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Evaluating Insulin Resistance As A Prognostic Indicator of Mortality in Diabetic and Non Diabetic Patients With Myocardial Infarction

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Abstract

Aims and Objective: To determine the predictive value of Insulin Resistance as measured by HOMA-IR & TyG index with one-month survival outcome in Patients with Myocardial Infarction

Materials and Method: This study was Baseline Cross sectional Observational study of 165 patients admitted with Myocardial Infarction between November 2022 and February 2024. Brief history was taken and baseline demographic details were noted. Fasting Blood sample was collected & HbA1c, TyG Index and HOMA IR, was estimated. Patients were divided into Diabetics and Non diabetics based on history & HbA1c. Patients were followed up after 1 month to know the survival outcome.

Results: The average age of 1 month survivors in the study is 54.56± 11.20 years. In contrast, the average age of non-survivors is significantly higher, at 66.91± 9.39 years. In assessing BMI for predicting short-term mortality due to acute MI, at a cut-off of 26.4 kg/m², sensitivity was 90.90%, with p-value 0.042, indicating statistical significance. In the analysis of HOMA-IR for predicting short-term mortality, at a cut-off of 8.55 specificity was 94.80%, with p-value 0.03, suggesting statistical significance. In the analysis of the TyG index for predicting short-term mortality, at a cut off of 8.9, sensitivity was 72.70%, while specificity was 68.80%,and the p-value was 0.429, suggesting the results were not statistically significant.

Conclusion: Individuals aged ≥65 years, A HOMA IR of ≥8.55 , BMI> 26.4Kg/m^2 was associated with a very high risk of mortality, presenting a critical predictor of adverse outcomes.

Keywords: HOMA IR, Insulin resistance , Mortality, Myocardial Infarction, TyG Index

Introduction

Acute myocardial infarction (AMI) is a leading cause of death in many countries, claiming over a million lives annually in the United States alone, with a prevalence of nearly 3 million cases(1). Atherosclerotic plaque rupture and thrombosis are the primary causes, while other factors include coronary artery embolism, cocaine-induced vasoconstriction, and vasospasm(2). Obesity, Insulin Resistance (IR), and type 2 diabetes mellitus are increasing and are powerful risk factors for Ischemic Heart Disease(3). Insulin resistance, a common feature of diabetes, exacerbates myocardial and microvascular dysfunction, contributing to larger infarct sizes and poorer clinical outcomes in diabetic patients experiencing myocardial infarction(9).

The Homeostatic Model Assessment (HOMA) index is a simple and inexpensive Insulin Resistance marker. It was recently proven to be feasible for evaluating IR in STEMI patients when compared to euglycemic hyper-insulinemic clamp which is the gold standard(4).

In addition, the Triglyceride Glucose (TyG) index is derived from fasting triglyceride (TG) and fasting

plasma glucose (FPG) levels, and it has been suggested as a reliable surrogate marker of insulin resistance (IR). Several studies have shown a positive correlation between the TyG index and cardiovascular risk factors, including systemic arterial stiffness, carotid atherosclerosis, coronary artery calcification, coronary artery stenosis, symptomatic coronary artery disease, hypertension, and metabolic syndrome(5). Furthermore, growing evidence has indicated that the TyG index is related to morbidity and mortality of cardiovascular disease in the general population and many patient cohorts, including patients with and without diabetes (6)

This is a cross sectional study which aims to evaluate the association between Insulin Resistance as measured using HOMA IR & TyG Index and the short-term outcomes in patients of Acute Myocardial Infarction with & without diabetes mellitus in the form of mortality.

Materials & Methods

A cross sectional observational study was conducted in a tertiary care hospital in Western India, following the approval by the Institutional Review Board (Ethical committee) of the hospital. The patients included during a study period between November 2022 and February 2024.We included the patients admitted in the hospital under Department of Medicine diagnosed with Myocardial infarction above 20 years of age of either sex after obtaining an informed consent.

Following data are collected from the patient,

1. Demographic data (Name, age, geographical location)

2. Body mass index (kg/m^2)

The following data are obtained from the fasting blood sample collected,

1) HbA1c *(Reference Range : < 6%)*

2) HOMA IR= Fasting insulin (U/ml) X fasting glucose (mg/dl)/405 [or fasting glucose (mmol/l)/22.5] *(Reference Range : <1.9mU/ml)*

3) TyG Index= Ln fasting Triglyceride(mg/dL) × Fasting plasma glucose(mg/ dL) /2 *(Reference Range : 4-8)*

The patients were followed up after a month to record their mortality status.

