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Original Article

The Association between CHA_2DS_2-VASc Score with Increased Serum Creatinine Level in ACS Patients Undergoing PCI at RSUD dr. Saiful Anwar Malang

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ABSTRACT

Background: The current literature on the relationship between the congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category (CHA_2DS_2-VASc) score and increased Serum Creatinine (SCr) among Acute coronary syndrome (ACS) patients is noticeably limited in scope.
Objective: Therefore, the primary objective of this study was to assess the correlation between CHA_2DS_2-VASc score with increased of Serum Creatinine in patients with ACS undergoing Percutaneous coronary intervention (PCI) procedures.
Material and Methods: In this study, a total of 527 participants were recruited, comprising two groups: Increased SCr level (n=159) and normal SCr level (n=368). Data pertaining to clinical information and demographic characteristics, such as gender, age, diabetes mellitus (DM), hypertension (HT), congestive heart failure (CHF), history of stroke or transient ischemic attack (TIA), and vascular disease, were gathered from various sources, including registry data and medical records, diagnostic physical examination, electrocardiography and laboratory records. Logistic regression analysis was employed to assess the association between the CHA_2DS_2-VASc score and the incidence of increased SCr level.
Result: In our study, we observed that the CHA_2DS_2-VASc scores were significantly higher in the group of patients who increase SCr level compared to those who did not increase SCr level. Furthermore, our Receiver Operating Characteristic (ROC) analysis revealed that a CHA_2DS_2-VASc score cutoff of was determined to be the optimal threshold for estimating the increased SCr level (AUC= 0.805, 95% CI 0.762-0.848; p<0.01).
Conclusion: The CHA_2DS_2-VASc score serves as a valuable tool for estimating the likelihood of SCr in patients undergoing PCI, offering a foundational assessment. Additionally, in PCI patients, an increase in the CHA_2DS_2-VASc score exceeding 3 is indicative of a heightened incidence of increased SCr level.

1. Introduction

Percutaneous coronary intervention (PCI) is effective in reducing angina symptoms and myocardial ischemia rates in stable chronic coronary syndromes. However, despite these benefits, several studies have not found a significant improvement in survival rates. On the other hand, evidence indicated that patients with ST-segment elevation acute myocardial infarction (STEMI) experience a survival advantage from PCI.[1] There was evidence to support the reduction of ischemia burden in chronic coronary syndromes through PCI, especially in individuals with a history of high risk. However, it was important to note that the administration of intravenous contrast media during PCI procedures and pre-renal factors, increased the risk of renal impairment.

Additionally, the increased serum creatinine level has been associated with a longer average hospital stay, higher healthcare expenses, and in particular, a higher inpatient mortality rate.[2] In the 2018 European Society of Cardiology (ESC) Guidelines on Myocardial Revascularization, the evaluation of all patients at risk of increased creatinine level was upgraded from a suggestion (IIa) to a recommendation (1C). Recently, several risk scores have been devised to determine the possibility of developing renal impairment. Serum creatinine (SCr) level serves as the initial marker for all types of kidney injury risk scores. However, it should be noted that factors such as age, sex, and muscle mass can influence SCr levels, and these factors may not be promptly assessed to detect underlying renal dysfunction.[3,4,5]

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An investigation involving individuals with stable coronary artery disease who underwent PCI demonstrated a correlation between the CHA_2DS_2-VASc score and the development of renal impairment.[6] Moreover, in another study, it was observed that the factors comprising the CHA_2DS_2-VASc score were associated with a higher risk of unexpected clinical outcomes in cardiovascular disease.[5] Patients with stable coronary artery disease and ACS may experience renal impairment, one of the most significant side effects of PCI.[7] Patients who are susceptible to renal impairment continue to present a difficult challenge. The renal impairment risk factors include advanced age, being a woman, diabetes, heart failure or left ventricular dysfunction, and decreased renal function.[8,9,10] In fact, one study reported an association between hypertension and the development of increased serum creatinine level.[11] The same factor responsible for the occurrence of renal impairment also comprise the components of the CHA_2DS_2-VASc score.[12] Therefore, this study aimed to assess the value of the CHA_2DS_2-VASc score in determining the occurrence of increased serum creatinine level among patients with ACS undergoing PCI procedures.

2. Material and Methods

2.1. Study design

In this study, a retrospective cohort design was employed to investigate potential role of CHA_2DS_2-VASc score to estimate the incidence of increased SCr level among ACS patients, both those with STEMI and Non-STEMI, who underwent PCI at RSUD dr. Saiful Anwar Malang. The Health Research Ethics Committee at RSUD dr. Saiful Anwar Malang had verified that this study adhered to all ethical guidelines and conformed with the principles outlined in the Declaration of Helsinki (No. 400/098/K.3/102.7/2023).

