

# POSITIVE PREDICTIVE VALUE OF GRACE SCORE IN PREDICTING OBSTRUCTIVE CORONARY ARTERY DISEASE IN NSTEMI PATIENTS TAKING CORONARY ANGIOGRAPHY AS GOLD STANDARD

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## ABSTRACT:

### INTRODUCTION:

*The Global Registry of Acute Coronary Events (GRACE) risk score is widely utilized to predict major adverse cardiovascular events (MACE) in patients with non-ST-elevation myocardial infarction (NSTEMI). However, its effectiveness in prognostic stratification remains uncertain. This study aims to evaluate the positive predictive value of the GRACE score in identifying obstructive coronary artery disease (CAD) among NSTEMI patients in the local population. Early diagnosis and treatment of obstructive CAD using this approach may contribute to reducing the morbidity and mortality associated with the condition.*

### AIMS & OBJECTIVE:

*To determine the Positive Predictive Value (PPV) of GRACE score in predicting obstructive CAD in NSTEMI patients taking coronary angiography as gold standard.*

### MATERIAL & METHODS:

*This Cross-sectional study was conducted at Cardiology Department, Mayo Hospital, Lahore from August 1, 2023 to January 31, 2024. Total 135 patients fulfilling the selection criteria were enrolled. Patients with NSTEMI having suspected obstructive CAD on GRACE score underwent coronary angiography and true positive and true negative were labeled upon it.*

### RESULTS:

*In this study, 135 patients with NSTEMI were enrolled. Among these patients, 81(60.0%) were males, while 54(40.0%) were females. Age range in this study was from 30 to 70 years with mean age of 49.19±13.221 years. Mean BMI of patients was 27.6±5.74 kg/m<sup>2</sup>. Mean duration of NSTEMI was 8.4±2.5 hours. Mean GRACE score was 95.89±21.15. According to case outcome, 85(63.0%) were true positive and 50(37.0%) were false positive.*

### CONCLUSION:

*The GRACE score demonstrates moderate predictive value in identifying obstructive coronary artery disease (CAD) in patients with NSTEMI. While it can serve as a useful screening tool, its effectiveness in assessing the extent of CAD remains limited.*

**KEY WORDS:**

*Acute Myocardial Infarction, NSTEMI, GRACE score, Angiography, Coronary Artery Disease.*

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**INTRODUCTION:**

Due to the significant narrowing or occlusion of the coronary artery, NSTEMI occurs which leads to reduced blood flow to the myocardium which results into myocardial injury. The extent of coronary obstruction varies among NSTEMI patients, resulting in diverse management approaches and an increased risk of adverse long-term outcomes.<sup>1</sup> NSTEMI typically arises from coronary artery narrowing, transient or partial occlusion, or micro-embolization of a thrombus and/or atheromatous material. It is characterized by elevated circulating cardiac enzyme levels without ST elevation. In contrast, unstable angina does not lead to a significant rise in cardiac biomarkers.<sup>2</sup>

CAD is one of the major causes of premature mortality globally while ACS is the most common clinical manifestation of it. ACS encompasses a diverse clinical spectrum, with significant variations in patient outcomes and hospital courses. Therefore, management guidelines emphasize individualized risk stratification to assess prognosis and optimize patient care.<sup>3</sup>

Effective risk stratification of ACS patients, particularly those with non-ST-elevation myocardial infarction (NSTEMI), is essential for optimizing management due to their variable prognosis and heightened risk of MI recurrence and rehospitalization. Several risk stratification tools have been developed, including the Global Registry of Acute Coronary Events (GRACE) score, the Framingham Risk Score, and the Thrombolysis in Myocardial Infarction (TIMI) score.<sup>3</sup>

Clinical practice guidelines by American and European recommend the TIMI or GRACE score use for risk stratification to assess short and mid-term outcomes.<sup>4-6</sup> There is limited literature available about these

scores for predicting the extent and severity of CAD. Accurately assessing coronary anatomy before invasive procedures like coronary angiography could significantly impact clinical decision-making, aiding in the timely and appropriate selection of therapeutic strategies and interventions.<sup>6</sup>

