Heart Score for Predicting In-Hospital Major Cardiovascular Event in Patient with Non ST Segment Elevation Acute Coronary Syndrome

Kamal Kharrazi Ilyas*, Sutomo Kasiman, Harris Hasan, Zulfikri Mukhtar , Refli Hasan, Abdul Halim Raynaldo

Department of Cardiology and Vascular Medicine, Faculty of Medicine, University of Sumatera Utara, H. Adam Malik Hospital, Medan, North Sumatera, Indonesia

ARTICLE INFO

ABSTRACT

Background: Acute Coronary Syndrome (ACS) is one of the main problems in the field of cardiovascular diseases because of high hospitalization rate, high mortality and high medical cost. Rapid and accurate risk stratification is needed to calculate the risk of complication and right now exist two most used score which is GRACE and TIMI. Heart score has 5 simple variables that can be calculated easily and this score considered to have better predictive ability compared to other score. The aim of this study is to examine HEART score as a predictor for in hospital Major Cardiovascular Event (MACE) in patient diagnosed as Non ST Segment Elevation Acute Coronary Syndrome (NSTEACS) that hospitalized at Haji Adam Malik (HAM) General Hospital Medan.

Methods: This is a prospective cohort study that includes 52 NSTEACS patient that hospitalized at HAM General Hospital since November 2018 until January 2019. Patient that diagnosed as NSTEACS were calculated for GRACE, TIMI, and HEART score then observed during hospitalization. Outcome of this study is MACE during hospitalization. Statistical analysis was performed to test HEART score as MACE predictor and then comparison was done with GRACE and TIMI

Results: By using ROC curve analysis, the cut-off value of HEART score was 5 (AUC 0.947, 95% CI 0.883-0.997, p<0.01). Study subject that experienced MACE with HEART score ≥5 was 21 patients (87.5%) compared to 2 patients (7.1%). HEART score ≥5 can predict MACE with sensitivity 87.5%, specificity 92.9%, negative predictive value (NPV) 89.7% and positive predictive value (PPV) 91.3%. ROC curve comparison was done between HEART with GRACE and TIMI then it was found that HEART score has better predictive ability compared to TIMI and GRACE (AUC 0.947 vs 0.829 vs 0.807, p < 0.01).

Conclusion: HEART score can be used as MACE predictor which is relatively simpler but have better predictive ability compared to GRACE and TIMI.

INTISARI

Latar Belakang: Sindrom koroner akut (SKA) sampai saat ini masih merupakan salah satu masalah yang paling utama di bidang kardiovaskular karena menyebabkan tingginya angka perawatan di rumah sakit, memiliki angka kematian yang tinggi, dan biaya perawatan yang cukup tinggi. Stratifikasi resiko yang cepat dan akurat dibutuhkan untuk menentukan resiko komplikasi dan saat ini terdapat dua skor yang paling sering digunakan yaitu GRACE dan TIMI. Skor HEART memiliki 5 komponen sederhana yang dapat dinilai dan skor ini dianggap memiliki kemampuan prediktif yang lebih baik dibandingkan dengan skor lainnya. Penelitian ini bertujuan untuk menguji kemampuan skor HEART sebagai prediktor kejadian kardiovaskular mayor (KKvM) selama rawatan pada pasien yang

didiagnosa sebagai sindroma koroner akut non elevasi segmen ST (SKANEST) di Rumah Sakit Umum Pusat Haji Adam Malik Medan (RSUP HAM).

Metode : Penelitian ini merupakan kohort prospektif 52 pasien SKANEST yang menjalani perawatan di RSUP HAM sejak November 2018 sampai Januari 2019. Semua subyek penelitian yang didiagnosa sebagai SKANEST dilakukan penghitungan skor GRACE, TIMI, dan HEART kemudian dilakukan pengamatan selama pasien dirawat. Luaran yang dipantau adalah kejadian KKvM selama rawatan. Analisa statistik dilakukan untuk menilai kemampuan skor HEART untuk memprediksi KKvM kemudian dibandingkan dengan skor GRACE dan TIMI.

