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Predictors of the Extent and Severity of Coronary Artery Disease in Patients with non-ST-Segment Elevation Acute Coronary Syndromes

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Abstract

Introduction: The proportion of patients visiting emergency department with chest pain indicative of non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is increasing. The current risk assessment of patients with NSTE-ACS may calculate patients risk for recurrent events but may fail to identify patients with severe coronary artery disease (CAD). The present study aimed to identify predictors of the extent and severity of CAD for prognosis of NSTE-ACS patients undergoing early angiography.

Methods: A total of 215 patients with NSTE-ACS were enrolled randomly and followed up between April-2015 and February-2017 at a tertiary healthcare center. The coronary angiography was performed. Patients were divided into two groups: high-risk coronary anatomy (HRCA) and low-risk coronary anatomy (LRCA). Patients were analyzed for baseline, demographic, clinical characteristics, and cardiovascular risk factors, during hospitalization and 30 days post discharge.

Results: Among 215 enrolled patients, 90 (mean age: 52.22 ± 10.24 year) and 125 (mean age: 57.78 ± 8.83 year) patients were in the LRCA and HRCA group, respectively. The presence of previous heart failure [Odds Ratio (OR): 3.95, 95% confidence interval (CI): 1.11-14.10; P = 0.03], chronic renal failure [OR: 5.11, 95% CI: 1.12-23.22; P = 0.03] and peripheral vascular disease [OR: 3.38, 95% CI: 1.09-10.42; P = 0.03] were significant independent predictors of HRCA. Additionally, Grace score >140 was the significant predictor of 30 days mortality [OR: 5.85; P = 0.02] and major adverse cardiac and cerebral events [MACCE; OR: 6.23, 95% CI: 2.22-17.50; P = 0.001].

Conclusions: The extent and severity of CAD in NSTE-ACS patients can be predicted by assessing HRCA through clinical parameters. However, the correlation of HRCA with 30 days MACCE and mortality was modest.

INTRODUCTION

Number of patients visiting emergency department with chest pain mimicking the symptoms of the non-ST-segment elevation acute coronary syndrome (NSTE-ACS) is increasing; among which approximately 50% of patients have cardiac disease. It was found that the proportion of NSTE-ACS is higher within various cardiac diseases [1-3]. Estimated 580000 new attacks and 210000 recurrent attacks occur annually [4]. NSTE-ACS represents a wide spectrum of clinical syndromes, ranging from unstable angina (UA) (without cardiomyocyte loss) to non-ST-segment-elevation myocardial infarction (NSTEMI, with cardiomyocyte necrosis). NSTEMI is characterized by an abnormal level of cardiac biomarkers (preferably troponin) accompanied by the electrocardiographic (ECG) changes. UA is distinguished by the absence of myocardial necrosis and hence only normal cardiac biomarkers are present with the ECG changes [5]. The traditional risk factors for NSTE-ACS include but are not limited to age, male gender, prior myocardial infarction (MI), hypertension, tobacco use, diabetes mellitus (DM), dyslipidemia, and family history of premature coronary artery disease (CAD; age of onset prior to 55 years in males and <65 years in females). Similarly, a sedentary lifestyle, metabolic syndrome, inflammation, chronic kidney disease and, obstructive sleep apnea are supposed to increase the risk of NSTE-ACS.

The management of patients with ACS requires accurate risk stratification to guide appropriate (early or late) therapy. A wide number of risks are associated with NSTE-ACS and requires careful assessment as early as the first medical contact. It remains a continuous process during hospitalization and after discharge. The 2015 ESC guideline for the management of ASC stratifies the patients into unstable angina, low-, intermediate- and high- risk arrhythmia groups [6]. For the prognosis of before-mentioned risk groups, corresponding factors like duration of chest pain, age, cardiac biomarkers, ECG changes and congestive heart failure (CHF) are used. Thrombolysis in myocardial infarction (TIMI) score, Receptor Suppression Using Integrilin Therapy (PURSUIT) score and Global Registry of Acute Coronary Events (GRACE) score are also used in risk stratification and prediction of risk group [7, 8].

