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Correlation of Clinical Risk Scores with Angiographic Extent of Coronary Artery Disease in Patients with Non ST-Elevation Myocardial Infarction/Unstable Angina and Their Effects on 6 Month Outcomes.

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BACKGROUND*:Patients with non ST elevation acute myocardial infarction(NSTEMI) and unstable angina (UA) have a wide variation in their disease severity.Thus,risk stratification is essential for adequate clinical decision-making. The accuracy of the GRACE, TIMI and PURSUIT scores in predicting coronary disease with NSTEMI/UA has not been established.*

AIM*:The aim of the study was to correlate clinical risk scores with angiographic extent of coronary artery disease(CAD) in patients with NSTEMI and UA and their sixmonth outcomes.*

METHODOLOGY: *It is a single centre, prospective study conducted ina tertiaryhealth care centre atTirupati, Indiabetween June 2016 to May 2017.Four hundred patients with UA and NSTEMI were evaluated for presence of 6 clinical predictors and 3 risk scores were calculated.Major adverse cardiovascular events (MACE) at six month follow up were studied and correlated with clinical predictors and risk scores.*

RESULTS: *Mean TIMI score was 3.04±0.97, mean PURSUIT score was 10.23±1.72 and mean GRACE score was 105.37±25.78.Mean Syntax score(SS) was 14.08±10.13.Pearson correlation analysis showed a moderate positive correlation of TIMI risk score with SS(r: 0.326;p<0.01), whereas PURSUIT(r:0.212;p<0.01)andGRACE(r:0.223;p<0.01) risk scores showed weak positive correlation. Significant association between SS and biomarker elevation (p=0.001), congestive heart failure(p=0.02) and ≥2 anginal episodes within 24 hrs(p=0.002) was found.There was no significant correlation between SS with MACE events(p=NS). The results showed statistically significant correlation between GRACE score and MACE (p=0.04). Out of the 6 clinical predictors only CHF(congestive heart failure) showed statistically significant correlation with MACE.*

CONCLUSION*: Patients with higher scores in TIMI, GRACE and PURSUIT scoring systems had significantly greater angiographic disease, when compared to those with low scores. Presence of CHF, >2 anginal episodes within 24 hrs and presence of elevated biomarker are stronger predictors of extent of coronary artery disease.TIMI score had more correlation with SS. Presence of CHF and higher GRACE risk score carries a significant correlation with MACE at 6 month follow up.*

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I. Introduction

Cardiovascular diseases have emerged as a major health burden in developing countries and are a subject of great concern for its significant contribution to mortality.[1]Acute coronary syndrome is a major cause of cardiovascular morbidity and mortality for which timely diagnosis and appropriate therapy is of paramount importance to improve clinical outcomes.[2]Unstable angina (UA) and Non ST elevation acute myocardial infarction (NSTEMI) patients account for approximately 2 million to 2.5 million hospital admissions annually worldwide.[3]Clinical predictors like duration of chest pain, age, cardiac biomarker positivity, congestive heart failure (CHF) help in predicting high risk group. Similarly, clinical risk scores like Thrombolysis in Myocardial Infarction (TIMI) score, Platelet Glycoprotein IIb-IIIa in Unstable Angina, Receptor Suppression Using Integrilin Therapy (PURSUIT) score and Global Registry of Acute Coronary Events (GRACE) scores have established role in risk stratification and predicting prognosis.[4,5]Specific subgroups of patients identified by clinical features, electrocardiographic findings and/or cardiac (or vascular) markers are at higher risk of adverse outcomes for whom angiography is advisable as there is high probability of significant coronary artery disease. In this regard we sought to evaluate suitable risk score and clinical predictors that best correlate with the severity of angiographic extent of coronary artery disease in patients presenting with NSTEMI/UA which helps in early risk stratification for efficient and aggressive treatment to prevent adverse long term clinical events.

II. Aim & Objectives

To calculate TIMI, PURSUIT andGRACE risk scores in patients presenting with NSTEMI/UA, to determine the angiographic extent of coronary artery disease by Syntaxscore(SS) in these patients and to correlate with angiographic severity andto study the major adverse cardiovascular events (MACE) at six month follow up.

