Association Between CHA2DS2-Vasc Score with In Stent Restenosis in Acute Coronary Syndrome Patients Undergoing Percutaneous Coronary in Haji Adam Malik General Hospital Medan

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Abstract:-
Background: Acute coronary syndrome is one of many primary causes of mortality and morbidity in the world. Interventional therapy has been known to cause complications, which is in-stent restenosis (ISR). The CHA2DS2-VASc score consisted of 8 components that were thought to be associated with ISR. Several studies have suggested using the CHA2DS2-VASc score to predict the occurrence of ISR.

Objective: The objective of this study was to determine whether the incidence of ISR in patients with acute coronary syndrome undergoing percutaneous coronary intervention at Haji Adam Malik General Hospital Medan was correlated with the CHA2DS2-VASc score.

Methods: This was an observational analytic study, with a retrospective cohort design. The study was carried out at Haji Adam Malik General Hospital Medan since July 2020. The research sample was ACS patients at Haji Adam Malik General Hospital Medan. ISR was assessed by finding ≥50% narrowing of the stent or peri-stent segments luminal diameter at follow-up coronary angiography. To assess the relation between the CHA2DS2-VASc score and the incidence of ISR, bivariate analysis was performed. A p value < 0.05 was considered to be significant statistically.

Results: From the total of 96 people, 46 (47.92%) of whom had ISR. The group that experienced ISR, in general, consisted of older mean age, more history of congestive heart failure, stroke, dyslipidemia, hypertension, and diabetes mellitus, as well as lower LVEF values, higher median FBG, lower mean HDL, and higher mean LDL. The variables that had a statistically significant association with ISR (p < 0.05) were hypertension, dyslipidemia, congestive heart failure, LVEF, HDL, LDL, and CHA2DS2-VASc score. Chi-square analysis of the CHA2DS2-VASc score and the incidence of ISR showed that the two variables had a significant correlation statistically (p < 0.0001; RR 14.58; CI = 6,026-44,997).

Conclusion: The CHA2DS2-VASc score was statistically significant with the incidence of ISR in patients with ACS undergoing percutaneous coronary intervention at Haji Adam Malik General Hospital Medan (p < 0.001; RR 14.58; CI = 6,026-44,997). Patient characteristics that were significant statistically with the occurence of ISR were hypertension, dyslipidemia, congestive heart failure, LVEF, HDL, and LDL.

Keyword:- CHA2DS2-VASc Score, In-Stent Restenosis, Acute Coronary Syndrome.

I. INTRODUCTION

One of the many major causes of mortality and morbidity in the world is cardiovascular diseases, primarily coronary heart disease (CHD).[1] Data from 2013 Basic Health Research (Riskesdas) in Indonesia shows that the most common cardiovascular diseases besides CHD is heart failure. The incidence of CHD is directly proportional with age, reaching 3.6%. The incidence of heart failure increases proportionately with age, ranging from 0.5% (65 - 74 years) to 1.1% (≥75 years).[2]

Acute Coronary Syndrome (ACS) describes various clinical signs of acute myocardial ischemia. Clinical manifestations of ACS can be as acute myocardial infarction with ST elevation (STEMI), non-ST elevation acute myocardial infarction (NSTEMI), or unstable angina pectoris (UAP).[3,4]

Smoking, hyperlipidemia, diabetes, and hypertension are the most common risk factors for CHD.[5] Risk stratification is of primary importance in predicting prognosis and determining treatment. The Global Registry for Acute Coronary Events (GRACE) score and the Thrombolysis in Myocardial Infarction (TIMI) score are recommended in recent guidelines for risk stratification of ACS-NSTEMI.[6]

In-stent restenosis (ISR) remains as an unsolved clinical challenge in the era of interventional cardiology. Several studies have shown that several factors, namely clinical, procedural, patient-related, and lesion-related related factors are related to the incidence of ISR. Chronic conditions associated with elevated inflammation such as diabetes, hypertension, heart disease, stroke, in addition to percutaneous coronary intervention (PCI) related procedural problems, are considered to be major risk factors for ISR.[7]

