ORIGINAL ARTICLE PROSPECTIVE VALIDATION OF HEART SCORE FOR SUSPECTED ACUTE CORONARY SYNDROME PATIENTS

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Background: The HEART score is reported to be a useful tool for the assessment of suspected acute coronary syndrome (ACS) patients, however, data regarding its validity in our population is scarce. Therefore, aim of this study was to evaluate the prognostic utility of the HEART score to predict major adverse cardiac events (MACE) within 6 weeks in patients presenting to emergency department with chest pain. Methods: This prospective observational study included suspected ACS patients presented with chest pain to the emergency department of a tertiary care cardiac center. Inclusion criteria for the study were consecutive adult patients with suspected ACS, patients with definite diagnosis of ACS based on history, electrocardiography (ECG), and cardiac enzymes were excluded from the study. HEART score was calculated and patients with ≥ 7 score were also excluded. MACE over the 6-weeks after discharge were observed. Results: Total of 281 patients were included in this analysis, 191 (68%) were male and mean age was 52.58±10.63 years. Mean HEART score was calculated to be 4.27±1.06 with 70.8% (199) in moderate risk [4-6]. Area under the curve of HEART score for the prediction of 6-weeks MACE was 0.874 [0.827-0.920] with MACE rate of 31.7% vs. 0% for low- and moderate-risk group respectively. Conclusion: HEART score showed good discriminating power for the prediction of 6-weeks MACE. Risk of MACE for the patients with HEART score of 0-3 is very low and such patients can be discharged from ER without extensive cardiac workup with proper follow-up planned. Keywords: HEART score, acute coronary syndrome, chest pain, MACE, emergency room

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INTRODUCTION

Millions of patients in Pakistan come to emergency services with chest pain.¹ Adult emergency department (ED) visits for chest discomfort are one of the most prevalent and potentially significant presenting ailments. Identifying those having acute coronary syndrome (ACS) is the foremost issue in these patients.² Timely proper diagnosis and risk stratification should be done as quick and efficient way so that patient should get targeted treatment as early as possible which improves the overall prognosis significantly.

Approximately 80% of patients with chest discomfort do not have a definite ACS at the time of presentation in today's practice.³ Even while 75-85 percent of patients with symptoms indicative of ACS go through extensive testing in the emergency department, most of these individuals do not receive final diagnosis of ACS.^{4–6} Without a perfect methodology, these evaluation processes differ from one institution to another. Clinicians frequently hospitalize these patients for observation while also treating them as ACS patients. Owing to this, over diagnosis and treatment are prevalent, leading to elevated patient burden, physician duplication of efforts, increased costs and poor patient outcomes, such as higher number of deaths.⁷ Patients

having all causes of chest pain are examined at the emergency department (ED) with a simple certified measure called the HEART score to enhance risk evaluation.

Six AJ and colleagues created the HEART score in Netherlands during the year 2008 as a fast risk evaluation instrument for individuals having chest pain on basis of their short term risk of major adverse cardiovascular events (MACE) to spot low risk patients who might be discharged from the ED sooner.⁸ This instrument is useful for a variety of causes such as its simplicity of use, readily available variables, and the recognition of three distinct sub-populations (low, moderate, and high risk) of emergency department chest pain individuals who believed to have an ACS. Patients with low risk were considered as suitable and secure for emergency department release exclusive of any further heart evaluation or inpatient admission; on the other hand, an elevated score was linked to a greater MACE rate, implying that extra evaluation or interference was required.8-10

The HEART score is a trustworthy predictor of prognosis for individuals having chest pain in the emergency area. The accuracy of the HEART score has been demonstrated in numerous investigations and significant sensitivity, negative likelihood ratio, and negative predictive value for the prediction of immediate MACE.¹¹ Another meta-analysis published in 2018 also showed that the HEART score offers a high sensitivity for detecting individuals at low risk of chest pain while at risk of having a significant adverse cardiac event in the short term. A HEART score of 4 or higher was linked to a significant susceptibility for major adverse cardiac events in short term, notably short term death and acute myocardial infarction.^{12,13} Furthermore Heart score if applied correctly could lead to significant reduction in cardiac testing in a population with low pretest prospect of ACS.¹⁴

The rationale behind conducting this study was to evaluate the validity of HEART score in our population. With the data obtained we can teach health care providers to use such a useful tool in their routine practice and get reliable information regarding patient condition and possibility of MACE so timely action should be taken. The implication of the study will reduce the burden of subsequent admission of patients with MACE. Therefore, aim of this study was to evaluate the prognostic utility and precision of the HEART score to predict the occurrence of major adverse cardiac events (MACE) within 6 weeks in patients presenting to emergency department with chest pain.