The objective was to correlate TyG index, HbA1c and HOMA IR with short term (1 month) mortality in patients admitted with Myocardial infarction. The records of patients were analyzed, and baseline demographic data were extracted. Fasting Blood sample was collected to analyze laboratory parameters such as fasting glucose, HOMA IR, HbA1c, TyG index. The patients were followed up after one moth to record their mortality status.

According to literature, the prevalence of IHD from previous study was found to be 10% and with absolute error of 4% the sample size came as 165.

Methods of estimation

Table 1 Method for estimation of various Tests

Parameter	Method
Fasting Glucose	Colorimetry(Glucose-hexokinase)
Triglycerides	Colorimetry (Glycerol 3 phosphate oxidase)
Insulin	Electrochemiluminescence Immunoassay
HbA1c	High performance liquid Chromatography (HPLC)

Statistical methods – The distribution of incidence of various qualitative characteristics was shown as n (% of cases), while the distribution of various quantitative characteristics was shown using Mean ± Standard deviation across two study groups. The statistical comparison of continuous variables across two groups

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was done using independent sample 't' test after confirming the underlying normality assumption. The significance of difference of categorical variables across two groups was tested using Chi-square test or Fisher's exact probability test. P-values less than 0.05 was considered to be statistically significant. All statistical analysis was done using SPSS 25.

Results

In this study, 165 patients admitted with Myocardial Infarction, were included and were followed up after one month and their mortality status was noted(2022-2024).

Demography

Table 2 Demography and One Month Mortality

Demography	P value
Gender	0.483
Age	<0.0001
BMI	0.062

Based on 1 month survival outcome between genders, it was observed that no gender was predisposed to mortality.

The average age of 1-month survivors in the study is 54.56± 11.20 years. In contrast, the average age of non-survivors is significantly higher, at 66.91±9.39 years. The difference in ages between survivors and non-survivors is statistically significant (P=0.0001)

The BMI of non-survivors was higher than who survived 1 month. But this difference was just short of being statistically significant.

Biochemical parameters:

Table 3 Comparison of average Fasting Glucose, Fasting insulin, TyG Index, HOMA-IR in Survivors &Non survivors

Parameter	Survivor (N=154)		Non-survivors (N=11)		Total (N=165)		p
	Mean	SD	Mean	SD	Mean	SD	
HbA1C%	7.09	2.01	7.16	1.98	7.09	2.01	0.906
Fasting Insulin (uIU/ml)	9.78	6.03	23.15	21.14	10.67	8.51	<0.0001
TyG Index	9.08	0.53	9.22	0.58	9.09	0.53	0.42
HOMA IR	3.7	3.11	10.8	9.13	4.17	4.15	<0.0001

HOMA IR & Fasting Insulin was significantly raised in participants who did not survive after a month than in participants who survived.

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Table 4 ROC Analysis for each test to determine cut off with significance

Test	AUC	Std. Error	p-value	95% CI (Lower–Upper)	Sensitivity	Specificity	Cut-off
HbA1C%	0.503	0.098	0.971	0.310 – 0.696	45.5%	68.8%	7.1%
HOMA-IR	0.696	0.116	0.030	0.469 – 0.922	63.6%	94.8%	8.55
TyG Index	0.571	0.087	0.429	0.401 – 0.742	72.7%	68.8%	8.9
BMI (kg/m²)	0.684	0.076	0.042	0.535 – 0.833	90.9%	51.3%	26.4

In the ROC curve analysis for HbA1C% concerning short-term mortality due to acute MI, the area under the curve (AUC) was 0.503, indicating poor predictive ability. But In the analysis of HOMA-IR ,the area under the curve (AUC) was 0.696, indicating moderate predictive ability. At a cutoff of 8.55, sensitivity was 63.60%, indicating it correctly identified 63.60% of short-term mortality cases, while specificity was 94.80%, indicating it accurately identified 94.80% of non-mortality cases. The p-value was 0.03, suggesting statistical significance.

