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Original Article

Internal Medicine Section

Prediction of Angiographic Extent of Coronary Artery Disease on the Basis of Clinical Risk Scores in Patients of Unstable Angina

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ABSTRACT

Background: The correlation of clinical risk predictors and clinical risk scores: Thrombolysis in Myocardial Infarction (TIMI), Platelet Glycoprotein IIb-IIIa in Unstable Angina, Receptor Suppression Using Integrilin Therapy (PURSUIT) and Global Registry of Acute Coronary Events (GRACE) scores in Unstable Angina with angiographic extent of Coronary Artery Disease (CAD) is not known.

Aim: To know the correlation of clinical risk scores with angiographic extent of coronary artery disease.

Materials and Methods: This was a hospital based single centre, cross-sectional, observational, descriptive study conducted at a tertiary care teaching institute. One hundred and sixty patients with acute unstable angina were evaluated for presence of 9 clinical predictors and their 3 risk scores were calculated. All patients underwent coronary angiography. Correlation with Modified Gensini score and percentage stenosis in culprit artery was done.

Statistical Analysis: Data were summarized in the form of Mean, Standard Deviation and Proportions. Multiple linear regressions, Student's t-test and Pearson's coefficient 'r' were also used.

Results: Use of aspirin, age >= 65 years & presence of Congestive Heart Failure (CHF) were stronger predictors of Modified Gensini score. Presence of elevated enzymes and age >65 years were more significant predictors of percentage stenosis of culprit artery. GRACE score had better correlation with Modified Gensini score, PURSUIT score had more correlation with percentage stenosis in culprit artery.

Conclusion: Use of Aspirin, age >= 65 years, presence of CHF and presence of elevated enzymes are stronger predictors of extent of CAD. Hence we recommend that these factors be given more importance. GRACE and PURSUIT risk scores had more correlation with angiographic extent of CAD.

Keywords: Angiographic severity, GRACE score, Modified gensini score, PURSUIT score, TIMI score

INTRODUCTION

Unstable angina and Non ST elevation acute myocardial infarction patients account for approximately 2 million to 2.5 million hospital admissions annually worldwide [1]. The high risk unstable angina patients are at risk for death, myocardial infarction or recurrent ischemic events [2,3]. Angiography clearly predicts Major Adverse Cardiovascular Events (MACE) in unstable angina and helps in deciding revascularization [4]. Angiography is advisable only in high risk group who have more probability of significant coronary artery disease. Clinical predictors like duration of chest pain, age, cardiac biomarker positivity, ST segment depression in ECG, Congestive Heart Failure (CHF) - help in predicting high risk group. Similarly, clinical risk scores – 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 [5,6].

AIM OF STUDY

To determine the correlation of TIMI, PURSUIT and GRACE risk scores with angiographic extent of coronary artery disease and to predict the angiographic severity on the basis of various independent clinical predictors (age, ECG changes, cardiac biomarker positivity, etc).

MATERIALS AND METHODS

This hospital based single centre, cross-sectional, observational, descriptive study conducted at a tertiary care teaching institute. One hundred and sixty patients were recorded between April 2012 and November 2013. Study patients comprised patients presenting with unstable angina with most recent episode occurring within 72 hours of admission. Unstable angina was defined as angina or its equivalent with atleast one of the 3 features: occurring at rest or minimal exertions & usually lasting >20 minute, being severe, or occurring with a crescendo pattern (more severe, prolonged, or frequent than previous) [7]. Patients with >72 hours since chest pain, or those with previous MI, Percutaneous Transluminal Coronary Angioplasty (PTCA) or Coronary Artery Bypass Grafting (CABG) or contraindications to coronary angiography were excluded. 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 Non-ST Elevation Myocardial Infarction (NSEMI). Informed consent was taken from each patient. Institutional Ethical committee reviewed the study and cleared it. All patients were assessed by use of a structured questionnaire regarding main risk factors and medical history. All patients underwent a detailed examination, 12 lead surface ECG, standard biochemical tests including lipid profile, cardiac serum markers and two dimentional echocardiography. Following 9 clinical risk predictors were recorded - Pain lasting for > 20 minutes, presence of 3 or more risk factors, presence of 2 or more episodes of pain in prior 24 hour, use of Aspirin within prior week, ECG finding of ST deviation of >=0.5 mm, ECG finding of T-wave inversion >=3 mm, Age >= 65 years, presence of elevated cardiac enzymes and presence of CHF in acute unstable angina cases. TIMI, GRACE & PURSUIT Scores were calculated based on history, vital parameters, lab investigations & ECG.