Such an approach can help identify patients who require more aggressive management to improve outcomes while also preventing unnecessary invasive procedures in those with non-obstructive CAD.<sup>6</sup> Ishaq et al. conducted a study and found that the positive predictive value of GRACE score in predicting obstructive coronary artery disease in NSTEMI patients was 91.1%.<sup>7</sup> In another study, positive predictive value of GRACE score in predicting obstructive coronary artery disease in NSTEMI patients was 34.1%.<sup>8</sup> In another study, positive predictive value of GRACE score in predicting obstructive coronary artery disease in NSTEMI patients was 77%.<sup>9</sup>

The purpose of this study is to repeat in local population so that the positive predictive value of GRACE score in predicting obstructive coronary artery disease in NSTEMI patients could be determined in local population and it can be useful to diagnose and treat obstructive CAD resulting in less mortality and morbidity affiliated with this condition.

**OPERATIONAL DEFINITIONS:**

**NSTEMI:** It was defined as presence of chest pain >30minutes on rest, ST-segment elevation <1mm on ECG with troponin >100mIU, CK-MB >25mIU at time of presentation.

**Coronary artery disease on angiography:** It was defined as presence of >50% stenosis in one or more coronary arteries detected on coronary angiography.

**Coronary artery disease on GRACE score:** It was considered as likelihood if cutoff value of GRACE score was  $\geq 84$ .<sup>10</sup>

Positive predictive value of GRACE score in predicting obstructive CAD in NSTEMI patients: It was calculated by the following formula.

True Positive: Patients found to have obstructive CAD on GRACE score later found to be true on coronary angiography.

False Positive: Patients found to have obstructive CAD on GRACE score later found to be false on coronary angiography.

#### **MATERIALS AND METHODS:**

This Cross-sectional study was carried-out in the department of Cardiology, Mayo Hospital, Lahore from August 1, 2023 to January 31, 2024. Total 135 patients fulfilling the selection criteria were enrolled. Patients with NSTEMI having suspected obstructive CAD on GRACE score underwent coronary angiography and true positive and true negative were labeled upon it.

We included patients of both genders age ranging from 30-70 years with suspected obstructive CAD suffering from NSTEMI as per operational definition. We excluded patients who were diagnosed recurrent NSTEMI or previous STEMI, valvular heart or neurological disease, renal failure (creatinine >1.2mg/dl), liver disease (AST >40IU, ALT >40IU, bilirubin >5mlU).

#### **DATA COLLECTION PROCEDURE:**

Study participants who presented in the cardiology department fulfilling the inclusion/exclusion criteria were informed about the research. Informed consent was taken who were enrolled in the study. Patients with NSTEMI having suspected obstructive CAD on GRACE score underwent coronary angiography and true positive and true negative were labeled. Study participants underwent coronary angiography according to the guidelines. Explanatory variables like place of residence, socio-economic status, diabetes (FBS >126mg/dl), hypertension (BP >140/90mmHg), family history of CAD, and smoking (>5 packs/year) were also noted.

#### **DATA ANALYSIS PROCEDURE:**

Data analysis was done using SPSS v25.0. Numerical variables i.e. age, BMI, GRACE score and duration of NSTEMI were presented by Mean  $\pm$  S.D. Categorical variables i.e. positive predictive value of

obstructive CAD on angiography and GRACE score, place of residence, socio-economic status, diabetes, family history of CAD, hypertension and smoking were presented as frequencies and percentages. Data was stratified for gender, age, BMI, duration of NSTEMI, place of residence, socio-economic status, diabetes, hypertension, family history of CAD and smoking to deal with effect modifiers. Post stratification, PPV was calculated.

#### **RESULTS:**

Among 135 participants, there were 54(40%) females and 81(60%) males. Age ranging from 30-70 years with mean age of  $49.19 \pm 13.221$  years. Mean BMI of participants was  $27.6 \pm 5.74$  kg/m<sup>2</sup>. It was observed that 48(35.6%) participants had normal BMI, while 67(49.6%) and 20(14.8%) were overweight and obese respectively. Among 135 patients, 62(45.9%) had diabetes mellitus, 54(40.0%) had hypertension, 56(41.5%) were smokers, 38(28.1%) were urban resident and 97(71.9%) were rural resident. According to socio-economic status distribution, 48(43.0%) had low income, while 52(38.5%) and 25(18.5%) patients had middle and high income respectively. Mean duration of NSTEMI was  $8.4 \pm 2.5$  hours. According to duration of NSTEMI distribution, 42(31.1%) had  $\leq 5$  hours duration, while 93(68.9%) had >5 hours. Mean GRACE score was  $95.89 \pm 21.15$ . According to case outcome, 111(82.2%) had likelihood obstructive CAD positive on GRACE score, while 119(88.1%) had likelihood obstructive CAD positive on angiography (Table-1).