MATERIAL AND METHODS

This prospective observational study included suspected ACS patients presented with chest pain to the emergency department of a tertiary care cardiac center of Karachi, Pakistan between November 2020 and April 2021. Study was approved by the ethical review committee of the institution and informed consent was obtained from all the patients for inclusion in study, follow-up, and publication of collected data without disclosing patients' identity in any form. Inclusion criteria for the study were consecutive adult patients $(\geq 18 \text{ years})$ with suspected (probable or possible) ACS, patients with definite diagnosis of ACS based on history, electrocardiography (ECG), and cardiac enzymes were excluded from the study. Also, patients categorized as high risk (score \geq 7) as per the HEART score were excluded. Course of management and outcomes during index hospitalization and over 6-weeks of follow-up period after discharge from hospital were observed for all the patients.

The HEART score was calculated based on the five factors as defined by the Six AJ *et al.*⁸ History of the patients was assessed regarding symptoms such as localization, pattern, and duration chest pain and its relation to the sublingual nitrates, cold, stress, and exercise and categorized as highly suspicious, moderately suspicious, or non-specific and points were assigned accordingly. Presentation ECG was obtained by interpreted for significant ST-segment deviation,

non-specific changes, normal and scores were assigned accordingly by the treating cardiologist. Information regarding conventional risk factors, hemodynamic profile, and history of atherosclerotic cardiovascular disease (ASCVD) were obtained as per the requirement for the calculation of HEART score. Similarly, data regarding age and troponin were obtained and categorized to compute an additive score of the five factors. Based on the computed HEART score patients were categorized as low, moderate, or high-risk group with score cut-offs of 0 to 3, 4 to 6, and \geq 7 respectively. High risk patients were excluded from this study and were managed as per the intuitional protocol for highrisk patients and low- to moderate-risk group of patients were followed for the occurrence of major adverse cardiac event (MACE) up to six weeks after discharge. MACE was defined as occurrence of any of the acute myocardial infarction event, need for percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG) surgery, or any invasive testing revealing significant disease needed conservative or procedural management, or all cause death. Disposition of patients in the emergency room were as per the institutional management protocol.

Sample size for the study was calculated based on anticipated area under the curve (AUC) of 0.83 for HEART score for predicting the 6-weeks MACE, at 95% confidence interval and 4% margin of error the required sample size for the study was calculated to be n=258. Considering the expected loss to follow-up a total of 300 patients were recruited. At the end of study duration 19 patients in low-risk group were loss to follow-up, hence, data analysis were performed for 281 patients with successful 6-weeks follow-up. All the analysis were performed with the help of IBM SPSS version 21. Patients were stratified by gender as well as HEART score risk categorization and outcomes and clinical characteristics were compared. Categorical response variables were compared with the help of the Chi-square test or Fishers Exact test and summarized frequency and percentages. Continuous variables such as age of the patient and HEART score were compared with the help of independent sample t-test and summarized as mean \pm standard deviation. To determine the prognostic value of the HEART score the receiver operating characteristic curve (ROC) analysis was performed taking 6-weeks MACE as state variable and HEART score as test variable and AUC along with 95% confidence interval were obtained. For all the analysis were performed under the 5% level of significance criteria.

RESULTS

A total of 281 suspected ACS patients with chest pain were included in this analysis, 191 (68%) were male and mean age was 52.58 ± 10.63 years with a majority, 64.4% (181), belong to the middle age (45–65 years) group. ECG at the presentation showed significant ST-depression in about 5.3% (15) of the patients, 3.2% (9) patients had \geq three risk factors or history of ASCVD, 4.3% (12) were with highly suspicious history, and 15.3% (43) had troponin raised above 2 times the normal limit. Mean HEART score was calculated to be 4.27±1.06 with 70.8% (199) in the range of moderate risk. [4 to 6]. Clinical disposition was discharge from

ED after some observation for 21.7% (61), a majority of the patients were admitted in ward, 61.9% (174) discharged from ward after workup advised and remaining 16.4% (46) discharged from ward after cardiac workup. During the 6-weeks of index hospitalization, 35.9% (101) patients undergone invasive testing, 28.8% (81) suffered chest pain, and 6.4% (18) visited emergency room. Overall MACE was reported in 22.4% (63) of the patients (Table-1).

