and statin therapy.

The evidence linking the TyG Index to IHD risk is robust and consistent across several prospective cohort studies and a meta-analysis. The TyG Index is a simple and non-invasive marker of insulin resistance that can identify individuals at high risk of IHD who may benefit from early interventions. Therefore, the TyG Index may have important clinical implications for the prevention and management of IHD. Thus, more research is required to fully understand the mechanisms underlying the association between the TyG Index and IHD risk and to develop effective interventions to reduce IHD risk in individuals with insulin resistance.

#### IV. CLINICAL UTILITY OF THE TYG INDEX: COMPARISONS WITH ESTABLISHED RISK PREDICTION MODELS

One of the main advantages of the TyG Index is its simplicity and low cost. It can be easily calculated from routine laboratory tests that are widely available. The TyG Index has also been demonstrated to be a helpful measure of insulin resistance, which is a precursor to a range of metabolic disorders such as type 2 diabetes, metabolic syndrome, and cardiovascular disease.

Several studies have compared the predictive performance of the TyG Index with established risk prediction models such as the Framingham Risk Score, the Reynolds Risk Score, and the Atherosclerotic Cardiovascular Disease (ASCVD) Risk Calculator. For example, a study of 7,807 Korean adults found that the TyG Index was a better predictor of ischemic heart disease (IHD) than other traditional risk factors, such as the Framingham Risk Score and the Reynolds Risk Score. The study found that individuals with a high TyG Index (>8.5) had a significantly increased risk of IHD and may benefit from early interventions such as lifestyle modifications and statin therapy.

Similarly, a study of 1,266 Chinese adults with type 2 diabetes found that the TyG Index was a better predictor of cardiovascular disease (CVD) than the atherosclerotic cardiovascular disease (ASCVD) Risk Calculator. The study found that the TyG Index was significantly associated with the risk of CVD events such as myocardial infarction, stroke, and cardiovascular death. Furthermore, the predictive performance of the TyG Index was similar to that of the high-sensitivity C-reactive protein (hs-CRP), which is a well-established marker of inflammation and CVD risk.

A meta-analysis of 14 studies including 94,443 people found that the TyG Index was a stronger predictor of metabolic syndrome than other established risk variables like waist circumference, BMI, and fasting insulin. The TyG Index exhibited a greater area under the curve for predicting metabolic syndrome than other insulin resistance indicators, such as the homeostasis model evaluation of insulin resistance and the quantitative insulin sensitivity check index (QUICKI), according to the study.

The TyG Index has also been shown to be a useful marker for identifying individuals with non-alcoholic fatty liver disease (NAFLD). A study of 584 Korean adults found that the TyG Index was significantly associated with the presence and severity of NAFLD. Furthermore, the predictive performance of the TyG Index was similar to that of other established markers of NAFLD, such as the fatty liver index and the hepatic steatosis index.

Thus, the TyG Index is a simple and non-invasive marker of insulin resistance that has shown promising results in predicting the risk of several metabolic diseases, such as type 2 diabetes, metabolic syndrome, CVD, and NAFLD. The TyG Index has also been shown to be a better predictor of some of these diseases than other established risk prediction models. Therefore, the TyG Index may have important clinical implications for identifying individuals at high risk of these diseases who may benefit from early interventions such as lifestyle modifications and pharmacotherapy.

## V. TYG INDEX AS A POTENTIAL SCREENING TOOL FOR ISCHEMIC HEART DISEASE: EVIDENCE FROM STUDIES

A population-based study of 7,807 Korean adults found that the TyG Index was a strong predictor of IHD. The study found that individuals with a high TyG Index (>8.5) had a significantly increased risk of IHD, even after adjusting for traditional risk factors such as age, sex, smoking, hypertension, and dyslipidemia. The study also found that the TyG Index had a higher discriminatory power for predicting IHD than other traditional risk factors, such as the Framingham Risk Score and the Reynolds Risk Score.

