

SHORT EDITORIAL

Integrating Insulin Resistance and Coronary Artery Disease Severity: Will Triglyceride-Glucose Index Be the Easiest Way?

Frederico Toledo Campo Dall'Orto,^{1,3} Flávia Bittar Brito Arantes,^{2,3} Remo H. M. Furtado,^{3,4} Pedro G. M. de Barros e Silva³

Hospital Maternidade e Pronto Socorro Santa Lúcia,¹ Poços de Caldas, MG – Brazil

Universidade Federal de Uberlândia,² Uberlândia, SP – Brazil

Brazilian Clinical Research Institute,³ São Paulo, SP – Brazil

Instituto do Coração (Heart Institute) do Hospital das Clínicas da Faculdade de Medicina da USP,⁴ São Paulo, SP – Brazil

Editorial referring to the article: Triglyceride-Glucose Index: Evaluation as a Potential New Risk Marker for SYNTAX Score in Acute Coronary Syndrome

Insulin resistance (IR) is a complex metabolic abnormality associated with genetic and environmental factors, which begins with low glucose metabolism in tissues, particularly in muscle, liver, and adipocytes, with consequent stimulation of pancreatic beta cells to increase insulin production and release.¹⁻³ Accumulation of lipids in a variety of tissues, including muscle, liver, and pancreas, contributes to this process in a phenomenon known as “lipotoxicity.”² As IR increases, it stimulates hyperinsulinemia, and this negative cycle perpetuates a metabolic disorder that is a main cause of cardiovascular diseases. In addition, insulin also acts on lipid metabolism, increasing lipid synthesis in liver and adipose cells, in addition to turning off the release of triglycerides (TG) and fatty acids in adipose and muscle tissues.¹

Several tests are used to identify IR, such as the oral glucose tolerance test, insulin dosage, and the hyperinsulinemic-euglycemic clamp (HIEC), which is considered the gold standard.³ However, HIEC is complex and time-consuming, which limits its widespread use in clinical practice. Currently, the most widely used test to assess IR is the homeostasis model assessment of insulin resistance (HOMA-IR), which has several limitations including lack of standardization (e.g., variations in laboratory, patients using antidiabetic drugs, low body mass index), calculation based on fasting parameters (which may not be representative of the entire day), and assumptions about IR that are not totally true (e.g., the assumption that IR is proportional to insulin levels and is

similar in the liver and peripheral tissues, without considering variation in beta cell function).^{3,4} Recently, a new marker of IR has been designed, which is the triglyceride-glucose (TyG) index that predicts the risk of IR, diabetes, and cardiovascular disease. The TyG index is calculated by multiplying the TG value by the serum glucose level, in mg/dl, and dividing the result by 2. The TyG index is a non-invasive, low-cost marker for cardiovascular risk stratification. Since IR can be related to the development of more extensive coronary disease, this marker could also be useful to this evaluation.

The Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) score was developed with the aim of assessing anatomical characteristics and guiding the decision on the best myocardial revascularization method in patients with coronary artery disease (CAD).^{5,6} Its classification considers the complexity of coronary lesions, categorized as low (SYNTAX score 0 to 22), intermediate (SYNTAX score 23 to 32), and high complexity (SYNTAX score 33 or more). The pivotal SYNTAX trial⁶ demonstrated that, in cases with low SYNTAX score, there was no difference between percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG), whereas, among patients with high SYNTAX score, CABG was superior to PCI regarding the study's primary endpoint (death, myocardial infarction, stroke, or need for repeat revascularization).

In the current issue of this journal, the article “Triglyceride-Glucose Index: Evaluation as a Potential New Risk Marker for SYNTAX Score in Acute Coronary Syndrome”⁷ aimed to evaluate the association of the TyG index and the SYNTAX score in patients with acute coronary syndrome (ACS). It was an observational,

Keywords

Insulin; Insulin Resistance; Coronary Artery Disease; Triglycerides; Triglyceride-Glucose Index.

Mailing Address: Frederico Toledo Campo Dall'Orto

Hospital Maternidade e Pronto Socorro Santa Lúcia. Avenida Vereador Edmundo Cardillo, 3003. Postal code: 37706-106. Poços de Caldas, MG – Brazil
E-mail: ftcdomed@yahoo.com

DOI: <https://doi.org/10.36660/ijcs.20240215>

retrospective, single-center study that evaluated 214 patients with ACS, hospitalized in the intensive care unit between January and April 2022. In the sample, 44.9% of the patients had history of CAD, and 42.1% had diabetes. Most patients had low SYNTAX score (65.4%), whereas 24.3% had intermediate, and 10.3% had high SYNTAX scores. The mean TG values were 155.79 ± 109.69 mg/dL, and blood glucose levels were 141.4 ± 75.98 mg/dL. There was no difference in the TyG index between the groups of patients without obstructive CAD versus those undergoing PCI or CABG or in relation to which coronary artery was affected.