The clinical assessment along with clinical score is significant for the risk stratification. The GRACE score provides the most accurate risk stratification [7, 9]. The GRACE 2.0 risk calculator provides the direct estimation of mortality during hospitalization and, after discharge up to 3 years. It also provides the combined risk of death or MI up to 1 year [10]. Variables required for the GRACE 2.0 risk calculation are age, systolic blood pressure, pulse rate, serum creatinine, elevated cardiac biomarkers, ST deviation, Killip class at presentation and cardiac arrest at admission. Although the TIMI risk score is simple to use, has less accuracy than the GRACE risk score and the GRACE 2.0 risk calculator. The TIMI risk score uses seven variables viz. age, CAD risk factors, known CAD, aspirin use in the past 7 days, severe angina (two or more episodes within 24 h), ST change ≥0.5 mm and, positive cardiac marker. The risk scores have a high prognostic value, however, its impact on patients in the real world hasn't been adequately investigated [11, 12].

The therapeutic strategy depending on the risk groups such as obstructive CAD-invasive treatment or non-obstructive CAD-conservative treatment has been decided. However, current risk assessment of NSTE-ACS patients fails to identify some patients with severe CAD. The present study aimed to identify predictors of the angiographic extent and severity of CAD in patients with NSTE-ACS undergoing early angiography and its impact on prognosis.

METHODS

Study Population

A total of 215 patients with NSTE-ACS were enrolled randomly and followed up between April-2015 and February-2017 undergoing early invasive strategy at a tertiary healthcare center. The study was approved by the institutional ethics committee and the all patients have provided written informed consent. The coronary angiography was performed according to the standard technique through femoral or radial route, for eligible patients. Patients were divided into two groups: high-risk coronary anatomy (HRCA) and low-risk coronary anatomy (LRCA). Baseline, demographic, other clinical characteristics and cardiovascular risk factors of patients were recorded and compared between the two groups. For the purpose of the study, HRCA was defined as one of the following: left main stenosis > 50%, proximal left anterior descending artery (LAD) lesion > 70%, and/or a two to three vessel disease involving the LAD.

Study End Points

In-hospital complications including pulmonary edema, cardiogenic shock, moderate to severe mitral regurgitation (MR), acute renal failure, major bleeding event, and mortality were recorded. Major adverse cardiac and cerebral events (MACCE), defined as a composite of cardiac death, recurrent MI, major bleeding, definite stent thrombosis, and mortality were analyzed at 30 days.

Statistical Analysis

Statistical analysis was performed using SPSS version 22. Categorical variables were expressed as a percentage and, continuous variables were expressed as a mean ± standard deviation. Categorical variables were compared using chi-square statistics. Continuous variables were compared using Student's t-test. Odd's

ratio was calculated for predictors of HRCA, 30 days MACCE and 30 days mortality.

RESULTS

Baseline Characteristics

A total of 215 patients were enrolled in the study, of which 90 patients were in LRCA group and 125 patients in HRCA group. The mean age of patients in the HRCA group was 57.78 ± 8.83 year and in the LRCA group was 52.22 ± 10.24 year. The difference was statistically significant, suggesting that the patients with higher age are at more risk of HRCA than lower age patients. The mean BMI in both the groups was similar (P = 0.61). Previous MI, angina pectoris, percutaneous coronary intervention, previous stroke, history of hypertension, diabetes, and smoking and, aspirin therapy were not significantly different in HRCA and LRCA groups. In the same group, patients with previous heart failure, chronic renal failure, and peripheral vascular disease were significantly (P < 0.05) higher in HRCA compared to LRCA group. Moreover, a number of patients with Grace Score > 140 (P = 0.001) and, Killip Class > I (P = 0.0108) were significantly higher in the HRCA group. Additionally, laboratory parameters like eGFR, Serum blood glucose, and creatinine level have a significant correlation with HRCA. (Table 1).