According to presence of likelihood obstructive CAD on GRACE score vs. angiography, GRACE score had 97.2% PPV in detecting likelihood obstructive CAD (Table-2).

Stratification of presence of obstructive CAD on GRACE score vs. angiography with respect to gender, age, BMI, diabetes, hypertension, smoking, residence, socio-economic status and duration of NSTEMI was done and had high PPV values in each strata (Table-3 to 11).

| Table-1: Distribution of various parameters. |             |           |            |
|--|-------------|-----------|------------|
|  |             | Frequency | Percentage |
| Gender                                       | Male        | 81        | 60.0       |
|  | Female      | 54        | 40.0       |
| Age groups                                   | 30-50 years | 60        | 44.4       |
|  | 51-70 years | 75        | 55.6       |
| Body mass index                              | Normal      | 48        | 35.6       |
|  | Overweight  | 67        | 49.6       |
|  | Obese       | 20        | 14.8       |
| Diabetes mellitus                            | Yes         | 62        | 45.9       |
| Hypertension                                 | Yes         | 54        | 40.0       |
| Smoking                                      | Yes         | 56        | 41.5       |
| Residence                                    | Urban       | 38        | 28.1       |
|  | Rural       | 97        | 71.9       |
| Socio-economic status                        | Low         | 58        | 43.0       |
|  | Middle      | 52        | 38.5       |
|  | High        | 25        | 18.5       |
| Duration of NSTEMI                           | ≤5 hours    | 42        | 31.1       |
|  | >5 hours    | 93        | 68.9       |
| Obstructive CAD on angiography               | Positive    | 119       | 88.1       |
|  | Negative    | 16        | 11.9       |
| Obstructive CAD on GRACE score               | Positive    | 111       | 82.2       |
|  | Negative    | 24        | 17.8       |

| Table-2: Presence of obstructive CAD on GRACE score vs. angiography. |                                |          |       |       |
|--|--------------------------------|----------|-------|-------|
| Likelihood Obstructive CAD on GRACE score                            | Obstructive CAD on Angiography |          | Total | PPV   |
|  | Positive                       | Negative |       |       |
| Positive   | 108                            | 3        | 111   | 97.2% |
| Negative   | 11                             | 13       | 24    |       |
| <b>Total</b>   | 119                            | 16       | 135   |       |

| Table-3: Stratification of obstructive CAD on GRACE score vs. angiography with respect to gender. |   |                                |          |       |        |
|---|---|--------------------------------|----------|-------|--------|
| Gender  | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV    |
|   |   | Positive                       | Negative |       |        |
| Male  | Positive                                  | 66                             | 3        | 69    | 95.6%  |
|   | Negative                                  | 7                              | 5        | 12    |        |
|   | <b>Total</b>                              | 73                             | 8        | 81    |        |
| Female  | Positive                                  | 42                             | 0        | 42    | 100.0% |
|   | Negative                                  | 4                              | 8        | 12    |        |
|   | <b>Total</b>                              | 46                             | 8        | 54    |        |

**Table-4: Stratification of obstructive CAD on GRACE score vs. angiography with respect to age.**

| Age groups  | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV   |
|-------------|---|--------------------------------|----------|-------|-------|
|             |   | Positive                       | Negative |       |       |
| 30-50 years | Positive                                  | 46                             | 2        | 48    | 95.8% |
|             | Negative                                  | 6                              | 6        | 12    |       |
|             | <b>Total</b>                              | 52                             | 8        | 60    |       |
| 51-70 years | Positive                                  | 62                             | 1        | 63    | 98.4% |
|             | Negative                                  | 5                              | 7        | 12    |       |
|             | <b>Total</b>                              | 67                             | 8        | 75    |       |

