Type of the Paper (Research Article)

Insulin Resistance and Severity of Coronary Lesions in Patients with Acute Coronary Syndrome

Samiha M. Gaballah[1]*, Khaled A. El-khashab[1], Haitham Soliman[1], Noha Khalifa[1], Gomaa Abdelrazeik[1], Mahmoud Elmallwany[1]

[1] Cardiology Department, Faculty of Medicine, Fayoum University, Fayoum, 63514 Egypt.

*Correspondence: Samiha M. Gaballah, Sms12@fayoum.edu.eg, Tel: (002) 01000167037.

Received: 21 October, 2024 Reviewed: 2 February, 2025
Accepted: 20 May, 2025 Published online: 26 June 2025

Abstract:

Introduction: Insulin resistance (IR) has been identified as an independent risk factor for atherosclerosis and an increased likelihood of coronary artery disease (CAD) in both diabetics and non-diabetics.

Aim of the study: To assess the relation between IR and CAD severity.

Subjects and Methods: A cross-sectional study included one hundred patients who presented with ACS, then Coronary angiography was performed at the cardiology department of Fayoum University in 2022. Blood samples for insulin level were taken. IR was estimated utilizing the homeostatic model assessment index of IR (HOMA-IR) and the TYG index. Finally, Coronary angiography and severity calculation using the Gensini Scoring system.

Results: There was no significant disparity in Genseni level among HOMA-IR levels & TYG index levels.

Conclusions: Gensini score for CAD severity is not the best to correlate with IR indices, and better to use another scoring system for CAD severity.

Keywords: Insulin resistance; severity of CAD; Gensini.

1. Introduction

Adults are more likely to experience cardiovascular events if they have hypertension, dyslipidaemia, or are overweight. In addition to the risk posed by each cardiovascular risk factor, those with metabolic syndrome are 3 times more likely to develop CVD than individuals without the

syndrome, according to the WHO definition of metabolic syndrome.

IR and the onset of cardiovascular disease have been linked in several ways. In particular, one of those processes occurs in the endothelium of blood vessels. Vasodilation and endothelin-mediated vasoconstriction are counteracting factors that, in a healthy state, dictate vascular tone. Blood vessels constrict rather than dilate in an IR situation because the NO signaling pathway is less activated and the endothelin pathway is more activated [1].

Obesity, impaired glucose tolerance, as well as early onset of T2DM are all risk factors for CAD, and they all contribute to the acceleration of atherosclerosis in insulin-resistant conditions.

The activation of the hexosamine biosynthetic route is another way that excessive glucose impacts vascular parameters. This process leads to an increase in glucosamine synthesis, which in turn decreases endothelial NO generation. Advanced glycation end products (AGEs) are formed when free amino acids react with excess glucose, which happens in hyperglycemia. Interactions between AGEs and the endothelial receptor for AGE (RAGE) are associated with distinct procoagulant alterations, in accordance with the available research. In particular, the anticoagulatory protein C pathway is not activated because this interaction decreases thrombomodulin activity. Enhanced tissue factor activity is another procoagulatory effect of this ligand-receptor interaction that activates coagulation factors IX as well as X via factor VIIa binding. In animal and human models, there is evidence that AGEs deactivate NO in a manner that is dependent on the dose [2].

2. Subjects and Methods

2.1 Subjects

100 patients at the cardiology department of Fayoum University in 2022

Inclusion criteria

Cross cross-sectional study included 100 patients admitted with acute coronary

syndrome, who then underwent coronary angiography.

Exclusion criteria

Cases with a history of myocardial infarction, revascularization with PCI or prior cardiac operation, heart failure, insufficient medical history or steroid use,

Patients were subjected to medical history, examination, and 12-lead electrocardiogram., Trans thoracic echocardiography.

HOMA-IR

Based on the clinical data collected by Mono-bind and in line with the existing literature, the following ranges have been assigned: plasma glucose levels, fasting insulin levels. Diabetic adult Hypoglycemic 0.7-25 µg/ml.

IR was evaluated utilizing HOMA-IR, which was computed utilizing the following formula: The formula is calculated by multiplying the serum insulin concentration (mU/L) with the baseline plasma glucose (mg/dL) and dividing by 405.

chronic kidney disease GFR less than sixty ml/min/1.73 m2; and chronic liver disease (Platelet count < 160,000, Albumin less than 3.8 milligram per deciliters, AST > ALT (in non-alcoholic etiologies), INR > 1.2, Bilirubin greater than 1.5 milligrams per deciliters) were excluded.