Table 1: Patient Characteristics in Relation to HRCA and LRCA

Variables	HRCA	LRCA	P value
Age	57.78 ± 8.83	52.22 ± 10.24	0.0001
BMI	24.61 ± 4.53	24.33 ± 3.71	0.61
Previous Myocardial Infarction	31 (24.8%)	22 (24.4%)	0.91
Previous angina Pectoris	52 (41.6%)	32 (35.6%)	0.45
Previous PCI	27 (21.6%)	19 (21.1%)	0.93
Previous Heart failure	15 (12%)	3 (3.3%)	0.04
Chronic Renal failure	13 (10.4%)	2 (2.2%)	0.04
Peripheral vascular disease	17 (13.6%)	4 (4.4%)	0.04
Previous stroke	9 (7.2%)	5 (5.6%)	0.83
Family history of heart disease	33 (26.4%)	29 (32.2%)	0.43
Hypertension	90 (72%)	61 (67.8%)	0.60
Diabetes	52 (41.6%)	29 (32.2%)	0.20
Smoking	42 (33.6%)	30 (33.3%)	0.91
Prior aspirin therapy	69 (55.2%)	44 (48.9%)	0.43
Presenting Symptoms			
Typical angina pectoris	98 (78.4%)	77 (85.6%)	0.24
Dyspnea	30 (24.1%)	15 (16.7%)	0.25
Killip Class >I	25 (20%)	6 (16.7%)	0.01
Heart rate mean ± SD	91.57 ± 17.81	83.91 ± 11.19	0.0004
Grace Score >140	23(18.4)	3(3.33)	0.001
Laboratory parameters			
eGFR	80.53 ± 24.54	102.49 ± 27.75	<0.0001
Elevated CKMB	89 (71.2%)	61 (67.7)	0.69
Elevated Troponin. I	85 (68%)	53 (58.8%)	0.21
Glucose	144.14 ± 72.13	124.22 ± 57.78	0.03
Creatinine	1.10 ± 0.57	0.87 ± 0.34	0.0008

Data are expressed as Mean ± SD and Frequency (percent). HRCA: High-risk Coronary Anatomy, LRCA: Low-risk Coronary Anatomy, GFR: Glomerular Filtration Rate, PCI: Percutaneous Coronary Intervention, BMI: Body Mass Index

Analysis for Predictors of HRCA

Odds ratio (OR) and 95% confidence interval (CI) has been calculated for all clinical parameters to find out the predictors for HRCA. It has been found that previous heart failure [OR 3.95, 95% CI: 1.11-14.10; P = 0.03], chronic renal failure [OR: 5.11, 95% CI: 1.12-23.22; P = 0.03] and, peripheral vascular disease [OR: 3.38, 95% CI: 1.09-10.42; P = 0.03] were significant independent predictors of HRCA. (Table 2)

Cardiovascular Outcomes in Relation to HRCA and LRCA

Table 3 represents the cardiovascular outcomes in both HRCA and LRCA groups. Patients with HRCA had significantly (P < 0.0001) lower ejection fraction than patients with LRCA. MACCE (P = 0.04) and CABG (P < 0.0001) were significantly higher in the HRCA group compared to the LRCA group. No significant difference was found for other cardiovascular outcomes between the two groups.

Predictors of 30 Days Mortality and MACCE

We found that the HRCA and peripheral vascular disease were not significantly associated with the incidence of mortality. However, we found that Grace

score >140 was the significant predictor of mortality [OR: 5.85; P = 0.02] and MACCE [OR: 6.23; 95% CI: 2.22-17.50; P = 0.001).

Table 2: Analysis of Predictors for High-risk Coronary Anatomy

Variables	Odds Ratio	95% CI	P-value
Previous Heart failure	3.95	1.11-14.10	0.03
Chronic renal failure	5.11	1.12-23.22	0.03
Peripheral vascular disease	3.38	1.09-10.42	0.03
Grace Score >140	1.41	0.6-3.34	0.42

CI: Confidence Interval

Table 3: Cardiovascular Outcomes in Relation to HRCA and LRCA

Variables	HRCA	LRCA	P value
Ejection Fraction	47.47 ± 9.10	52.22 ± 6.58	< 0.0001
In-hospital complications			
Moderate to Severe MR	5(4%)	1(1.1%)	0.39
Acute renal failure	9(7.2%)	1(1.1%)	0.07
Major Bleeding event	3(2.4%)	1 (1.1%)	0.85
In-hospital & 30 days Mortality	2(1.6%)	1(1.1%)	0.77
Recurrent MI at 30 days	5(4%)	3(3.3%)	0.91
Stent thrombosis at 30 days	2(1.6%)	0(0%)	0.17
MACCE	17(13.6%)	04(4.4%)	0.04
CABG	33(26.4%)	0(0%)	<0.0001

Data are expressed as Mean ± SD and Frequency (percent).HRCA: High-risk Coronary Anatomy, LRCA: Low-risk Coronary Anatomy, MACCE: Major Adverse Cardiac and Cerebrovascular Event, CABG: Coronary artery bypass grafting, MR: Mitral regurgitation

DISCUSSION

The major finding of this study was NSTE-ACS patients with HRCA signifying higher risk of CAD and can be predicted by demographic characteristic (age); clinical parameters (peripheral vascular disease, chronic renal failure and, previous heart failure); lab parameters (glucose, eGFR and, creatinine); and presenting symptoms (Killip Class >I and Grace Score > 140). Additionally, we found that peripheral vascular disease, chronic renal failure, and previous heart failure were independent predictors of HRCA. A significant number of patients with HRCA faced MACCE and had undergone CABG. Moreover, we found that Grace score >140 is the strongest independent predictor of MACCE and mortality in patients with NSTE-ACS.