Hasil : Melalui analisa kurva ROC, didapati nilai titik potong skor HEART adalah 5 (AUC 0.947, 95% CI 0.883-0.997, p<0.01). Subyek penelitian pada kelompok yang mengalami KKvM dengan skor HEART ≥ 5 yaitu 21 orang (87.5%) berbanding 2 orang (7.1%). Skor HEART ≥5 dapat memprediksi KKvMdengan sensitivitas 87.5%, spesifisitas 92.9%, negative predictive value (NPV) 89.7% dan positive predictive value (PPV) 91.3%. Dilakukan perbandingan kurva ROC antara skor HEART dengan GRACE dan TIMI dan dijumpai skor HEART memiliki kemampuan prediktif yang lebih baik dibandingkan dengan TIMI dan GRACE (AUC 0.947 vs 0.829 vs 0.807, p < 0.01)

Kesimpulan : Skor HEART dapat digunakan sebagai prediktor KKvM yang relatif lebih sederhana tetapi memiliki kemampuan prediktif yang lebih baik daripada skor GRACE dan TIMI.

Introduction

Acute coronary syndrome (ACS) is one of the main problem in the field of cardiovascular disease because of high hospitalization rate, high mortality rate, and high medical cost.[1] Globally, there are higher incidence of NSTEMI compared to STEMI probably because of changes in diagnostic criteria and usage of more sensitive cardiac marker according to survey and studies from 1990 until 2006.[2]

Mortality in patient with NSTEMI varies, where almost all studies shows in hospital mortality relatively low with higher mortality for longer term compared to STEMI.[3] NSTE-ACS can be diagnosed easily if there are typical changes in ECG and cardiac marker, but in patient with normal examination, missed diagnosis can happen and patient can be diagnosed as normal. This kind of missed diagnosis can cause out of hospital sudden death due to transformation of unstable angina pectoris into myocardial infarction.[4]

Fast and accurate risk stratification are needed for clinician to identify patient with high risk of having complication and to identify which patient need intensive care and early intervention. Several scoring system has been developed to identify patient with high risk of having major cardiovascular event (MACE). Two most frequent scoring system used are Global Registry in Acute Coronary Events (GRACE) score and Thrombolysis in Myocardial Infarction(TIMI) score.[5,6]

HEART Score created and developed in Netherlands in 2008 by Six, Backus, and Kelder as a tool to stratify risk for patient with chest pain to predict risk of having MACE in short term and help identify low risk patient. This score has several benefits such as high applicability, focusing in short term outcome and able to classify chest pain patient into three category (low risk, moderate risk, and high risk). HEART score has 5 variables which is history, ECG, age, risk factor and troponin. Lowest score possible for HEART score is 0 with maximal score of 10 that categorized into low risk ((≤ 3), moderate risk (4 – 6) and high risk (7 – 10).[7]

Poldervaart et al. (2017) did a comparison between GRACE, TIMI, and HEART score to predict short term MACE (6 weeks) and conclude that HEART score can better predict short term MACE compared to GRACE and TIMI especially in patient with low risk of having MACE.8

Because of the importance of HEART score in predicting MACE in patient with NSTE-ACS, the aim of this study is to assess the role of HEART score in predicting in hospital MACE in patient NSTEACS in Haji Adam Malik General Hospital.

Methods

Study Design

This is an observational prospective study conducted at Haji Adam Malik (HAM) General Hospital in Medan, Indonesia, with permission from the Research Ethics Committee of the Faculty of Medicine, University of North Sumatra. The study subjects were patients that diagnosed as NSTEACS that admitted to the emergency department (ED) from November 2018 until January 2019. Diagnosis of NSTEACS based on the ESC diagnostic criteria. The inclusion criterias were patients with a diagnosis of NSTEACS without any non cardiac condition that could cause increased cardiac enzyme. Patient with incomplete data were excluded from this study. HEART, GRACE, and

TIMI score was calculated in the ED then the patient observed during hospitalization..In this study, 52 peoples have met the inclusion and exclusion criterias.