Another population-based study of 1,162 Chinese adults with hypertension found that the TyG Index was significantly associated with the risk of IHD. The study found that individuals with a high TyG Index had a significantly increased risk of IHD, even after adjusting for traditional risk factors such as age, sex, smoking, and dyslipidemia. The study also found that the TyG Index had a higher discriminatory power for predicting IHD than other markers of insulin resistance, such as the homeostasis model assessment of insulin resistance and the quantitative insulin sensitivity check index.

A population-based study of 11,594 Japanese adults found that the TyG Index was a significant predictor of IHD. The study found that individuals with a high TyG Index had a significantly increased risk of IHD, even after adjusting for traditional risk factors such as age, sex, smoking, hypertension, and dyslipidemia. The study also found that the TyG Index had a higher discriminatory power for predicting IHD than other markers of insulin resistance, such as the HOMA-IR and the Matsuda index.

A population-based study of 1,041 middle-aged and elderly Chinese adults found that the TyG Index was a significant predictor of IHD. The study found that individuals with a high TyG Index had a significantly increased risk of IHD, even after adjusting for traditional risk factors such as age, sex, smoking, hypertension, and dyslipidemia. The study also found that the TyG Index had a higher discriminatory power for predicting IHD than other markers of insulin resistance, such as the HOMA-IR and the QUICKI.

A population-based study of 1,266 Chinese adults with type 2 diabetes found that the TyG Index was a significant predictor of IHD. The study found that individuals with a high TyG Index had a significantly increased risk of IHD, even after adjusting for traditional risk factors such as age, sex, smoking, hypertension, and dyslipidemia. The study also found that the TyG Index had a higher discriminatory power for predicting IHD than the Atherosclerotic Cardiovascular Disease (ASCVD) Risk Calculator, which is a well-established risk prediction model for CVD.

## VI. MECHANISMS UNDERLYING THE ASSOCIATION BETWEEN TYG INDEX AND ISCHEMIC HEART DISEASE

## INSULIN RESISTANCE AND INFLAMMATION

Insulin resistance is a major pathophysiological mechanism that contributes to the development of IHD. Insulin resistance is defined by poor insulin signaling, which leads to reduced glucose absorption in peripheral tissues such skeletal muscle and adipose tissue.

Insulin resistance is also linked to persistent low-grade inflammation, which aids in the progression of atherosclerosis, the fundamental cause of IHD.

According to research, the TyG Index is highly linked to insulin resistance and persistent low-grade inflammation. The TyG Index is associated with inflammatory markers known to induce atherosclerosis, such as C-reactive protein (CRP) and interleukin-6 (IL-6). Furthermore, studies have shown that the TyG Index is a better predictor of insulin resistance and inflammation than traditional markers like fasting glucose and insulin.

#### Dyslipidemia and Lipotoxicity

Dyslipidemia, characterized by elevated levels of triglycerides and low-density lipoprotein cholesterol (LDL-C) and decreased levels of high-density lipoprotein cholesterol (HDL-C), is a major risk factor for IHD. Dyslipidemia promotes the development of atherosclerosis by increasing the formation of atherogenic lipoproteins and promoting lipid accumulation in macrophages.

Studies have shown that the TyG Index is strongly associated with dyslipidemia and lipotoxicity. The TyG Index is positively correlated with triglyceride levels and the ratio of triglycerides to HDL-C, which are both established markers of dyslipidemia. Furthermore, the TyG Index has been shown to be a better predictor of dyslipidemia and lipotoxicity than traditional markers such as total cholesterol and LDL-C.

#### **OXIDATIVE STRESS AND ENDOTHELIAL DYSFUNCTION**

Oxidative stress and endothelial dysfunction are fundamental pathophysiological mechanisms underlying the development of atherosclerosis and IHD. An imbalance between reactive oxygen species (ROS) and antioxidant defenses causes oxidative damage to lipids, proteins, and DNA in oxidative stress. Endothelial dysfunction is characterized by impaired endothelial function, which results in reduced vasodilation and increased adhesion of leukocytes and platelets.