The CHADS2 score is known for being a tool in predicting the risk of stroke occurrence in non-valvular atrial fibrillation patients. In daily practice, the CHA2DS2-VASc is

preferred over CHADS2 score, since the former is better in risk stratification in patients that are low-risk. The CHA2DS2-VASc score consists of components of history of congestive heart failure (C), history of hypertension (H), having the age of ≥75 years old (A2), history of diabetes (D), history of transient ischemic attack (TIA) or stroke (S2), history of vascular disease (V), having the age of 65–74 years old (A), the male gender (Sc, Sex category).[8]

The author in this study evaluates the CHA2DS2-VASc score as a predictive tool of the incidence of IRS during treatment in ACS patients at the Haji Adam Malik General Hospital Medan.

II. METHODS

Study population

The data were taken from acute coronary syndrome patient that undergoes percutaneous coronary intervention at Haji Adam Malik General Hospital Medan, with nonprobability sampling method, namely purposive sampling. This study involved 96 acute coronary syndrome patients, taken from medical record that fulfils the inclusion and exclusion criteria. Patient with incomplete medical record, under long-term steroid treatment, evidence of malignancy, and metabolic comorbid disease, with atrial flutter and atrial fibrillation, and that are loss to follow up were excluded.

CHA2DS2-VASc score and In Stent Restenosis evaluation

This was an observational analytic study, with a retrospective cohort study design. Researchers examined the patients' medical records for history, physical examination, electrocardiography (ECG), blood laboratory, and angiography, then recorded the CHA2DS2-VASc scoring data. The study samples were split into 2 groups, the first being ACS patients that experienced ISR. Meanwhile, the second was ACS patients that did not experience ISR. ISR was determined by finding ≥50% narrowing of the stent or peri-stent segment luminal diameter (defined as the length from distal and proximal to the edge of the stent of 5 mm) at coronary angiography follow up, while non-ISR was determined by finding <50% narrowing to no stenosis at all.

Statistical analysis

Data were analysed using SPSS version 24. Bivariate analysis used the Independent T-test (T-test), otherwise Mann-Whitney test is used if it did not meet the requirements. Chi-square test will then be carried out if the requirements are met or an alternative Fisher's exact test. Relative risk was assessed by comparing the number of ISR patients in the risk group (CHA2DS2-VASc score of ≥4) with the number of ISR patients in the no-risk group (CHA2DS2-VASc score of <4), RR was said to be significant if it did not pass 1, with confidence interval (CI) 95%.

III. RESULTS

The number of samples that fulfilled the inclusion and exclusion criteria in this study were 96 people. The main data required were a history of ISR events and a total CHA2DS2-VASc score. Patient characteristics data were also analysed for the incidence of ISR. The results of the analysis can be seen in table 1.

Table 1. Characteristics of the samples

Variable	ISR (+); n=46	ISR (-); n=50	p
Age (years old), mean ± SD	59,33 ± 8,54	56,32 ± 8,36	0,085[a]
Sex, n (%)			
Male	37 (80,43)	40 (80)	0,957[b]
Female	9 (19,57)	10 (20)	
Diabetes mellitus, n (%)			
Yes	27 (58,70)	22 (44)	0,150[b]
No	19 (41,30)	28 (56)	
Hypertension, n (%)			
Yes	37 (80,43)	20 (40)	<0,001[b]
No	9 (19,57)	30 (60)	
Dyslipidemia, n (%)			
Yes	19 (41,30)	0 (0)	<0,001[b]
No	27 (58,70)	50 (100)	
Smoking, n (%)			
Yes	32 (69,57)	34 (68)	0,869[b]
No	14 (30,43)	16 (32)	
Stroke, n (%)			
Yes	2 (4,35)	0 (0)	0,227[c]
No	44 (95,65)	50 (100)	
Congestive heart failure, n (%)			
Yes	45 (97,83)	37 (74)	0,001[b]