In the analysis of the TYG index for predicting short-term mortality due to acute MI, the area under the curve (AUC) was 0.571, suggesting limited predictive ability. At a cut off of 8.9, sensitivity was 72.70%, indicating it correctly identified 72.70% of short-term mortality cases, while specificity was 68.80%, indicating it accurately identified 68.80% of non-mortality cases. The p-value was 0.429, suggesting the results were not statistically significant.

In assessing BMI for predicting short-term mortality due to acute MI, the area under the curve (AUC) was 0.684, indicating moderate predictive ability. At a cutoff of 26.4 kg/m², sensitivity was 90.90%, suggesting it correctly identified 90.90% of short-term mortality cases, while specificity was 51.30%. The p-value was 0.042, Indicating statistical significance.

Table 5 Relative Risk Assessment for factors associated with mortality in MI

Risk Factor	Number	Number in mortality	RR	95% CI	P
DM v/s Non DM	77	5	0.95	0.3 to 2.99	0.93
Diabetic with poor glycaemic control v/s good control	36	4	4.55	0.53 to 38.9	0.16
Female v/s male	41	4	1.52	0.46 to 4.95	0.48
Age≥65 v/s < 65 years	39	6	3.87	1.25 to 12.4	0.01
TyG >8.55 v/s ≤ 8.55 TyG	144	10	1.45	0.19 to 10.8	0.79
HOMA IR ≥8.5 v/s <8.5	15	7	17.5	5.78 to 52.9	<0.0001

In the assessment of mortality risk factors associated with myocardial infarction (MI), certain factors stood out significantly in influencing outcomes. Notably, individuals aged ≥65 years showed a significantly increased risk of mortality (RR 3.87, 95% CI 1.25-12.4, p=0.01), underscoring the impact of age on MI

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outcomes. Furthermore, a HOMA IR of ≥8.55 was associated with a very high risk of mortality, presenting a critical predictor of adverse outcomes (RR 17.5, 95% CI 5.78-52.9, p<0.0001).

On the other hand, several factors did not show a statistically significant association with mortality. Diabetes mellitus (DM) versus non-DM indicated no significant difference in mortality risk (RR 0.95, 95% CI 0.3-2.99, p=0.93). Similarly, diabetics with poor glycemic control compared to those with good control showed an elevated risk, though it was not statistically significant (RR 4.55, 95% CI 0.53-38.9, p=0.16). The analysis also found that being female compared to male and having a higher TYG index both presented increased risks that were not statistically significant (Female vs. Male: RR 1.52, 95% CI 0.46-4.95, p=0.48; TYG >8.5: RR 1.45, 95% CI 0.19-10.8, p=0.79).

Discussion

The cross sectional observational study included 165 patients admitted with Myocardial Infarction over a period of 2 years (2022-2024). The study participants were evaluated for Insulin Resistance using HOMA IR & TyG Index to study the impact of insulin resistance on one month mortality in both Diabetics and Non diabetics. Based on the literature review, it is well-established that hypertension, dyslipidemia, obesity, impaired glucose tolerance, coronary artery disease, insulin resistance, and hyperinsulinemia are associated and collectively referred to as the insulin resistance syndrome or 'syndrome X'. Among these disorders, the connection between atherosclerosis and insulin resistance is least established. Insulin resistance is a well-known factor in the development of dyslipidemia and diabetes, but it is not routinely measured. The HOMA IR model illustrates how glucose and insulin interact in the body to predict the levels of both when insulin resistance and beta-cell function are taken into account. Also, studies have shown that the TyG index not only reflects glycemic control but also serves as a good predictor of insulin resistance. We studied the effect on insulin resistance as a predictor of one month mortality in these patients.

Demography:

Gender: Based on 1 month survival outcome between genders it was observed that no gender was predisposed to mortality.

But, In a study by Samaneh Mozaffarian et al on short- and long-term survival rates following myocardial infarction and its predictive factors, using national registry data, a high incidence rate of MI was found in men compared to women (72.4% vs. 27.6%)(7).