III. Materials And Methods

It is a single centre,prospective study conducted in a tertiary care teaching institute. Four hundred patientspresenting with NSTEMI/UA with age of >18 yearsadmitted between June 2016 toMay 2017were included in the study.Post coronary artery bypass graft(CABG)/post percutaneous coronary intervention(PCI), contrast allergy, bleeding diathesis, collagen vascular diseases, pregnant women and patients not willing to participate in the study were excluded. Institutional Ethical committee reviewed the study protocol and cleared it. Informed consent was taken from each patient. Baseline clinical and demographic characteristics were obtained. UA was defined as angina or its equivalent with atleast one of the 3 features: being severe, or occurring with a crescendo pattern (more severe, prolonged, or frequent than previous)occurring at rest or minimal exertions & usually lasting >20 minute.[6]Patients with unstable angina who had evidence of myocardial necrosis on the basis of elevated cardiac serum markers such as Troponin T or I or Creatine kinase-Muscle Brain (CK-MB) enzyme were diagnosed as NSTEMI.Cardiovascular risk factors like hypertension, diabetes mellitus, and smoking were recorded. A detailed physical examination was performed including past medical history. Complete blood count, lipid profile and serum creatinine levels were obtained. Hypertension was identified based on prior prescription of antihypertensive drugs or when blood pressure exceeded 140/90 mmHg in at least three measurements. Dyslipidemia and diabetes were defined as prior prescription of anti-hyperlipidemic and anti-diabetic medications or total cholesterol level > 200 mg/dL and fasting glucose levels above 126 mg/dL, respectively. Comprehensive two-dimensional transthoracic echocardiography, was performed. Measurements were performed according to the American Society of Echocardiography guidelines. Emphasis was placed on the following clinical data, presence of 3 or more risk factors, presence of 2 or more episodes of pain in previous 24 hours, use of aspirin within prior week,age ≥ 65 years, presence of elevated cardiac enzymes andCHF(congestive heart failure). TIMI, GRACE & PURSUIT scores were calculated. All patients underwent diagnostic coronary angiography (CAG). All obstructive lesions were visualized in two orthogonal views and lesion with a visual diameter stenosis of 50% was considered significant. Assessment of angiographic lesion severity was done by SS. The SS has been described and validated previously.[7]Thiswas calculated by using dedicated software that integrates the number of lesions with their specific weighting factors based on the amount of myocardium distal to lesion and the morphological features of each lesion.The SS was divided into threetertiles: low- risk tertile is ≤ 22, intermediate risk 22-32 and high-risk tertile is > 32. All the patients were followed up at 6 months for major adverse cardiovascular events.

IV. Statistical Analysis

Data was collected in pre-designed Microsoft excel spread sheets. Data was presented as mean and standard deviation for continuous variables and numberswith percentages for categorical variables. Differences observed were tested for significance with Unpaired student's t-test for continuous data and with Chi-square test for categorical data.Relationship between angiographic severity and different scoring systems was performed by Pearson's correlation test. The interpretation of correlation coefficient was done as weak (positive/negative) if<0.3, moderate if 0.3 to 0.7 and strong if>0.7. All the statisticalanalysis was performed on Microsoft Excel spread sheets and Statistical Package for Social sciences (SPSS) for Microsoft Windows,Version 20.0.IBM,Chicago,USA. A p-value of ≤0.05 was considered as significant.

V. Results

The mean age of the patients was 56.37±10.43 years. Majority of the patients were in the age group 51-60 yrs. Out of 400 patients, 257(64.5%) were males. In the study population, 220(55%) had NSTEMI and 180(45%) had UA.In the study population 212(53%) were hypertensive,155(38.7%) were diabetics,120(30%)were smokers,41(10.2%) had dyslipidemia,32(8%) were tobacco chewers(Table1). Majority of the patients presented in NYHA class II. Mean ejection fraction was 56.36±8.95. Among the study population,61 had ≥3 risk factors,88 had age ≥ 65yrs, 15 presented with CHF,32 were already using aspirin within the last week, 342 had >2 anginal episode within 24 hours and 220 had biomarker elevation(Table 2). Risk scores were calculated for all the patients in the study group. Mean TIMI score was 3.04±0.97, mean PURSUIT score was 10.23±1.72 and mean GRACE score was 105.37±25.78.All the patients in the study group underwent CAG and Syntax score was calculated. Mean Syntax score was 14.08±10.13.Table 3 shows the comparision of the 3 the risk scores for angiographic extent of CAD. For all the 3 risk scoring systems, the high score patients had significantly greater extent of CAD than low score ones. Of all the patients, 32.5% had single