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. CAG was done by the cardiologist other than the investigator. Investigator had demarcated risk factor & risk scores before comparing it with CAG finding. Assessment of angiographic lesion severity was done by Modified Gensini score and stenosis in culprit angina related artery (ARA).

The Modified Gensini score has been described and validated previously [8]. The most severe stenosis in each of eight coronary segments was graded from 1 to 4 (1.1% to 49% lumen diameter reduction, 2. 50% to 74% stenosis; 3, 75% to 99% stenosis, 4, 100% occlusion) to give a total score ranging between 0 and 32. The proportion of each vessel involved by atheroma was multiplied by a factor for each vessel: left main, (5), left anterior descending, (20), main diagonal branch (10), first septal perforator, (5), left circumflex, obtuse marginal, and posterolateral vessels, (10), right coronary, (20), and main posterior descending branch, 10. When the major lateral wall branch was a large obtuse marginal or intermediate vessel, the factor used was 20, with a factor of 10 for the left circumflex [9,10].

Patients who had single vessel disease, the ARA localization was straight forward. In patients who had multivessel disease, the coronary lesion was considered culprit angina related if there was obvious eccentric thrombus with scalloped or overhanging edges and a narrow neck or if it had dissection showing Regional Wall Motion Abnormality (RWMA) in echocardiography was considered as angina related . Also the coronary artery supplying the myocardial segments. Features suggesting thrombus included globular intraluminal mass with rounded or polypoidal shape or "haziness" of a lesion. A panel of three fixed cardiologists analysed each angiography and gave the report after consensus, thus minimizing interobserver and subjective variability.

STATISTICAL ANALYSIS

Quantitative data were summarized in the form of Mean & Standard Deviation (SD). Qualitative data were summarized in the form of proportions. Multiple Linear Regression was done for 9 independent predictors to assess their influence over Modified Gensini Score and percentage stenosis in culprit artery. Categorization of high versus low score was done for TIMI, GRACE and PURSUIT Scores. Pearson's coefficient 'r' was calculated to assess the relationship of these three Risk Scores with Modified Gensini Score and percentage stenosis in the culprit artery. The interpretation of correlation coefficient was done as weak (positive/negative) < 0.3, moderate 0.3 to 0.7 and strong > 0.7 [11,12]. Student's t-test was applied to find correlation of low v/s high risk score values with angiographic severity. Multiple Linear Regression Model with F statistics and Adjusted R-square were used for assessing influence of the 9 independent predictors on angiographic parameters.

RESULTS

[Table/Fig-1] shows clinical characteristics of the study group. Mean age ± SD of the study group was 56±34 years, range being 38 – 80 years. Out of total, 75.6 % were males and smoking was the most important risk factor (51.2 %).

[Table/Fig-2] summarizes the values of Modified Gensini score, percentage stenosis of culprit artery, and the number of vessels involved relative to the various independent predictors. Out of total, 27.5% patients had chest pain for more than 20 minutes, 25.6% patients had more than 3 risk factors for CAD present and 10% patients were taking aspirin within prior week. A 43.7% patients had more than 2 angina episodes in last 24 hours, 37.5% patients had ST depression > = 0.5 mm in >= 2 contiguous leads and 27.5 % patients had T wave inversion >=3mm in >= 2 contiguous leads. A 56.8% patients had cardiac enzyme elevation in form of qualitative

Age (Mean + SD) in years 56 ± 34	Number of patients (n =160)
Males	121 (75.6%)
Diabetes	61 (38.1%)
Hypertension	77 (48.1%)
Smoking	82 (51.2%)
LDL Cholesterol > 130 mg%	44 (27.5%)
Family h/o CAD/CVA	40 (25%)