| Table-1: Clinical characteristics, HEART score risk stratification, and 6-weeks outcomes of the low- to |
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| moderate-risk suspected acute coronary syndrome patients | | | | | |
|--|--------------------------|-------------------------|------------------------|-------------|--|
| Characteristics | Total | Gei | nder | p-value | |
| | | Male | Female | | |
| Total (N) | 281 | 191 (68%) | 90 (32%) | - | |
| Age (years) | 52.58 ± 10.63 | 52.46 ± 10.64 | 52.83 ± 10.66 | 0.782 | |
| \leq 45 years | 21.7% (61) | 22.5% (43) | 20% (18) | 0.634 | |
| 45 to 65 years | 64.4% (181) | 63.4% (121) | 66.7% (60) | 0.588 | |
| \geq 65 years | 13.9% (39) | 14.1% (27) | 13.3% (12) | 0.856 | |
| Co-morbid | | | | | |
| Diabetes mellitus | 33.1% (93) | 29.3% (56) | 41.1% (37) | 0.05* | |
| Hypertension | 67.3% (189) | 61.3% (117) | 80% (72) | 0.002* | |
| Obesity | 5.7% (16) | 5.8% (11) | 5.6% (5) | 0.945 | |
| Smoking | 15.3% (43) | 22% (42) | 1.1% (1) | < 0.001* | |
| Dyslipidemia | 0.7% (2) | 1% (2) | 0% (0) | 0.330 | |
| Congestive heart failure | 2.5% (7) | 3.7% (7) | 0% (0) | 0.066 | |
| Cerebrovascular accident | 1.4% (4) | 1.6% (3) | 1.1% (1) | 0.000 | |
| Risk Factors | 1.4% (4) | 1.0% (3) | 1.1% (1) | 0.702 | |
| No risk factors known | 18.5% (52) | 20.9% (40) | 13.3% (12) | 0.125 | |
| | | | | 0.125 | |
| 1 or 2 risk factors | 78.3% (220) | 74.9% (143) | 85.6% (77) | | |
| ≥ 3 risk factors or ASCVD history | 3.2% (9) | 4.2% (8) | 1.1% (1) | 0.172 | |
| History | | | | | |
| Slightly suspicious | 14.9% (42) | 16.8% (32) | 11.1% (10) | 0.216 | |
| Moderately suspicious | 80.8% (227) | 78.5% (150) | 85.6% (77) | 0.163 | |
| Highly suspicious | 4.3% (12) | 4.7% (9) | 3.3% (3) | 0.594 | |
| Electrocardiography (ECG) | | | | | |
| Normal | 28.1% (79) | 26.7% (51) | 31.1% (28) | 0.443 | |
| Nonspecific | 66.5% (187) | 67.5% (129) | 64.4% (58) | 0.608 | |
| Significant ST-depression | 5.3% (15) | 5.8% (11) | 4.4% (4) | 0.647 | |
| Troponin | | | | | |
| Within normal limits | 31.7% (89) | 32.5% (62) | 30% (27) | 0.679 | |
| 1 -2 times above normal limit | 53% (149) | 50.8% (97) | 57.8% (52) | 0.273 | |
| > 2 times above normal limit | 15.3% (43) | 16.8% (32) | 12.2% (11) | 0.325 | |
| HEART Score | 4.27 ± 1.06 | 4.26 ± 1.05 | 4.29 ± 1.09 | 0.843 | |
| Low Risk [0-3] | 29.2% (82) | 27.7% (53) | 32.2% (29) | 0.441 | |
| Moderate Risk [4-6] | 70.8% (199) | 72.3% (138) | 67.8% (61) | 0.441 | |
| Disposition | | | | | |
| DC from ER after some observation | 21.7% (61) | 20.4% (39) | 24.4% (22) | 0.445 | |
| DC from ward after workup advised | 61.9% (174) | 60.7% (116) | 64.4% (58) | 0.550 | |
| DC from ward after workup done | 16.4% (46) | 18.8% (36) | 11.1% (10) | 0.102 | |
| Six weeks follow-up outcomes | 20.00/ (01) | 20.20((5.1) | 2004 (27) | 0.7.5 | |
| Suffered chest pain | 28.8% (81) | 28.3% (54) | 30% (27) | 0.765 0.531 | |
| Undergone invasive testing Visited emergency room | 35.9% (101) 6.4% (18) | 37.2% (71) 7.9% (15) | 33.3% (30) 3.3% (3) | 0.531 | |
| LHC done and CABG advised/done | 4.6% (18) | 4.7% (9) | 4.4% (4) | 0.149 | |
| LHC done and PCI advised/done | 17.1% (48) | 17.8% (34) | 15.6% (14) | 0.921 | |
| LHC non-significant | 14.2% (40) | 14.7% (28) | 13.3% (12) | 0.767 | |
| Medical management only | 63.3% (178) | 62.3% (119) | 65.6% (59) | 0.598 | |
| Mortality | 1.1% (3) | 1% (2) | 1.1% (1) | 0.961 | |
| Major adverse cardiac event | 22.4% (63) | 23% (44) | 21.1% (19) | 0.718 | |