Age:

The average age comparison of 1 month survival was statistically significant (<0.0001) of mean age of patients who succumbed within a month being 66.91±9.39 in contrast to the rest being 54.56±11.20

A study by Al-Ali SA et al. 2022 (8) describing the association between insulin resistance (IR), assessed by the Homeostatic Model Assessment (HOMA) index and TyG index, and short-term outcomes in non-diabetic patients with acute ST-segment elevation myocardial infarction (STEMI), the mean age of 61 participants was 54.6 ± 11.6 years

A study by S. Capewell et al on Measuring outcomes: one month survival after acute myocardial infarction in Scotland revealed odds of dying within 30 days effectively doubled for each decade of age (odds ratio compared with patients aged under 55: 2.3 aged 55-64, 4.4 aged 65-74, 8.2 aged 75-84, 12.0 aged 85 plus).

A study on Risk Factors for In-Hospital Mortality from Cardiac Causes After Acute Myocardial Infarction by Gabriel Vasconcelos Oliveira (9) advanced age along with systolic Blood pressure and female gender were significant risk factors for death within 30 days after STEMI.

BMI & 1-month mortality prediction: In our study at a cut-off of 26.4 kg/m², sensitivity was 90.90%, suggesting it correctly identified 90.90% of short-term mortality cases

However, was no statistical correlation of body mass index with one month survival outcome (p=0.062)

In line to our study, Kragelund et al. (10)showed that abdominal obesity appeared to be an independent predictor of mortality in men admitted with AMI.

On the other hand Angerås et al. (11)examined associations between BMI and mortality in patients with acute coronary syndromes and found that the risk for mortality decreased with increasing BMI up to 35 kg/m2 and then increased. Also, Khalid et al. (12) observed a similar results & demonstrated that patients who were overweight or obese before heart failure

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development had lower mortality compared with normal BMI patients.

Biochemical findings :

In our study we enrolled patients admitted with Myocardial Infarction irrespective of their glycaemic status and grouped them as diabetes and non-diabetes based on history and HbA1c levels. There were 88 diabetic and 77 non diabetics in our study.

Insulin Resistance & 1-month survival outcome prediction:In the present study the patients were followed up for one month it is observed that patients who died after one month also showed statistically significant levels of HOMA IR & insulin. Thus we can imply that HOMA IR & insulin levels can be used as predictive markers of mortality in myocardial infarction. These findings are in agreement with a study conducted by Stubbs and colleagues with a median follow-up time of 3 years, indicated that insulin resistance upon admission appears to be a predictor of future cardiac death in non-diabetic patients with acute coronary syndrome. The study suggested that evaluating the insulin resistance index upon admission may be more effective than measuring admission plasma glucose in these patients..(13)

Similar results were observed by Al-Ali SA et al. who investigated the association between insulin resistance (IR), assessed by the Homeostatic Model Assessment (HOMA) index and TyG index, and short-term outcomes in non-diabetic patients with acute ST-segment elevation myocardial infarction (STEMI) & the findings suggest that IR is significantly associated with poor outcomes in acute STEMI patients, particularly in terms of EF < 55% and 4-week mortality. (8)

Mortality risk factors associated with Myocardial Infarction (MI)

Studies in the past have found several factors which increase the risk of mortality in myocardial infarction. We tried to predict the one month mortality using the parameters studied and we found that:

1. Individuals aged ≥65 years showed a significantly increased risk of mortality.
2. A HOMA IR of ≥8.55 was associated with a very high risk of mortality, presenting a critical predictor of adverse outcomes. Diabetics with poor glycemic control compared to those with good control showed an elevated risk, though it was not statistically significant.
3. The analysis also found that being female compared to male and having a higher TyG index both presented increased risks that were not statistically significant.
4. We found that at a BMI cutoff of 26.4 kg/m², the sensitivity was 90.90%, indicating that it correctly identified 90.90% of short-term mortality cases.

These findings highlight the importance of age and certain metabolic indices like Insulin Resistance as measured by HOMA IR & TyG Index, and BMI as key factors influencing mortality risk in Myocardial Infarction , guiding therapeutic strategies and risk management accordingly.

Our findings suggest that measuring the HOMA IR can predict the short term mortality in patients who suffered Myocardial Infarction. Thus, improving insulin resistance in these patients can improve the prognosis of Myocardial infarction.

Conclusion

This study reveals that HOMA IR is closely associated with one month survival outcome after Myocardial Infarction. Additionally, HOMA IR along with demographic factors like Age, BMI are associated with high risk of mortality and maybe used as predictors of adverse outcomes.

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