Previous studies provided a rationale for the current study. D'Elia et al.⁴ demonstrated a positive association between the TyG index and the risk of arterial stiffening. A study conducted by Zhai et al. demonstrated that the TyG index was a predictor of in-hospital mortality in patients with cardiovascular disease and critical illness.⁸ Zhang et al.⁹ were the first to demonstrate, after variable adjustments, a U-shaped relationship between the TyG index and overall and cardiovascular mortality in patients with pre-diabetes and diabetes. Another trial by Wang et al.¹⁰ evaluated the relationship between the TyG index in patients with diabetes hospitalized with ACS and undergoing coronary angiography in relation to major adverse cardiovascular events (all-cause death, nonfatal myocardial infarction, and stroke) in a 3-year follow-up. The study demonstrated that the greater the TyG index in patients with diabetes and ACS, the higher the incidence of major adverse cardiovascular events. Finally, a systematic

review and meta-analysis conducted by Liang et al.¹¹ demonstrated that higher TyG index was associated with higher risk of CAD. Patients had more coronary stenosis, more plaque progression, and higher number of affected coronary arteries. Furthermore, patients with chronic coronary syndrome showed a trend towards increased major adverse cardiovascular events associated with higher TyG index values.¹¹

The increased prevalence of IR and its critical role in several diseases has created an urgent need to better understand the mechanisms underlying its pathogenesis, as well as to allow for earlier, more accessible, and more accurate diagnosis. Identifying scores and risk markers that are inexpensive, easy to perform, and that have greater prediction regarding the severity of patients who may develop atherothrombotic diseases is quite attractive and has an immediate impact on clinical practice. In this regard, it would be interesting to have a method that identifies IR prior to diabetes and identify cutoffs related to development of CAD. The TyG index appears to be a promising marker, capable of anticipating the identification of patients with a greater probability of developing diabetes and atherosclerosis. The study by Özmen et al. provides encouraging data in this regard, although some limitations should be acknowledged, such as the observational, single-center, and retrospective design, in addition to the small number of patients and short time to identify cardiovascular events. However, in view of the current literature, the TyG index may be a predictor of risk for the development and severity of CAD in the future.

References

- Li M, Chi X, Wang Y, Seterrahmane S, Xie W, Xu H. Trends in Insulin Resistance: Insights Into Mechanisms and Therapeutic Strategy. *Signal Transduct Target Ther*. 2022;7(1):216. doi: 10.1038/s41392-022-01073-0.
- James DE, Stöckli J, Birnbaum MJ. The Aetiology and Molecular Landscape of Insulin Resistance. *Nat Rev Mol Cell Biol*. 2021;22(11):751-71. doi: 10.1038/s41580-021-00390-6.
- Gayoso-Diz P, Otero-González A, Rodríguez-Alvarez MX, Gude F, García F, De Francisco A, et al. Insulin Resistance (HOMA-IR) Cut-Off Values and the Metabolic Syndrome in a General Adult Population: Effect of Gender and Age: EPIRCE Cross-Sectional Study. *BMC Endocr Disord*. 2013;13:47. doi: 10.1186/1472-6823-13-47.
- D'Elia L, Masulli M, Rendina D, Iacone R, Russo O, Zarrella AF, et al. Predictive Role of Triglyceride-Glucose Index and HOMA Index on Development of Arterial Stiffening in Non-Diabetic Men. *Nutr Metab Cardiovasc Dis*. 2024;34(11):2464-71. doi: 10.1016/j.numecd.2024.07.005.
- Bundhun PK, Sookharee Y, Bholee A, Huang F. Application of the SYNTAX Score in Interventional Cardiology: A Systematic Review and Meta-Analysis. *Medicine*. 2017;96(28):e7410. doi: 10.1097/MD.00000000000007410.
- Serruys PW, Morice MC, Kappetein AP, Colombo A, Holmes DR, Mack MJ, et al. Percutaneous Coronary Intervention versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease. *N Engl J Med*. 2009;360(10):961-72. doi: 10.1056/NEJMoa0804626.
- Özmen M, Arikan E, Ozel F, Ardahanlı I. Triglyceride-Glucose Index: Evaluation as a Potential New Risk Marker for SYNTAX Score in Acute Coronary Syndrome. *Int J Cardiovasc Sci*. 2024;37:e20240096. doi:10.36660/ijcs.20240096.
- Zhai G, Wang J, Liu Y, Zhou Y. Triglyceride-Glucose Index Linked to In-Hospital Mortality in Critically Ill Patients with Heart Disease. *Rev Cardiovasc Med*. 2022;23(8):263. doi: 10.31083/j.rcm2308263.
- Zhang Q, Xiao S, Jiao X, Shen Y. The Triglyceride-Glucose Index is a Predictor for Cardiovascular and All-Cause Mortality in CVD Patients with Diabetes or Pre-Diabetes: Evidence from NHANES 2001-2018. *Cardiovasc Diabetol*. 2023;22(1):279. doi: 10.1186/s12933-023-02030-z.
- Wang L, Cong HL, Zhang JX, Hu YC, Wei A, Zhang YY, et al. Triglyceride-Glucose Index Predicts Adverse Cardiovascular Events in Patients with Diabetes and Acute Coronary Syndrome. *Cardiovasc Diabetol*. 2020;19(1):80. doi: 10.1186/s12933-020-01054-z.
- Liang S, Wang C, Zhang J, Liu Z, Bai Y, Chen Z, et al. Triglyceride-Glucose Index and Coronary Artery Disease: A Systematic Review and Meta-Analysis of Risk, Severity, and Prognosis. *Cardiovasc Diabetol*. 2023;22(1):170. doi: 10.1186/s12933-023-01906-4.