None of the risk factors known till date for stratification of NSTE-ACS is ideal, instead could not predict risk independently [Henderson, 2013 #13]. Such risk factors include patient history, clinical examinations, ECG changes, cardiac markers, and various risk scores. Additionally, for early risk stratification, a complicated clinical course, left ventricular systolic dysfunction, severity of CAD, revascularization status and evidence of residual ischemia on non-invasive testing may be used. All these risk factors can stratify patients into high-risk or low-risk CAD, but unable to predict the presence of HRCA and hence the severity of CAD [6, 13].

Al-Thani et al. analyzed 6705 consecutive ACS patients of which 177 were peripheral artery disease (PAD) patients. The study explored that most of the patients had high Killip class and GRACE risk score at presentation. They constituted the high-risk group as well as the independent predictors of mortality in NSTE ACS patients [14]. Marenzi et al. concluded that the frequency of chronic kidney disease was more in ACS patients and was a potent as well as the independent risk factor for adverse cardiac outcomes [15]. Many studies have established that in patients with NSTE-ACS, heart failure on admission was associated with increased risk of mortality and MI. Also, Killip classification was a powerful independent predictor of NSTE-ACS [16-18]. Additionally, some other studies have suggested that factors such as age, heart rate, systolic BP, ST-segment depression and cardiac enzymes as the strongest predictor of mortality and MI [19, 20]. Results of these studies are in line with the current study.

GRACE risk scoring system [21] is an important risk stratification system among ACS patients to decide early invasive strategy and predict clinical outcomes. Our study revealed that, in patients with NSTE-ACS, the GRACE score >140 has a predictive value for the presence of HRCA signifying a greater extent and burden of a CAD (P = 0.001). Additionally, we have

explored that GRACE score >140 is an independent predictor of 30 days mortality and MACCE. However, no relation was established between MACCE and mortality with HRCA. Beigel et al. [22] suggested that GRACE score > 140 and HRCA as the strongest predictor of 30 days mortality and HRCA alone as the strongest predictor of 30 days MACCE. Another study done by Avci et al. [23] found that a significant difference is available between GRACE score of HRCA and LRCA (P = 0.001). Furthermore, they explored that GRACE score > 123 is having 71% sensitivity and 60% specificity in predicting HRCA and hence the cutoff. However, they found that GRACE score is a modest predictor of HRCA. Isilak et al. [24] suggested that only ACC/AHA guidelines can predict the three vessels CAD. Further suggested that the GRACE score of 119 had higher sensitivity. GRACE investigators showed that in 27,406 patients with NSTE-ACS, the GRACE risk score had a direct relation to in-hospital mortality [25].

Based on the findings we could summarize that, instead of solely relying on conventional cardiac biomarkers and risk scores, clinical parameters can be used in combination to predict the patients with HRCA or LRCA in NSTEMI. Proper identification of these patients is important for opting an early invasive strategy to improve short- and long-term outcomes. Patients with predictors of HRCA should be treated as early as possible.

Limitations

The study was conducted at a high-volume tertiary center. Therefore, the results might not be applicable to other settings. Due to a small sample size of our study, the reliability of the result is limited. Hence, a large, prospective, randomized cohort study is needed to explore the new predictors of NSTEMI, which will provide substantially reliable results for future research.

CONCLUSIONS

The extent and severity of CAD in NSTE-ACS patients can be predicted by assessing HRCA through clinical parameters such as the previous history of heart failure, chronic kidney disease or, peripheral vascular disease. We found that the Grace score >140 are a strong predictor for 30 days MACCE and mortality. However, an only modest co-relation was found between HRCA and 30 days MACCE and mortality.

Authors Contributions

Chirag Patel: Data Acquisition, Manuscript writing, Patient enrollment
Jayesh Prajapati: Concept, Design, Manuscript review
Iva Patel: Bio-Statistical analysis, Manuscript editing, Data entry, Manuscript Preparation
Roopesh Singhal: Literature review,
Ashish Mishra: Manuscript editing,
Gaurav Singh: Literature search,

Conflicts of Interests

None.

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