2.2 Methods

TyG index

Formula-based: Ln (Fasting triglycerides (mg/dL) x Fasting blood glucose (mg/dL)/2).

Coronary angiography and severity calculation using Genseni Scoring system:

The following steps were utilized for calculating the GSs [3] (**Figure 1**):

1) establish the degrees of concentric or eccentric luminal narrowing (2% to 25% stenosis, 26% to 50% stenosis, 51% to 75% stenosis, 76% to 99% stenosis, 100% stenosis are assigned scores of 1, 2, 4, 8, 16, 32, correspondingly)
2) The importance of each segment of the coronary arteries in supplying blood to the heart is determined by its specific coefficient. As an illustration, the coefficient for the left main coronary artery is 5, the coefficient for the proximal

segment of the left anterior descending coronary artery is 2.5, the coefficient for the proximal segment of the circumflex artery is 2.5, the coefficient for the mid-segment is 1.5, the coefficient for the RCA is 1.0, the coefficient for the distal segment is 0.5, and the coefficients for the remaining segments are 1.0, 2.5, 1.0, and 0.5, in addition to 0.5, accordingly.

3) Calculating the final GS involves multiplying the narrowing score by the coefficient, which results in the final GS being the total of all variable segment scores.

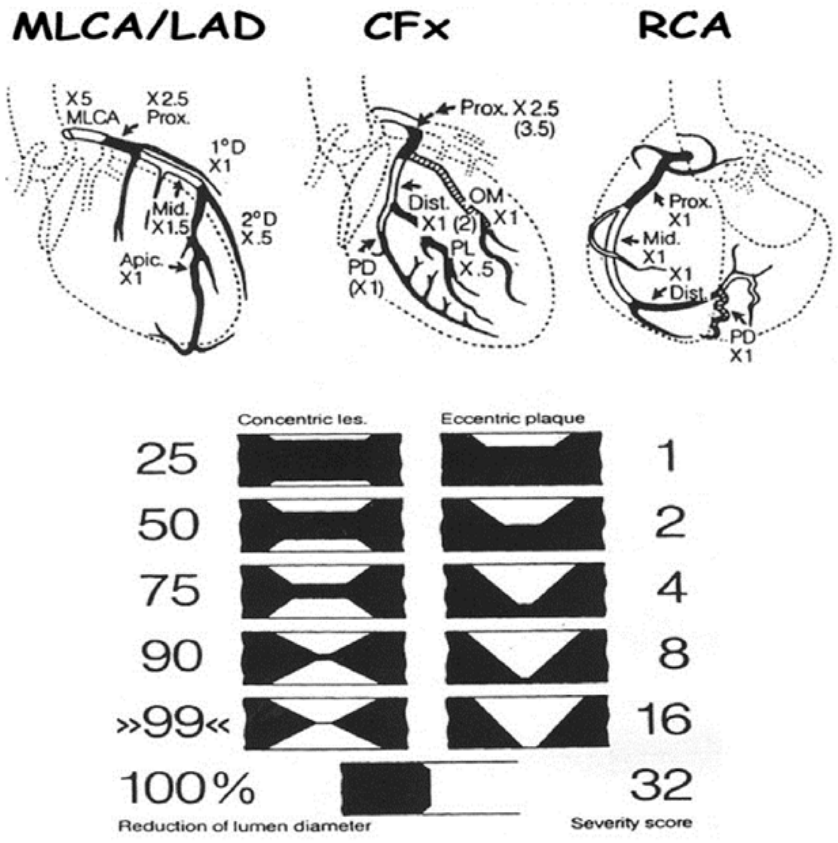

Figure 1: Gensini score calculation LCX: Circumflex; RCA: Right coronary artery; MLCA: Main left coronary artery; LAD: Left anterior descending artery.

2.3 Statistical analysis

All these data were collected, and statistical analysis was performed for these variants. Data analysis was carried out with SPSS 22 for Windows 7 (SPSS Inc., Chicago, IL, USA). Quantitative parametric data is typically measured by standard

deviations, while qualitative data is typically presented in the form of percentages and numbers for simple descriptive analysis. The study's quantitative data were subjected to a one-sample Kolmogorov-Smirnov test to ensure normalcy in each group before being subjected to inferential statistical testing. In cases where the data is quantitative and nonparametric, more than two independent groups can be compared using the Kruskal-Wallis test. To compare two separate groups, the Mann-Whitney test is employed. To compare multiple qualitative groups when working with qualitative data, the chi-square test is employed. To examine the relationship between variables, one can use the bivariate Spearman correlation test. The significance level was determined by a P-value below 0.05.