Study Procedure

Baseline clinical and demographic characteristics including age, sex, previous history of illness such as diabetes mellitus, hypertension, heart failure, stroke, vascular disease and hyperlipidemia, smoking history, family history of CHD, family history of drug use and also vital sign were completely recorded. The initial important data evaluated were HEART, TIMI, and GRACE score in the emergency room of HAM General Hospital. The patient also undergoes blood test and chest x-ray. Patient then observed for MACE which includes acute heart failure, transformation into STEMI, cardiogenic shock, death, and ventricular arrythmia during hospitalization

Statistical Analysis

All statistical analyseswere carried out using the SPSS statistical software. Categoric variables are presented by number or frequency (n) and percentage (%). Numeric variables are presented with mean values with standard deviations for normally distributed data. The normality test of numeric variables in all study subjects using the Kolmogorov-Smirnov test (n>50). Bivariate analysis was done by using Mann Whitney test for numerical variable and Fisher Test for categorical variable. Correlation between HEART score with MACE analyzed by using Spearman Correlation

Analysis of ROC curve was done to find cut-off point of significant HEART score value for MACE prediction. ROC curve then compared between HEART, TIMI, and GRACE score to find which score is better to predict MACE with p value < 0.05 considered statistically significant.

Results

Baseline Characteristics

Total subject of this study is 52 patient which consist of 38 male (73.1%) and 14 female (26.9%). Based on risk factor, smoking history is the most frequent risk factor that patient have which is 41 patients (78.8%) followed by hypertension, diabetes and dyslipidemia.

Based on diagnosis, 33 patient (63.5%) diagnosed as NSTEMI and 19 patient (36.5%) diagnosed as UAP. During hospitalisation, 24 patients (46.2%) experience MACE with acute heart failure were the most frequent MACE which is 10 case (19.2%) followed by inhospital death (6 case, 11.5%), transformation into STEMI (5 case, 9.6%), ventricular arrythmia (4 case, 7.7%) and cardiogenic shock (3 case, 5.8%). Based on HEART, TIMI, and GRACE score measurement, we found the median score for HEART score were 4, TIMI score were 3 and GRACE score were 113.

Bivariate analysis by using Fisher Exact and Mann Whitney was done to assess the correlation or significant difference between baseline characteristic of this study toward MACE and we found that several characteristic had

statistical significance (p value <0.05) which is history of diabetes, heart rate, TIMI score, GRACE score, HEART score and type of NSTE-ACS. High score in GRACE, TIMI, and HEART correlate with MACE and patient with NSTEMI as a diagnosis correlate with MACE compared to UAP. Baseline characteristic according to MACE can be seen in table 1.

Table 1.
Baseline Characteristic According to MACE

| Characteristic	MACE		p
	Yes (n=24)	No (n=28)	
Sex			
Male	19 (79.2%)	19 (67.9%)	0.532
Female	14 (26.9%)	9 (32.1%)	
Age	58 (49-78)	58.5 (40-72)	0.298
Risk Factor			
Hypertension	14 (58.3%)	17 (60.7%)	> 0.05
Diabetes Melitus	15 (62.5%)	9 (32.1%)	0.05
Dislipidemia	13 (54.2%)	14 (50%)	0.788
Smoking History	21 (87.5%)	20 (71.4%)	0.191
Clinical Parameter			
Heart Rate (bpm),	97 (50-134)	75 (50-90)	<0.01
SBP (mmHg)	140 (90-180)	130 (100-160)	0.191
DBP (mmHg)	80 (60-100)	80 (60-100)	0.491
Diagnosis NSTEACS			
NSTEMI	21 (87.5%)	12 (42.9%)	0.01
UAP	3 (12.5%)	16 (57.1%)	0.01
Score			
GRACE	133 (75-181)	98 (64-145)	<0.01
TIMI	4 (2-6)	3 (1-5)	<0.01
HEART	7 (3.9)	3 (3.6)	<0.01

Correlation of HEART Score with Major Adverse Cardiac Events (MACE) in NSTE-ACS patients

We found strong positive correlation between HEART score with MACE with correlation coefficient 0.8 (p value < 0.001). HEART score have moderate positive correlation with acute heart failure incidence (r =0.522), weakly positive correlation with STEMI transformation (r =0.227) and cardiogenic shock (r =0.31) but did not have correlation with death and ventricular arrythmia during hospitalization.