[Table/Fig-1]: Clinical characteristics of the study group

Predictors	Number of patients (n)	Gensini Score Mean (± SD)	Culprit stenosis (%) Mean (± SD)	Single Vessel (n)	Multi Vessel (n)
Overall	160	115 (± 76.8)	88 (± 10.27)	72	88
Chest pain duration in mins					
>=20	44	115.9 (± 77.7)	85.58 (± 3.5)	23	21
< 20	116	114.2 (± 77)	82.63 (± 10.3)	49	67
Number of risk factors					
>=3	41	117.56 (± 77.36)	89.58 (± 10.28)	20	21
<3	119	114.18 (± 77.36)	85.5 (± 10.3)	52	67
Use of aspirin in last week					
Yes	16	100 (± 79.4)	85 (± 10.1)	12	4
No	144	121.9 (± 76.8)	89.1 (± 10.26)	62	82
>2 pain episodes in last 24 hours					
Yes	70	108.8 (± 77.1)	81.56 (± 10.1)	30	40
No	90	119.2 (± 76.7)	84.75 (± 10.3)	42	48
ECG ST depression					
Yes	60	139.47 (± 78.3)	90.46 (± 10.4)	22	38
No	100	111.1 (± 77.1)	87.7 (± 10.3)	50	50
ECG T wave inversion >= 3mm					
Yes	44	114.1 (± 77.1)	89.80 (± 10.28)	19	15
No	116	123.4 (± 78.3)	88.21 (± 10.31)	53	63
Cardiac enzyme raised					
Yes	91	126.68 (± 77)	89.20 (± 10.31)	44	47
No	69	110.15 (± 76.94)	85.56 (± 10.25)	28	37
Age >= 65 years					
Yes	38	156 (± 76)	94.57 (± 10.1)	11	27
No	122	105.39 (± 78.2)	85.61 (+ 10.2)	61	61
CHF					
Yes	3	266.68 (± 79.7)	99 (± 0)	1	2
No	157	144.57 (± 79)	87.8 (± 10.23)	71	86

[Table/Fig-2]: Mean (± SD) values of angiographic parameters for various clinical predictors by extent of CAD and number of vessels

Troponin T positive, 23.7% patients had age >=65 years. 72 (45 %) patients had single vessel disease (SVD), 50 (31.2%) had double vessel disease (DVD), 38 (23.7%) patients had triple vessel disease (TVD), 3 (0.018%) patients had LMCA. Culprit angina related artery (ARA) could be recognized in 107 (66.8%) patients- 72 patients were SVD, 16 patients by echo delineation of RWMA & 19 patients by presence of thrombus. Mean Gensini score was 115 and mean stenosis in culprit ARA was 88%.

[Table/Fig-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.

Results of Multiple Linear Regression Analysis suggested a significant influence of the 9 independent predictors on Modified Gensini score,

Score (number of patients)	Gensini Score Mean (± SD)	p-value	Culprit stenosis (%) Mean (± SD)	p-value	Single Vessel (n)	Multi Vessel (n)
TIMI Score						
3 – 7 (53)	140.6 (± 77)	0.01	91.27 (± 10.23)	<0.001	21	32
0 – 2 (107)	107.27 (± 76.8)		85.2 (± 10.26)		51	56
Grace Score						
>= 96 (57)	143.86 (± 77.3)	0.007	90.1 (± 10.23)	0.022	19	38
<96 (103)	108.9 (± 76.8)		86.2 (± 10.26)		52	51
Pursuit Score						
>=10 (101)	128.7 (± 76.8)	0.027	90.1 (± 10.28)	0.001	32	27
<10 (59)	100.6 (± 77.3)		84.57 (± 10.26)		40	61

[Table/Fig-3]: Mean (± SD) values of angiographic parameters for the various risk scores by extent of CAD and number of vessels

F statistics	df	Significance	Adjusted R^2
3.409	9	0.001	0.121
	158		

[Table/Fig-4]: Multiple regression analysis for influence of the 9 independent predictors on Modified Gensini score

Predictor variable	Standardized Coefficient (B)	p value
Use of Aspirin	-0.688	0.038
Age >= 65 years	1.686	0.007
Presence of CHF	0.457	0.006

[Table/Fig-5]: Significant Clinical variable for Modified Gensini Score

F statistics	df	Significance	Adjusted R^2
2.668	9	0.008	0.126
	105		

[Table/Fig-6]: Multiple regression analysis for influence of the 9 independent predictors on percentage stenosis in the culprit artery

Predictor variable	Standardized Coefficient (B)	p value
Presence of elevated enzymes	0.269	0.01
Age >= 65 years	0.099	0.003

[Table/Fig-7]: Significant clinical variable for percentage stenosis in culprit artery

as shown in [Table/ Fig- 4]. Around 12 % of the observed variation in data can be explained by this relationship between Modified Gensini score and a clinical predictor when adjusted for possible effect of other predictors in this model. [Table/Fig-5] shows the significant variables.

Use of aspirin brought negative 68.8% change in Modified Gensini score, CHF brought 45.7% change and age above 65 yrs changed Modified Gensini score one and half times. Presence of pain lasting for >= 20 minutes, presence of more than 3 risk factors, presence of more than 2 episodes of pain, ECG finding of ST elevation, ECG finding of T wave inversion, and presence of elevated Enzymes were not significant predictors in this model.