3. Results

Table 1 illustrates that there was a significant positive correlation with *p*-value 0.01, 0.001, <0.001, <0.001 and <0.001 amongst levels of TyG index and each of LDL, cholesterol, triglyceride, fasting glucose, and fasting insulin levels. In addition, a significant negative correlation between the TyG index and HDL level was found with a *p*-value of 0.01. An increase in LDL, cholesterol, triglyceride, fasting glucose, and fasting insulin levels and a decrease in HDL will be associated with an increase in the TyG index level. Although other variables did show some association, it was not significant.

Table 1: Correlation between HOMA-IR with other study variables among the study group.

Variables		HOMA-IR	
		R	***P*-value**
Age (years)		0.05	0.6
BMI (kg/m^2)		-0.03	0.7
Lipid profile	LDL	0.09	0.4
	HDL	-0.08	0.4
	Cholesterol	0.16	0.1
	Triglyceride	**0.27**	**0.007**

Glucose profile	Fasting glucose	**0.64**	**<0.001**
	Fasting insulin (mlU/L)	**0.95**	**<0.001**
	Genseni score	-0.08	0.4
	TyG index	**0.58**	**<0.001***

Table 2 demonstrated that there was no significant distinction in Genseni levels among HOMA-IR levels.

Table 2: Correlation among the TyG index with other study variables among the study group.

Variables		**TyG index**	
		R	***P*-value**
Age (years)		-0.03	0.7
BMI (kg/m^2)		-0.01	0.9
Lipid profile	LDL	0.25	**0.01**
	HDL	-0.24	**0.01**
	Cholesterol	0.33	**0.001**
	Triglyceride	0.75	**<0.001**
Glucose profile	Fasting glucose	**0.64**	**<0.001**
	Fasting insulin (mlU/L)	**0.95**	**<0.001**
	Genseni score	-0.08	0.4

There was no statistically significant difference with *p*-value <0.05 in Genseni level between HOMA-IR levels Nd Tyg Index levels (**Table 3, Figure 2).**

Table 3: Comparisons of the Genseni score in different HOMA-IR and TyG index levels among cases.

Variables		Gensini score		*P*-value
		Median	IQR	
HOMA-IR	Normal (< 2)	46	30	0.6
	High (≥2)	48	44	
TyG index	Normal (< 4)	---	---	---
	High (≥4)	47	41	

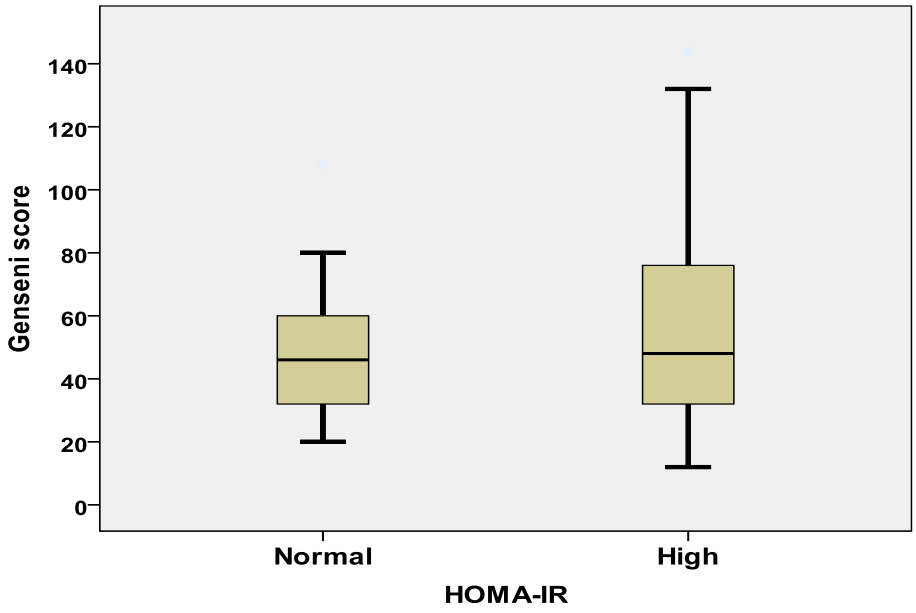

Figure 2: Gensini score value in different HOMA IR levels.