vessel disease, 20.8% had double vessel disease,17.5% had triple vessel disease and 29.3% had normal or insignificant disease.Left anterior descending artery was the most common diseased artery involved followed by left circumflex artery and right coronary artery. Left main artery was involved in 0.8 %.Depending on the disease burden, 191 patients underwent PCI,69 underwent CABG and 140 were on medical management. Pearson correlation analysis showed a positive correlation between TIMI and SS(r:0.326), PURSUIT and SS(r:0.212) GRACE and SS(r:0.223). There was a moderate positive correlation of TIMI risk score with SS whereas PURSUIT and TIMI risk scores showed weak positive correlation.Multiple regression analysis showed significant association between SS and biomarker elevation (p=0.001), CHF(p=0.02) and ≥2 anginal episodes within 24 hours(p=0.002)(Table 4).All the patients in the study group were followed up at 6 months and MACE were recorded. Out of 400 patients in the study group 1 patient was readmitted with unstable angina,8 with non-ST elevation myocardial infarction, 1 with ST-elevation myocardial infarction, 6 with stroke, 3 with bleeding manifestations,3 with CHF and 12 patients died.In this study we also aimed to assess the correlation between MACE and angiographic severity of CAD through SS. There was no significant correlation between SS with MACE events(p=0.873).We sought to find the relation between MACE and risk scores. The results showed statistically significant correlation between GRACE score and MACE(p=0.04).For the study population, MACE was correlated with clinical predictors.Out of the 6 clinical predictors only CHF showed statistically significant correlation with MACE.

VI. Discussion

Risk scores are simple prognostication scheme that categorize a patient's risk of death and ischemic events.In this study we tried to compare commonly used clinical risk scores and clinical predictors with the predictive value of angiographic severity in patients with NSTEMI and UA and correlated them with the MACE events at 6 month follow up. In a study by Huang et al.,[8] the prognostic value of the atherosclerotic burden determined using coronary scoring systems was explored and suggested that the prediction of atherosclerotic burden, as well as the risk for the patient, may have a prognostic significance. We stratified the patients into low and high risk category, and found that all patients with high risk scores have high disease burden on coronary angiogram. In our study risk scores were compared with angiographic severity determined by SS. A positive correlation was found between TIMI and SS (r: 0.326, p < 0.001), PURSUIT and SS (r:0.212, p<0.001) GRACE and SS (r:0.223, p<0.001). There was a moderate positive correlation of TIMI risk score with SS whereas PURSUIT and GRACE risk scores showed weak positive correlation. Our study showed that among the various clinical predictors of the severity,> 2 anginal episodes within 24 hours (p<0.001), biomarker elevation(p=0.002) and CHF(p=0.026) affectedSS significantly.A positive correlation between angiographic scores and troponin values indicate that these patients have an increased risk of poor outcome, which may be an additional benefit of the TIMI risk score. It suggests that all patients with high risk score should be treated with early invasive strategy in order to decrease the short and long term mortality. In a study by Gaurav Khandelwal et al,[9]they found GRACE score had better correlation with modified Gensini score and use of aspirin, age ≥ 65 years & presence of CHF were stronger predictors of higher modified Gensini score. In a study by Zhao et al.,[10] there was a significant reduction in combined cardiovascular events with patients with moderate and high TIMI risk score. Walsh et al.,[11] showed that in high-risk TIMI scores population, PCI can provide symptomatic and mortality benefit in elderly. Our study is in agreement with the study by Garcia et al.,[12] which showed that most of the low clinical risk patients had normal angiography or limited CAD, and high clinical risk patients had severe CAD and clear relations existed between TIMI risk score and angiography score in patients with NSTEMI. All the patients in the study group were followed up at 6 months and MACE were recorded. Out of the 400 patients in the study group, 1 patient was readmitted with UA, 8 with NSTEMI, 1 with STEMI, 6 with stroke, 3 with bleeding manifestations, 3 with CHF and 12 patients died. We found no significant correlation between SS and MACE(p=NS). There was a significant correlation between GRACE score and MACE (p=0.04). Our study is in accordance with the study by Pedro de AraújoGonçalves et al.,[13] in which they found GRACE score is superior to TIMI or PURSUIT risk scores and was best for predicting the risk of death or MI at 1 year after admission. Clinical predictors were correlated withMACEand only CHF showed significant correlation (p=0.04). Patients with heart failure usually have neurohumoral and inflammatory response, some of which are associated with atherosclerosis pathogenesis. High levels of inflammatory markers, especially high sensitive C-reactive protein, have been associated with left ventricular systolic dysfunction. Risk stratification is synonymous with prognosis determination. Management decisions in ACS should be based on a rapid and accurate assessment of risk. If the scores could better identify the presence of obstructive disease, they would identify patients to whom the invasive strategy would be more useful.