**Table-5: Stratification of obstructive CAD on GRACE score vs. angiography with respect to BMI.**

| Body mass index | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV    |
|-----------------|---|--------------------------------|----------|-------|--------|
|                 |   | Positive                       | Negative |       |        |
| Normal          | Positive                                  | 38                             | 2        | 40    | 95.0%  |
|                 | Negative                                  | 5                              | 3        | 8     |        |
|                 | <b>Total</b>                              | 43                             | 5        | 48    |        |
| Overweight      | Positive                                  | 55                             | 1        | 56    | 98.2%  |
|                 | Negative                                  | 5                              | 6        | 11    |        |
|                 | <b>Total</b>                              | 60                             | 7        | 67    |        |
| Obese           | Positive                                  | 15                             | 0        | 15    | 100.0% |
|                 | Negative                                  | 1                              | 4        | 5     |        |
|                 | <b>Total</b>                              | 16                             | 4        | 20    |        |

**Table-6: Stratification of obstructive CAD on GRACE score vs. angiography with respect to diabetes mellitus.**

| Diabetes mellitus | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV   |
|-------------------|---|--------------------------------|----------|-------|-------|
|                   |   | Positive                       | Negative |       |       |
| Yes               | Positive                                  | 48                             | 1        | 49    | 97.9% |
|                   | Negative                                  | 5                              | 8        | 13    |       |
|                   | <b>Total</b>                              | 53                             | 9        | 62    |       |
| No                | Positive                                  | 60                             | 2        | 62    | 96.7% |
|                   | Negative                                  | 6                              | 5        | 11    |       |
|                   | <b>Total</b>                              | 66                             | 7        | 73    |       |

**Table-7: Stratification of obstructive CAD on GRACE score vs. angiography with respect to hypertension.**

| Hypertension | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV   |
|--------------|---|--------------------------------|----------|-------|-------|
|              |   | Positive                       | Negative |       |       |
| Yes          | Positive                                  | 44                             | 1        | 45    | 97.7% |
|              | Negative                                  | 4                              | 5        | 9     |       |
|              | <b>Total</b>                              | 48                             | 6        | 54    |       |
| No           | Positive                                  | 64                             | 2        | 66    | 96.9% |
|              | Negative                                  | 7                              | 8        | 15    |       |
|              | <b>Total</b>                              | 71                             | 10       | 81    |       |

**Table-8: Stratification of obstructive CAD on GRACE score vs. angiography with respect to smoking.**

| Smoking | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV   |
|---------|---|--------------------------------|----------|-------|-------|
|         |   | Positive                       | Negative |       |       |
| Yes     | Positive                                  | 48                             | 2        | 50    | 96.0% |
|         | Negative                                  | 5                              | 1        | 6     |       |
|         | <b>Total</b>                              | 53                             | 3        | 56    |       |
| No      | Positive                                  | 60                             | 1        | 61    | 98.3% |
|         | Negative                                  | 6                              | 12       | 18    |       |
|         | <b>Total</b>                              | 66                             | 13       | 79    |       |

**Table-9: Stratification of obstructive CAD on GRACE score vs. angiography with respect to residence.**

| Residence | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV    |
|-----------|---|--------------------------------|----------|-------|--------|
|           |   | Positive                       | Negative |       |        |
| Rural     | Positive                                  | 32                             | 0        | 32    | 100.0% |
|           | Negative                                  | 3                              | 3        | 6     |        |
|           | <b>Total</b>                              | 35                             | 3        | 38    |        |
| Urban     | Positive                                  | 76                             | 3        | 79    | 96.2%  |
|           | Negative                                  | 8                              | 10       | 18    |        |
|           | <b>Total</b>                              | 84                             | 13       | 97    |        |

**Table-10: Stratification of obstructive CAD on GRACE score vs. angiography with respect to socio-economic status.**

| SES    | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV    |
|--------|---|--------------------------------|----------|-------|--------|
|        |   | Positive                       | Negative |       |        |
| Low    | Positive                                  | 48                             | 2        | 50    | 96.0%  |
|        | Negative                                  | 4                              | 4        | 8     |        |
|        | <b>Total</b>                              | 52                             | 6        | 58    |        |
| Middle | Positive                                  | 42                             | 1        | 43    | 97.6%  |
|        | Negative                                  | 5                              | 4        | 9     |        |
|        | <b>Total</b>                              | 47                             | 5        | 52    |        |
| High   | Positive                                  | 18                             | 0        | 18    | 100.0% |
|        | Negative                                  | 2                              | 5        | 7     |        |
|        | <b>Total</b>                              | 20                             | 5        | 25    |        |