Cut-off Value of HEART Score for MACE Prediction in NSTE-ACS patients

By using ROC curve, we could analyze area under curve (AUC) of HEART score which shows very high predictive ability for MACE prediction with AUC value 0.947 (p value < 0.01). Cut-off value ≥5 was considered able to predict MACE during hospitalization in NSTEACS patients with 87.5% sensitivity and 92.9% specificity (Figure. 1)

From 52 patients, 23 patients has HEART score ≥5 and 29 patients has HEART score <5. In group with HEART score ≥5, as many as 21 patients had MACE (87.5%) compared to 2 patients that did not have any MACE (7.1%).
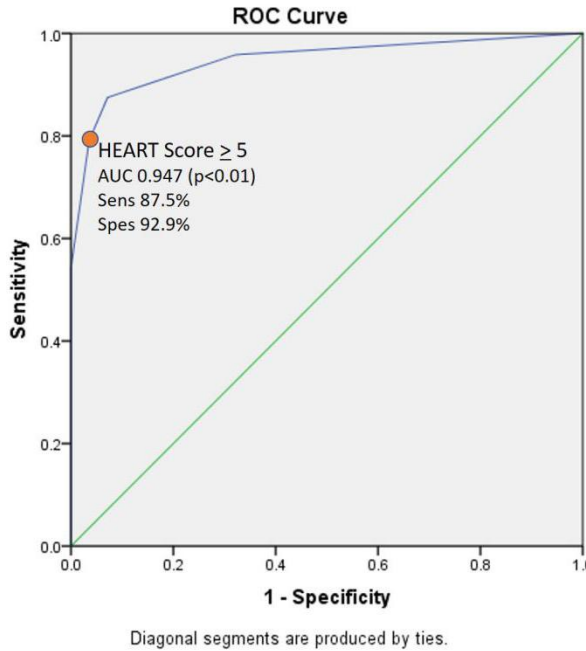
Figure 1. ROC Curve of HEART Score to Predict MACE

In HEART score <5 group, we found 26 patients (87.5%) that did not experienced MACE compared to 3 patients (12.5%) that experienced MACE. HEART score ≥5 was able to predict MACE during hospitalization for patients with NSTE-ACS with 87.5% sensitivity, 92.9% specificity, 89.7% negative predictive value, and 91.3% positive predictive value (Table 2).

Table 2.
HEART Score Analysis Result to Predict MACE

|	MACE		Sensitivity (%)	Specificity (%)	NPV	PPV
	Yes	No				
HEART Score >5	21 87.5%	2 7.1%	87.5	92.9	89.7	91.3
HEART Score < 5	3 12.5%	26 87.5%				

Comparison analysis of HEART Score with GRACE Score and TIMI Risk Score to Predict MACE in patient with NSTEACS

Because of strong correlation between HEART score and MACE, we continued with comparing HEART score with other score, such as, GRACE score and TIMI score. Comparison was done by comparing ROC curve from each score to predict MACE during hospitalization for NSTEACS patients.

From statistical analysis, we found that HEART score ≥5 has higher correlation with in hospital MACE (r =0.8, AUC =0.947) compared to TIMI score ≥ 4 (r =0.58, AUC =0.829) and GRACE score ≥108 (r =0.53, AUC =0.807) with p value < 0.01.

From three scores that can be used to predict MACE, we did diagnostic test comparison where HEART score ≥ 5 had better sensitivity, specificity, and predictive value if compared to TIMI score ≥4 (sensitivity 70.8%, specificity 78.6%) and GRACE ≥ 108 (sensitivity 75%, specificity 78.6%) with p value<0.01 (Figure 2).
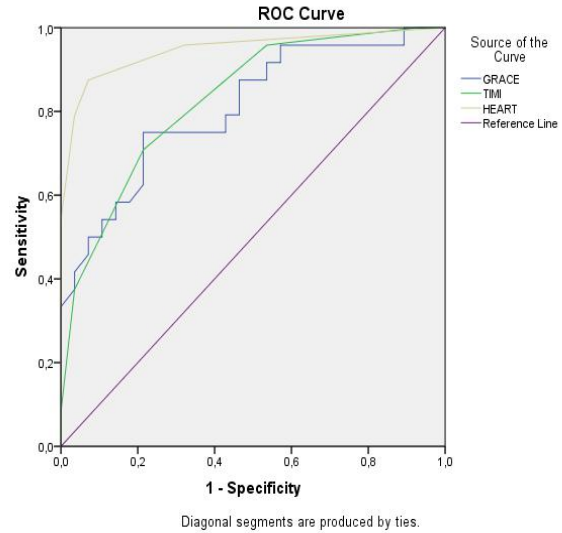
Figure 2. AUC of ROC Curve Comparison of HEART, GRACE, and TIMI