No	1 (2,17)	13 (26)	
LVEF (%), mean ± SD	46,3 ± 10,21	53,92 ± 10,53	0,001[a]
Hb (g/L), mean ± SD	13,44 ± 2,31	13,87 ± 1,52	0,286[a]
Platelet (x10³/μL), mean ± SD	269,82 ± 77,79	277,85 ± 63,23	0,579[a]
Leukocyte (x10³/μL), median ± SD	8,76 ± 5,53	7,53 ± 2,55	0,081[d]
FBG (mg/dL), median ± SD	108 ± 82,7	102,5 ± 97,7	0,939[d]
HDL (mg/dL), mean± SD	42,17 ± 11,26	47,18 ± 11,74	0,036[a]
LDL (mg/dL), mean ± SD	135,46 ± 40,18	94,1 ± 17,58	<0,001[a]
TG (mg/dL), median ± SD	132,5 ± 45,99	142 ± 45,29	0,122[d]
Post angiography ISR period (days), median ± SD	27 ± 34,12	23,5 ± 39,77	0,023[d]
CHA₂DS₂-VASc score, median ± SD	3 ± 0,81	2 ± 0,77	<0,001[d]

Description: analysis using [a]Unpaired T test [b]Chi-Square test [c]Fisher test [d]Mann-Whitney test.

Based on the occurrence of ISR, the sample of 96 people was split into 2 groups, 46 of 96 of whom had ISR. Table 1 represents the characteristics of research subjects based on several variables, namely age, gender, hypertension and dyslipidaemia, history of diabetes, history of smoking, stroke, congestive heart failure, LVEF values, haemoglobin, platelets, leucocytes, fasting blood sugar, HDL, LDL, and triglycerides. Compared to the group that did not experience In Stent Stenosis, the group that experienced ISR in general consisted of an older mean age, more history of diabetes, hypertension, dyslipidaemia, stroke, and congestive heart failure, and a lower mean LVEF value, higher median FBG, mean HDL was lower, and mean LDL was higher. When it comes to median, the CHA2DS2-VASc score was higher significantly in the group that experienced In Stent Stenosis than in those who did not. Statistically, the variables that were associated significantly with the occurrence of ISR (p < 0.05) based on table 1 were hypertension, dyslipidaemia, congestive heart failure, LVEF, HDL, LDL, post angiography ISR period, and CHA2DS2-VASc score.

Table 2. ACS patient category based on CHA2DS2-VASc score and ISR incidence

Category	Number (n)	Percentage (%)
CHA₂DS₂-VASc score		
High	48	50
Low	48	50
Total	96	100
ISR incident		
Yes	46	47,92
No	50	52,08
Total	96	100

Table 2 presents the number and percentage of ACS patients according to their CHA2DS2-VASc score and the incidence of ISR. According to their CHA2DS2-VASc score, the high and low risk groups were 50% each (n = 48). Based on the incidence of ISR, it was found that more samples did not experience ISR, namely 52.08% (n = 50).

Table 3. Location of the ISR

Location of the ISR	ISR (+)	ISR (-)	Total
Left arterior descending artery	29 (30,2%)	67 (69,8%)	96
Left circumflex artery	8 (8,3%)	88 (91,7%)	96
Right coronary artery	15 (15,6%)	81 (84,4%)	96

Table 3 describes the arterial locations where ISR occurs. The most common locations for ISR were the left arterior descending (LAD) artery, then right coronary artery (RCA), and finally left circumflex (LCX) artery with a percentage of 30.2%, 15.6%, and 8.3%, respectively.