ASCVD= atherosclerotic cardiovascular disease, DC=discharge, ER=emergency room, LHC=left heart catheterization, CABG=coronary artery bypass grafting, PCI=percutaneous coronary intervention. *Significant at 5%

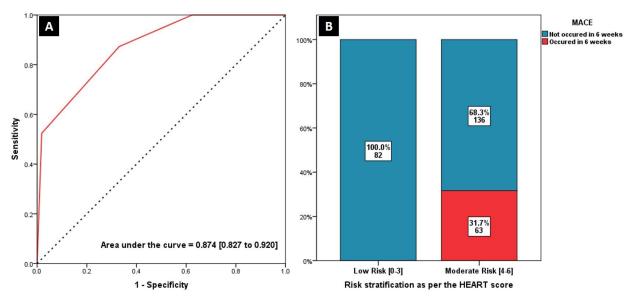


Figure-1: The receiver operating characteristic curve (ROC) analysis of HEART score (A) and 6-weeks MACE by HEART score risk stratification (B)

| Table-2: Six weeks follow-up outcomes of the low- to moderate-risk suspected acute coronary syndrome |
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| patients stratified by HEART score |

| Characteristics | Low Risk [0-3] | Moderate Risk [4-6] | <i>p</i> -value |
|-----------------------------------|----------------|---------------------|-----------------|
| Total (N) | 82 (29.2%) | 199 (70.8%) | - |
| Disposition | | | |
| DC from ER after some observation | 47.6% (39) | 11.1% (22) | < 0.001* |
| DC from ward after workup advised | 45.1% (37) | 68.8% (137) | < 0.001* |
| DC from ward after workup done | 7.3% (6) | 20.1% (40) | 0.008* |
| Six weeks follow-up outcomes | | | |
| Suffered chest pain | 18.3% (15) | 33.2% (66) | 0.012* |
| Undergone invasive testing | 12.2% (10) | 45.7% (91) | < 0.001* |
| Visited emergency room | 4.9% (4) | 7% (14) | 0.502 |
| LHC done and CABG advised/done | 0% (0) | 6.5% (13) | 0.018* |
| LHC done and PCI advised/done | 0% (0) | 24.1% (48) | < 0.001* |
| LHC non-significant | 12.2% (10) | 15.1% (30) | 0.530 |
| Medical management only | 87.8% (72) | 53.3% (106) | < 0.001* |
| Mortality | 0% (0) | 1.5% (3) | 0.264 |
| Major adverse cardiac event | 0% (0) | 31.7% (63) | < 0.001* |

DC=discharge, ER=emergency room, LHC=left heart catheterization, CABG=coronary artery bypass grafting, PCI=percutaneous coronary intervention. *Significant at 5%

The area under the curve of HEART score for the prediction of 6-weeks MACE was 0.874 [95% CI: 0.827 to 0.920]. Rate of MACE during following 6-weeks of index hospitalization were significantly higher among moderate risk group with rate of 31.7% (63/199) as against 0% for the low risk group (Figure-1).

Patients in low risk groups were more likely to discharge from ER after some observation (47.6% vs.11.1%) and more likely to get medical management without any invasive testing (87.8% vs. 53.3%) after discharge. Invasive testing during first 6-weeks of index hospitalization is more likely for the moderate risk group (45.7% vs. 12.2%), also more likely to suffered chest pain (33.2% vs. 18.3%) as compare to the low risk group. Similar, patients in the moderate risk group were also more likely to advised/undergone invasive management such as PCI (24.1% vs. 0%) or CABG (6.5% vs. 0%). Mortality at 6-weeks was observed to be 1.5% vs. 0%; p<0.001 for moderate and low risk group respectively.