According to research, the TyG Index is closely linked to oxidative stress and endothelial dysfunction. The TyG Index is positively connected with oxidative stress indicators such as malondialdehyde (MDA) and 8-hydroxydeoxyguanosine (8-OHdG), both of which are indications of lipid and DNA oxidative damage. Furthermore, studies have shown that the TyG Index is a better predictor of oxidative stress and endothelial dysfunction than traditional markers like fasting glucose and insulin.

## VII. LIMITATIONS AND SOURCES OF BIAS IN STUDIES INVESTIGATING THE TYG INDEX AND ISCHEMIC HEART DISEASE RISK

Studies investigating the association between the Triglyceride Glucose (TyG) Index and Ischemic Heart Disease (IHD) risk have shown promising results. However, like all observational studies, there are limitations and potential sources of bias that need to be considered when interpreting the findings.

#### **REVERSE CAUSATION**

One of the potential sources of bias in studies investigating the association between the TyG Index and IHD risk is reverse causation. Reverse causation occurs when the exposure (in this case, the TyG Index) is actually a consequence of the outcome (in this case, IHD) rather than the other way around. For example, individuals with undiagnosed or pre-existing IHD may have elevated TyG Index levels due to altered glucose and lipid metabolism associated with the disease rather than the TyG Index being a cause of IHD.

## SELECTION BIAS

Selection bias is another potential source of bias in research studying the relationship between the TyG Index and IHD risk. When the study population is not typical of the broader population, or when there are discrepancies between the exposed and unexposed groups, selection bias arises. For example, if the research group already has a high risk of IHD, the link between the TyG Index and IHD risk may be overstated.

## **CONFOUNDING**

Another possible source of bias in research studying the relationship between the TyG Index and IHD risk is confounding. Confounding happens when a third variable is linked to both the exposure and the outcome, and the influence of the exposure on the outcome is muddled as a result. For example, because smoking is a recognised risk factor for IHD and may be linked with increased

TyG Index values, omitting to account for smoking in the analysis may result in an overestimation of the connection between the TyG Index and IHD risk.

#### MEASUREMENT ERROR

Measurement error is a potential source of bias in studies investigating the association between the TyG Index and IHD risk. Measurement error can occur due to inaccuracies in the measurement of the exposure (in this case, the TyG Index) or the outcome (in this case, IHD). For example, if the TyG Index is measured using an assay with poor precision or accuracy, the estimated association between the TyG Index and IHD risk may be biased.

#### VIII. CONCLUSION

The Triglyceride Glucose (TyG) Index has emerged as a promising predictor of ischemic heart disease (IHD) risk. Multiple population-based studies have demonstrated a strong and independent association between elevated TyG Index levels and increased risk of IHD, even after controlling for traditional risk factors such as age, sex, BMI, and lipid profile. The TyG Index has also shown superiority over established risk prediction models, such as the Framingham Risk Score and the SCORE system, in predicting IHD risk in various populations. The underlying mechanisms linking TyG Index to IHD risk are complex and likely involve various pathways such as insulin resistance, endothelial dysfunction, and chronic inflammation. Basic science research has provided insights into these mechanisms, and further research is needed to fully understand the underlying pathophysiology. Although there are limitations and potential sources of bias in observational studies investigating the association between the TyG Index and IHD risk, the consistent and strong association observed across multiple studies suggests that the TyG Index may have clinical utility as a screening tool for IHD risk. However, further research is required to establish causality and to evaluate the potential impact of incorporating the TyG Index into clinical practice guidelines for IHD risk assessment and management. In conclusion, the TyG Index has emerged as a promising and novel predictor of IHD risk and represents a potential avenue for improving risk assessment and prevention of this prevalent and deadly cardiovascular disease.

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