VII. Limitations

Firstly, sample size is small in number to generalize the results and it is asingle centre study. Secondly, sampling method was not random but rather purposive, so there is risk of selection bias. Third, because there was a male dominance in our study, the results may not be applicable in groups with female dominance.

VIII. Conclusion

Our study confirmed strong correlation between higher risk scores and severity of coronary artery disease assessed by SS. The higher scores in TIMI, GRACE and PURSUIT scoring systems had significantly greater angiographic disease, when compared to low scores. In TIMI score, each of the variable is given equal point. In this study, we found that presence of CHF, > 2 anginal episodes within 24 hours and presence of elevated biomarkers are stronger predictors of extent of coronary artery disease. Hence we recommend that these factors be given more weightage, when predicting angiographic extent of coronary artery disease. TIMI score had more correlation with SS.Higher GRACE risk score andpresence of CHFshowed a significant correlation with MACE at 6 month follow up. This study emphazises the usage of risk scores for stratifying patients and tailoringcare for each individual patient.

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Table1. Baseline characteristics

	SEX		TotaL (n=400)
	Male (n=257)	Female (n=143)	
Age	55.44±10.63	58.03±9.89	56.37±10.43
EF	55.84±9.15	57.28±8.55	56.36±8.95
S.creatinine	1.17±2.65	0.87±0.28	1.06±2.13
TC	161.19±45.41	156.67±47.33	159.46±46.09
LDL	94.67±31.49	96.29±37.46	95.25±33..71
Smoking	118	2	120
Diabetes mellitus	97	58	155
Hypertension	134	78	212
Dyslipidemia	30	11	41
Tobacco chewing	31	1	32

EF=Ejection fraction ; TC=total cholesterol ;LDL=low density lipoproteins

Table 2. Mean (± SD) values of angiographic parameters for the various risk scores by extent of CAD and number of vessels.

Risk score	No.of patients	Syntax score	Diseased	SVD	MVD
TIMI					
0-2	127	10.3±11.0	59	29	30
3-7	273	15.8±9.2	224	101	123
Total	400	14.0±10.1	283	130	153
PURSUIT					
<10	81	9.4±9.6	37	18	19
≥10	319	15.2±9.9	246	112	134
Total	400	14.0±10.1	283	130	153
GRACE					
<96	154	11.7±10.4	92	50	42
≥96	246	15.5±9.7	191	80	111
Total	400	14.0±10.1	283	130	153

SVD-single vessel disease ; MVD-multivessel disease

Table 3 .Mean (± SD) values of angiographic parameters for various clinical predictors by extent of CAD and number of vessels

	No.of patients	**Syntax score**	**SVD**	**MVD**
ASPIRIN USAGE				
Yes	32	19.9±7.2	8	24
No	368	13.5±10.1	122	131
CHF				
Yes	15	20.7±10.9	4	9
No	385	13.8±10.0	126	146
AGE				
<65	312	13.5±10.4	102	112
>65	88	15.8±8.6	28	43
RISK FACTOR				
>3	61	17.2±10.1	21	33
<3	339	13.5±102	109	122
ANGINA >2 EPISODES in 24 Hours				
Yes	342	14.8±10.1	108	149
No	58	9.2±8.3	21	6
BIOMARKER ELEVATION				
Yes	220	16.5±9.1	80	108
No	180	11.0±10.4	50	47

CHF=congestive heart failure; SVD-single vessel disease ; MVD-multivessel disease

Table 4. Multivariate regression analysis to assess determinants of Syntax score

VARIABLES	**Standardized Beta Regression Coefficients**	**p-value**
RF ≥3	0.076	0.113
AGE≥65	0.088	0.061
ASA_USE	0.087	0.077
> 2 ANGINA	0.147	0.002
BIOMARKER ELEVATION	-0.221	0.001
CHF	0.107	0.026

RF-Risk factors ; CHF- Congestive heart failure

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