Discussion

In NSTE-ACS, which includes NSTEMI and UAP, quantitative measurement by using scoring system is better if compared to clinical assessment only. Several score that can be used to stratify risk at the moment are TIMI (Thrombolysis in Myocardial Infarction) and GRACE (Global Registry of Acute Coronary Events). Until now, GRACE score is the most accurate score that can be used for risk stratification during admission or when patients discharged.[9,10]

Baseline characteristic comparison between two groups shows no significant differences in sex and age of the patients, but we found significant differences in heart rate. In group that experiences MACE, we found higher rate of patient with diabetes as risk factor compared to group without MACE. Studies shows that there are several factor that affect short term MACE such as diabetes, older age, worsening of kidney function, male sex, recurrent chest pain with ECG changes, ventricular or supraventricular arrythmia and heart failure.[11,12]

From baseline characteristic, we found that from 52 subject, 24 patients (46.2%) experienced MACE and 28 patients (53.8%) did not. Patient evaluation by using HEART, TIMI, and GRACE score, we found significance difference between group whereas higher HEART, TIMI, and GRACE score correlate with MACE incidence during hospitalization with statistical significance p value <0.001. HEART score has very strong positive correlation with MACE incidence during hospitalization with AUC 0.947.

Study by Roffi (2016) shows that GRACE and TIMI score are one of the most objective measurement to predict mortality risk on admission, during hospitalization, and

long term where at the moment, GRACE score is the most accurate. Study by Goncalves et al (2005) also compares TIMI, GRACE, and PURSUIT score to predict prognosis in patient admitted because of acute myocardial infarction.[10,13]

Study by Backus (2008) has produced HEART score that can be used to predict risk of MACE in patient with chest pain that comes to ER where this study then validated at 2010 and it is found that score 0-3 has MACE risk around 1%, 4-6 has MACE risk 11.6% and score ≥ 7 has MACE risk 65.2%.[4,14]

We analyzed the cut-off value of HEART score to predict MACE from ROC curve. HEART score ≥5 considered as optimal value to predict MACE according to ROC curve with sensitivity 87.5% and specificity 92.9%. Subject in this study with HEART score ≥5 had higher MACE rate if compared to HEART score < 5 which is 21 patients (87.5%) versus 3 patients (12.5%). Our study consistent with meta analysis by Van den Berg and Body (2017) that shows HEART score ≤ 3cosidered as patient with low risk with MACE risk 3.3% with sensitivity 96.7% (95% CI 94-98.2%) and specificity 47% (95% CI 41-53.5%). Studies by Byrne et al (2018) also shows the same result which is HEART score ≥ 4 correlates with higher MACE even though further study was needed.[15,16]

We then compare HEART score with GRACE and TIMI to analyze this score predictive value to MACE during hospitlaization in patient with NSTEACS by comparing ROC curve and we found that HEART score has better correlation wih higher sensitivity and specificity if compared to TIMI and GRACE score.

The result of this study is consistent with study by Poldevaart (2017) which directly compare HEART, TIMI, and GRACE score in patients that come with chest pain as chief complaint and found that HEART score has higher discriminative ability to predict MACE especially in patient with low risk without compromising safety of the patient with AUC of GRACE, HEART and TIMI were 0.73 (95% CI: 0.70–0.76%), 0.86 (95% CI: 0.84–0.88%) dan 0.80 (95% CI: 0.78–0.83%) respectively. Same study also done by Sakamoto et al (2016) with consistent result which is if compared between HEART, TIMI, and GRACE in patient with typical cardiac chest pain then HEART score is better than TIMI or GRACE for 30-days MACE prediction.[8,17]

Study Limitation

Sample size in this study is relatively smaller than other study and only collected from one hospital so this study has bias potential and subject observation only done during hospitalization so we need longer and continual observation for patient for HEART score to be more representative to be used for daily practice.