DISCUSSION

The HEART score was created to evaluate individuals in the emergency department who had undifferentiated chest pain. According to the research, the short term MACE rate (AMI or death) lies in between 0.6 and 1.4 percent.^{9,14,15} In order to consider a patient candidate for discharge without any additional examination, these MACE rates were high. According to a poll of emergency department physicians, a majority of ED physicians felt that a missed rate of AMI and consequent MACE of less than 0.5 percent is considerable.¹⁶ In this study, we evaluated the HEART score as a potential risk stratification modality in order to find the low risk patients with chest discomfort that can benefit from discharge from ER and at the same time to identify the high risk patients in whom rate of adverse event can be minimized with proper timely management. In literature based on the relationship between the HEART score and poor outcomes, classified as the occurrence of MACE in duration of six weeks, three risk strata, 0 to 3, 4 to 6, and 7 to 10 were identified.10,17 We observed HEART score has good discriminating potential in identifying patients at increased risk of MACE with AUC of 0.874 [95% CI: 0.827 to 0.9201 and event rate at 6-weeks was 0% for the low risk group but a significant (31.7%) number patients in moderate risk group experienced MACE within 6-weeks of index hospitalization. Patients in moderate risk group are more likely to require invasive testing and management coupled with increased risk of mortality. These findings suggested good calibration of HEART score in identifying high risk patients and application of HEART score in the emergency department can be paving way for a more systematic decision making in ER based on firm clinical evidence.8 Contrary to ours, in the original development cohort of HEART score most of the patients were found to have low risk.8

In a study carried out by Leite L *et al.*¹⁸ the appropriate discriminatory power to predict short term incidence of MACE was confirmed for the three risk categories of the HEART score. A score of <4, indicating low risk group, showed a good negative predictive value, and the high risk group with a score of \geq 7 had a fair positive predictive value even for the patients with atypical symptoms. Study favored the use of HEART score to improve the accuracy of decision making regarding appropriate management, in which a significant uncertainty still exits, due to its strong predictive value in predicting event free survival.

McCord J *et al.*¹⁹ investigated whether a modified HEART Score (m-HS), which combines HEART Score with serial hs-cTnT readings and the 1-hour AMI exclusion criteria, might discover a population with low-risk among individuals assessed for potential AMI in the emergency department. In this study the individuals with HEART score ≤ 3 at were ruled out for AMI using the 1-hour delta method showed a MACE of 0.2 percent only. Study suggested such patients can be considered for discharge from ED without any additional cardiac assessment.

A meta-analysis was undertaken by Laureano-Phillips J *et al.*¹¹ to assess the data regarding the diagnostic precision of a HEART score to predict MACE in ED patients. They used a variety of patient demographics and reported the authenticity of the HEART score in diverse patient groups. Furthermore, some studies have increased their duration of follow-up from 3 months to 1 year and negative likelihood ratio and sensitivity of HEART score remains majorly unaffected, suggesting that long-term MACE can also be predicted by the HEART score.^{20–24} Another meta-analysis by Van Den Berg P *et al.*²⁵ argued the use of HEART score of 0–3 for low risk categorization, as this criteria arguably reported to miss 3.3 percent of patients having MACEs. Hence, physicians should consider if this risk is acceptable for clinical application, and must be directed by indigenous factors affecting diagnostic performance.

In the light of above discussion and finding of our study patient with HEART score of 0–3 (low-risk) at the time of presentation can be considered candidates for discharge from the emergency department without extensive cardiac workup and with proper follow-up planned. However, considering the good predictive value to the HEART score for MACE within 6-weeks, ER physician should very careful in the disposition of moderate to high-risk category of patients.

To the best of our knowledge this is the first study on the validity of HEART score in the Pakistani population. Study has some limitations, such as this study was conducted at a single center with relatively small sample size and a majority of the patients were in the moderate risk group and patients with HEART score of \geq 7 (high risk) were excluded which may affect the generalizability of the study findings.

CONCLUSION

HEART score is a useful modality for the risk stratification of suspected ACS patients presenting to ER with chest pain. Risk of MACE during following 6-weeks of the index hospitalization for the patients with the HEART score of 0 to 3 is very low. Such patients can be discharged from ER without extensive cardiac workup with proper follow-up planned. While, there is a significant risk of 6-weeks MACE in patients with HEART score of 4 to 6, appropriate cardiac workup should be performed in these patients.

AUTHORS' CONTRIBUTION

RK, SK, ARM, and MK contributed to the concept and design of study, RK, SK, KZ, WR, FAAW, NA, AA, and BB contributed to the collection, analysis and interpretation of data, RK, SK, KZ, WR, FAAW, NA, AA, and MK contributed to the drafting of the manuscript, and RK and ARM critically analyzed for content. All authors have read and approved the manuscript.

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