4. Discussion

No statistically significant distinction was observed in Genseni levels among HOMA-IR levels and TYG index levels despite a strong correlation between IR parameters and the incidence of CAD in our study, another study found a significant correlation among these parameters and coronary severity as measured by the Genseni score because our used method for evaluation CAD with the percentage of lumen occlusion and the site of occlusion but assessment of the arterial wall with

another method like IVUS may give more detailed early data about the prostheses of atherosclerosis even before development of significant lumen occlusion.

A comparable study was conducted by P S Mukund in 2013, which agreed with our results involving patients with T2DM who had coronary angiography for the assessment of CAD. The severity of CAD was measured using the modified Gensini Score, and the HOMA-IR showed a correlation with each other. It was found that there was a strong correlation between the severity of CAD and the log HOMA-IR in diabetic persons (r = 0.303, *P* = 0.009) [4]. The research conducted by Rehab I. Yaseen in 2021 also disagreed that they utilized insulin levels as an indicator of IR, revealing a significant positive linear association among insulin levels and the Gensini score. The accuracy of insulin levels as a predictor for CAD is 96.6%, with a sensitivity of 96.7% and a specificity of 75% at a cutoff predictive value of <25.8 mIU/L [5].

Through the utilization of non-insulin-based IR metrics such as the TyG Index, the Metabolic Score for IR, as well as the Triglycerides/High-Density Lipoprotein Cholesterol ratio, Zhenguo Wu investigated the incidence and severity of coronary artery disease and its severity in the year 2022. The values of the TyG index, TG/HDL-C, as well as METS-IR, were significantly greater among the participants in the study who had CAD as compared to the control group. This study discovered that the groups that had high Gensini Scores (GS) had considerably higher levels of TG/HDL-C and METS-IR in contrast to the groups that did not have high Gensini score, which disagree with our study [6].

Among those examined by Jamshid Vafaeimanesh, Insulin resistance (HOMA-IR> 2.5) was positive in 49.3%) patients and negative in 50.7%) patients. Hence, the correlation between IR and CAD was not statistically significant (*P* =0.9), which disagrees with our finding (7).

In the investigation carried out by Strisciuglio in 2020, IR was assessed using the homeostasis model assessment of HOMA-IR. The severity of coronary atherosclerosis was measured using the SYNTAX score (SS). Results showed that IR is associated with more severe and extensive coronary atherosclerosis in diabetics. The HOMA index has the potential to serve as an independent marker of three-vessel disease at CA, which disagrees with our results, and may be due

to the use of a different measure of coronary severity [8].

5. Conclusion

Gensini score for CAD severity is not the best to correlate with IR indices, and better to use another scoring system for CAD severity.

Ethical committee approval: The study was authorized by the institutional ethics committee in the Faculty of Medicine, Fayoum University, Egypt. Ethical approval was obtained with approval number D232.

Competing interests: There are no conflicts of interest for the authors.

Funding: No particular grants from public, commercial, or nonprofit funding organizations were given to this research.

AI declaration statement: None declared.

References

1. Feldstein C, Julius S. The complex interaction between overweight, hypertension, and sympathetic overactivity. J Am Soc Hypertens. 2009;3(6):353–65.
2. Brownlee M. Lilly Lecture 1993. Glycation and diabetic complications. Diabetes. 1994;43(6):836–41.
3. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol. 1983;51:606.
4. Shetty P, Kamath P, Manjrekar P, Unnikrishnan B. Correlation of severity of coronary artery disease with insulin resistance. N Am J Med Sci. 2013;5(11):611–4. doi:10.4103/1947-2714.120799
5. Yaseen RI, Beda MY, Ibrahim FA. Correlation between severity of coronary artery disease and insulin resistance in diabetic patients. Egypt J Hosp Med. 2021;84(1):2084–9. doi:10.21608/ejhm.2021.180360
6. Wu Z, Cui H, Li W. Comparison of three non-insulin-based insulin resistance indexes in predicting the presence and severity of coronary artery disease. Front Cardiovasc Med. 2022;9:918359. doi:10.3389/fcvm.2022.918359
7. Vafaeimanesh J, Parham M, Norouzi S. Insulin resistance and coronary artery disease in non-diabetic patients: Is there any correlation? Caspian J Intern Med. 2018;9(2):121–6. doi:10.22088/cjim.9.2.121
8. Strisciuglio T, Izzo R, Barbato E. Insulin resistance predicts severity of coronary atherosclerotic disease in non-diabetic patients. J Clin Med. 2020;9(7):2144. doi:10.3390/jcm9072144.