Results of Multiple Linear Regression Analysis suggested a significant influence of the 9 independent predictors on percentage stenosis in the culprit artery, as shown in [Table/ Fig- 6]. A 12.6% of the observed variation in data can be explained by this relationship between percentage stenosis in the culprit artery and a clinical predictor when adjusted for possible effect of other predictors in this model. [Table/Fig-7] shows the significant variables.

Presence of elevated enzymes brought 26.9% change in percentage stenosis of ARA, age above 65 years brings 9.9% change in percentage stenosis in the culprit artery. Presence of pain lasting for >= 20 minutes, presence of more than 3 risk factors, presence of more than 2 episodes of pain, ECG finding of ST elevation, ECG finding of T wave inversion, and presence of CHF were not significant predictors in this model.

Pearson's 'r' Correlation coefficient of the 3 Risk Scores With Modified Gensini Score, at 95% Confidence Intervals, were - TIMI risk score : 0.166, GRACE risk score: 0.3, and PURSUIT risk score: 0.274. There is a moderate positive correlation of GRACE risk score with Modified Gensini Score whereas PURSUIT and TIMI risk scores showed weak positive correlation [11,12].

Correlation coefficient of the 3 Risk Scores with % blockage of culprit artery, at 95% Confidence Interval, were - TIMI risk score : 0.227, GRACE risk score: 0.266, and PURSUIT risk score : 0.293. These values suggested weak positive correlation of all the 3 risk scores, with maximum correlation for PURSUIT score.

DISCUSSION

Risk Scores help in risk stratification in unstable angina. Our study aims at comparing the predictive value of angiographic severity of various risk scores. The study is probably the first one to compare the various clinical predictors in risk scores, with angiographic severity. This study is also different from previous studies as- angiographic severity is seen in the form of Modified Gensini score and percentage stenosis in culprit vessels, rather than just the number of vessels involved [13-15]. Also, predictive value of individual risk stratification factors are assessed rather than just low/ intermediate or high risk group [16].

Our study shows that among the various clinical predictors of the severity of unstable angina: CHF, age >= 65 years and use of aspirin in the past week affects the Modified Gensini Score significantly. Similarly, presence of elevated cardiac enzymes and age >= 65 years were significant predictors of increased severity of culprit stenosis. It also shows that the 3 risk scoring systems – TIMI, GRACE& PURSUIT have weak/moderate correlation with angiographic severity.

The study by Pedro de Araújo Gonçalves et al., demonstrated that the 3 risk scores have a good predictive accuracy for death or MI at 1 year and enabled the identification of high-risk subsets of patients who will benefit most from myocardial revascularization performed during initial hospital stay [5]. In a study by Zhao et al., the NSTEMI patients with moderate and high TIMI risk score showed significant reduction in combined cardiovascular events with early invasive strategy as compared to early conservative strategy [17]. Walsh et al., showed that Percutaneous Coronary Intervention (PCI) can provide symptomatic and mortality benefit in an elderly, high-risk TIMI scores population [18]. These studies showed that the risk scoring systems have a good predictive value for risk stratification and prognosis [17-19]. As angiographic severity is independent predictor of Major Cardiovascular Events (MACE) [4], it would be helpful if angiographic extent of CAD could be predicted from various clinical measures and appropriate risk scoring system.

In a study by Matthew et al., risk stratification according to the Agency for Health Care Policy and Reasearch (AHCPR) guidelines correlates with the angiographic extent of CAD, such that intermediate and high risk patients have a high likelihood of angiographically significant coronary disease [16]. The study by Garcia et al., of correlation between clinical risks with extension of CAD in NSTEMI showed that the most low clinical risk patients had normal angiography or limited CAD, but severe CAD or left main artery disease in high clinical risk patients was more prevalent than that in low risk patients, so the clear relations existed between TIMI risk score and angiography score in patients with NSTEMI [13]. These studies defined angiographic severity on the basis of single/double/ triple vessel disease [13-16,20,21]. Our study used Modified Gensini score, which is a more comprehensive score that incorporates both, the number of lesions, as well as the degree of stenosis. We also measured extent of CAD in terms of percentage of stenosis in culprit artery, which is a more direct and relevant marker of CAD disease.

LIMITATION

A limitation of this study is that percentage stenosis in culprit artery is subjective, though it was based on the consensus of 3 cardiologists.

CONCLUSION

In TIMI Score, each of the 7 variables is given equal point. In this study, we have found that use of Aspirin, age >= 65 years, presence of CHF and presence of elevated enzymes 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. The higher scores in TIMI, GRACE and PURSUIT Scoring systems had significantly greater angiographic disease, when compared to low scores. GRACE score had more correlation with Modified Gensini score, PURSUIT score had more correlation with percentage stenosis in culprit artery.

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