Conclusion

This study concludes that HEART score can be used as predictor for major adverse cardiovascular event during hospitalization in patients with NSTEACS. HEART score ≥5 as cut off point to predict MACE during hospitalization in

patients with NSTEACS according to ROC curve has higher predictive value to predict MACE if compared to GRACE and TIMI score.

Funding

Reference

1. World Health Organization. 2017. The Top 10 Causes of Death. Diunduh dari: http://www.who.int/mediacentre/factsheets/fs310/en/

2. Gomar FS, Quilis CP, Leischik R, Lucia A. 2016. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med, 4:256.

3. Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al. 2002. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin – The Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ACS). Eur Heart J, 23: 1190-1201.

4. Six AJ, Backus BE, Kelder JC. 2008. Chest Pain in the emergency room : value of the HEART score. Neth Heart J, 16:191-196.

5. Lee TH, Goldman L. 2000. Evaluation of the patient with acute chest pain. N Engl J Med, 342:1187-1195.

6. Visser A, Wolthuis A, Breedveld R, ter Avest E. 2015. HEART score and clinical gestalt have similar diagnostic accuracy for diagnosing ACS in an unselected population of patients with chest pain presenting in the ED. Emerg Med J, 32:595-600.

7. Brady W, de Souza K. 2018. The HEART score: A guide to its application in the emergency department. Turk J Emerg Med, 18:47-51.

8. Poldervaart JM, Langedijk M, Backus BE, Dekker IMC, Six AJ, Doevendans PA, et al. 2017. Comparison of the GRACE, HEART and TIMI score to predict major adverse cardiac events in chest pain patients at the emergency department. Int J Cardiol, 227 : 656-61.

9. Juzar DA, Danny SS, Irmalita, Tobing DP, Firdaus I, Widyantoro B, dkk. 2018. Pedoman Tatalaksana Sindrom Koroner Akut. Edisi Keempat. Jakarta: Perhimpunan Dokter Spesialis Kardiovaskular Indonesia (PERKI).

10. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2016. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Task force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J, 37:267-315.

11. Grabowski M, Filipiak KJ, Opolski G, Główczyńska R, Gawałko M, Balsam P, et al. 2018. Risk factors for adverse outcomes of patients with acute coronary syndrome: single-centre experience with long-term follow-up of treated patients. Kardiol Pol, 76:881-888.

12. Chehab O, Qannus AS, Eldirani M, Hassan H, Tamim H, Dakik HA.2018. Predictors of in-hospital mortality in patients admitted with acute myocardila infarction in a developing country. Cardiol Res, 9:293-299.

13. Goncalves PA, Ferreira J, Aguiar C, Seabra-Gomes R. 2005. TIMI, PURSUIT, and GRACE risk scores : sustained prognostic value and interaction with revascularization in NSTE-ACS. Eur Heart J, 26:865-872.

14. Backus BE, Six AJ, Kelder JC, Mast TP, Acker F, Mast EG, et al. 2010. Chest pain in the emergency room: A multicenter validation of the HEART score. Crit Pathways in Cardiol, 9:164-169.

15. Van Den Berg P, Body R. 2018. The HEART score for early rule out of acute coronary syndromes in the emergency department: a systematic review and meta-analysis. Eur Heart J Acute Cardiovasc Care, 7:111-119.

16. Byrne C, Toarta C, Backus B, Holt T. 2018. The HEART score in predicting major adverse cardiac events in patients presenting to the emergency department with possible acute coronary syndrome: protocol for a systematic review and meta-analysis. Syst Rev, 7:148.

17. Sakamoto JT, Liu N, Koh ZX, Fung NX, Heldeweg ML, Ng JC, et al. 2016. Comparing HEART, TIMI, and GRACE scores for prediction of 30-day major cardiac adverse events in high acuity chest pain patients in the emergency department. Int J Cardiol, 221:759-764.