**Table-11: Stratification of obstructive CAD on GRACE score vs. angiography with respect to duration of NSTEMI.**

| Duration of NSTEMI | Likelihood Obstructive CAD on GRACE score | Obstructive CAD on Angiography |          | Total | PPV    |
|--------------------|---|--------------------------------|----------|-------|--------|
|                    |   | Positive                       | Negative |       |        |
| ≤5 hours           | Positive                                  | 35                             | 0        | 35    | 100.0% |
|                    | Negative                                  | 1                              | 6        | 7     |        |
|                    | <b>Total</b>                              | 36                             | 6        | 42    |        |
| >5 hours           | Positive                                  | 73                             | 3        | 76    | 96.1%  |
|                    | Negative                                  | 10                             | 7        | 17    |        |
|                    | <b>Total</b>                              | 83                             | 10       | 93    |        |

## DISCUSSION:

The aim of our research was to evaluate the positive predictive value (PPV) of the GRACE score in predicting severe CAD in patients with NSTEMI. Our findings indicated that the GRACE score demonstrated moderate accuracy in distinguishing obstructive CAD. The optimal cutoff value for the GRACE score was identified as  $\geq 84$ , which emerged as an independent predictor of obstructive CAD. Several other studies have reported similar correlations between the GRACE score and the extent of CAD, both across the full spectrum of acute coronary syndrome and specifically in NSTEMI patients.

By Roy SS et al.<sup>10</sup> who carried out a research and enrolled 205 NSTEMI participants and found a positive correlation between the GRACE score and the severity of CAD. Additionally, it highlighted the superior performance of the GRACE score over the TIMI score in predicting CAD severity. A similar advantage of the GRACE score over the TIMI score was observed in a comparative analysis conducted by Roy SS et al., which also focused on predicting CAD severity.<sup>11</sup>

In a study by Hammami R et al.<sup>9</sup> involving 238 research participants presented with NSTEMI, examined the correlation between severity of CAD and GRACE score. The study found moderate accuracy in predicting obstructive CAD, with an AUC of 0.599. At a cutoff value of 120, the GRACE score demonstrated a sensitivity of 57% and a specificity of 61.8%. However, the study observed a weak correlation between the GRACE score and the CAD severity. As a result, they assessed that GRACE score has stronger predictive value for distinguishing obstructive CAD, it is less effective in

prediction of extent of CAD severity.

Rahman ME et al.<sup>12</sup> also studied 50 participants of NSTEMI and found a positive and major correlation between the CAD and GRACE score. Additionally, at a cutoff value of 135, the GRACE score demonstrated a sensitivity of 82.4% and a specificity of 75.8% in predicting severe CAD. In another research by Cakar MA et al.<sup>13</sup> divided 245 participants of NSTEMI into low-, intermediate, and high-risk groups, finding a crucial correlation between CAD severity and GRACE score.

In a research by Mahmood M et al.<sup>14</sup> found that both the TIMI and GRACE scores had strong predictive value in assessing the extent of the disease. Similar findings have been reported in other researches across the spectrum of ACS.<sup>15-17</sup> One of the largest research by dos Santos Viana M et al.<sup>18</sup> has discussed the relationship of severity of anatomical CAD and GRACE score before angiogram. The research enrolled 733 patients, 81% of whom had obstructive CAD. The AUC for the GRACE score in predicting severe disease was 0.65, and at a cutoff value of 103, it showed a sensitivity of 67% and a specificity of 50%. Additionally, the GRACE score exhibited a weak correlation of 0.36 with the SYNTAX score. Based on these findings, the study recommended that the use of the GRACE score be limited to prognostic assessments.

## CONCLUSION:

The GRACE score demonstrates moderate predictive value in identifying obstructive coronary artery disease in patients presenting with NSTEMI. While it can serve as a useful screening tool, its effectiveness in assessing the extent of CAD remains limited.

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