Table 4. Chi-Square analysis of the CHA2DS2-VASc score and the incidence of ISR

		ISR Incidence				p
		Yes		**No**		
		n	%	n	%	
CHA₂DS₂-VASc score	High	37	77,08	11	22,92	<0,001
	Low	9	18,75	39	81,25	
Total		46	47,92	50	52,08	

Table 4 presents the results of the chi-square analysis of the CHA2DS2-VASc score and the incidence of ISR. This study reported that the CHA2DS2-VASc score was correlated with ISR incidence (p < 0.05). RR value in this study was 14.58 (95% confidence interval [CI] = 6.026 to 44.997), which suggests that patients in the category of high CHA2DS2-VASc score were at risk of experiencing ISR 14.58 times higher compared to patients in the category of low CHA2DS2-VASc score.

IV. DISCUSSION

The percentage of subjects with a CHA2DS2-VASc score of ≥4 and <4 was 50% on each score group, while the percentage of subjects who had an ISR incidence was 47.92% and who did not have an ISR incidence was 52.08%. ISR and stent thrombosis are still the most common complications in stent placement.[9] The occurrence of an ISR after BMS implantation has been known to be linked with several clinical factors, lesions, procedures, and patient-related. Patient-related factors referred to are age, gender, history of renal failure, congestive heart failure, hypertension, diabetes mellitus, and angiographic factors namely the diameter and length of the stent.[10]

In this study, variables of age, gender, history of smoking, stroke, diabetes mellitus, and blood profile did not show a significant association with ISR ($p > 0.05$). Meanwhile, hypertension, dyslipidaemia, history of congestive heart failure, ISR period after angiography, were found to be significantly correlated with ISR.

This study reported that the CHA2DS2-VASc score was associated significantly with the incidence of ISR ($p < 0.001$) with RR = 14.58; 95% CI = 6,026-44,997. CHA2DS2-VASc score comprises of history of congestive heart failure (C), history of hypertension (H), having the age ≥75 years old (A_2), history of diabetes (D), history of transient ischemic attack (TIA) or stroke (S_2), history of vascular disease (V), having the age of 65–74 years old (A), the male gender (Sc, Sex category).[8] Acute coronary syndrome is influenced by modifiable and non-modifiable risk factors. Age, gender, diabetes mellitus, smoking, and hypertension are risk factors that have been widely accepted as major risk factors for ACS. These risk factors are included in the component of the CHA2DS2-VASc score.[7]

Other studies regarding the CHA2DS2-VASc score and the incidence of ISR also found the same result. Yilmaz et al. concluded that the CHA2DS2-VASc score was an independent predictor of ISR in ACS patients (area under curve = 0.79; 95% CI = 0.71-0.86), thus the study concluded that the cheaper and simpler CHA2DS2-VASc score can be utilised as a predictive tool for the incidence of ISR, having the sensitivity value of 82% and a specificity value of 76%.[7] Another study with the same objective found that the CHA2DS2-VASc score was an independent risk factor for ISR (odds ratio [OR] = 2.004; 95% CI = 1.361-2.949, $p < 0.001$). Another study aimed at evaluating the association of CHA2DS2-VASc score with ischemic incidence in patients undergoing percutaneous intervention concluded that a high CHA2DS2-VASc score was associated with patient mortality (OR = 3.71; 95% CI = 1,89-7,3), thus concluding that this score is useful as a risk stratification tool in patients with ACS undergoing percutaneous intervention.[11]

V. CONCLUSION

CHA2DS2-VASc score was statistically significant and associated with the incidence of ISR in ACS patients who received percutaneous coronary intervention at Haji Adam Malik General Hospital Medan ($p < 0.001$). The RR value obtained from the study was 14.58 with a 95% CI of 6.026-44.997. The mean age of patients in the study was 57.76 ± 8.54 years old, gender was dominated by male patients as many as 77 people (80.21%), with a history of comorbidities with diabetes as many as 49 people (51.04%), hypertension 57 people (59.38%), dyslipidaemia 19 people (19.79%), stroke 2 people (2.08%), and congestive heart failure 82 people (85.42%). Several patients' characteristics were analysed for the incidence of ISR and it was found that hypertension, dyslipidaemia, congestive heart failure, LVEF, HDL, and LDL were statistically significant with the incidence of ISR.

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