2.2. Study covariates

Clinical data and demographic characteristics, such as gender, diabetes mellitus (DM), age, and hypertension (HT), were collected by reviewing medical records, conducting diagnostic physical examinations, analyzing electrocardiography results and examining laboratory data.

The diagnosis of STEMI was confirmed when specific criteria are met, including typical chest pain consistent with myocardial infarction (lasting more than 20 minutes and potentially radiating to the neck, lower jaw, or left arm, unresponsive to nitrates, and accompanied by autonomic nervous system activation symptoms such as nausea, vomiting, and cold sweats), persistent ST-segment elevation of more than 1 mm in other leads or 2 mm in leads V2 and V3, or new or recent onset of left bundle branch block (LBBB). Additionally, elevated serial cardiac enzyme markers (such as CKMB and troponin) indicating myocardial necrosis are considered in the diagnosis.[13] The diagnosis of NSTEMI is confirmed in the presence of acute chest pain consistent with myocardial infarction, without persistent ST-segment elevation on ECG leads. Patients meeting these criteria typically exhibited ST-segment depression, inverted or flat T waves, or even no apparent ECG changes. However, the diagnosis was supported by evidence of elevated cardiac enzymes.

Increased of creatinine level was defined in this study as an increase in SCr levels of at least 0.5 mg/dl (44 mol/L) or a relative increase of at least 25% from the baseline value within the first 48-72 hours in hospitalized patient.[14] PCI was defined as a coronary revascularization procedure that encompassed both coronary angiography and percutaneous transluminal coronary angioplasty. The CHA_2DS_2-VASc score is a risk scoring system developed by the ESC that incorporates multiple variables. These variables include congestive heart failure (score of 1), hypertension (score of 1), age ≥75 years (score of 2), DM (score of 1), history of stroke (score of 2), presence of vascular disease (score of 1), and age between 65 to 74 years (score of 1). The total score on the CHA_2DS_2-VASc scale can range from 0 to 9, with a higher score indicating a higher risk.[15] Congestive heart failure (CHF) is characterized by moderate to severe left ventricular dysfunction, indicated by a left ventricular ejection fraction (LVEF) of 40% or less, or the presence of new-onset heart failure requiring hospitalization. This definition applies irrespective of the ejection fraction value.[16] Chronic kidney disease is defined as a baseline SCr > 1.5 mg/dl or a decrease in kidney function with a GFR <60 ml/min/1.7 m2 for more than or equal to 3 months or a structural disorder with pathological abnormalities.[17] DM is characterized as individuals who have a history of taking oral hypoglycemic drugs or insulin, or those whose blood sugar levels were assessed during hospitalization and met at least one of the following criteria: HbA1c level of 6.5% or higher, fasting blood sugar level of 126 mg/dl or higher, or postprandial blood glucose level of 200 mg/dl or higher.[18]

2.3. Statistical analysis

Categorical variables were presented using numbers (n) and percentages (%), while continuous variables were presented by their mean, standard deviation, or median value. To evaluate the normal distribution of numerical variables among the study subjects, the one-sample Kolmogorov-Smirnov test was employed. The numerical data of the two groups were compared using either the unpaired t-test or the Mann-Whitney U test, depending on the data distribution. For categorical data, the Chi-Square test or Fisher's exact test was employed. Variables that exhibited statistical significance in the bivariate analysis were subsequently included in the multivariate analysis (logistic regression). A correlation test was performed using the Spearman correlation coefficient for normally distributed data and the Pearson correlation coefficient for data that did not follow a normal distribution. Receiver operating characteristic (ROC) curve analysis was conducted to assess the sensitivity and specificity of the CHA_2DS_2-VASc score in increased of SCr level. A significance level of $p<0.05$ was used to determine statistical significance. The software used for data analysis in this study was Statistical Package for the Social Sciences (SPSS) version 17 (SPSS Inc., Chicago, IL, RRID:SCR_002865).

3. Result

3.1. Baseline characteristics

The study participants had an average age of 57.2 years, ranging from 26 to 95 years, representing the youngest and oldest individuals in the sample, respectively. Of the study subjects, 385 individuals (73.1%) were male, while 142 individuals (26.9%) were female. Significant differences in age, sex category, hypertension, CHF, DM , stroke, vascular disease and Killip levels were observed between patients in the Increased of SCr group and those normal SCr level group, with a statistically significant finding ($p<0.05$). Regarding other characteristics, there were no statistically significant differences between the increased of SCr level group and the normal SCr level group (Table 1).

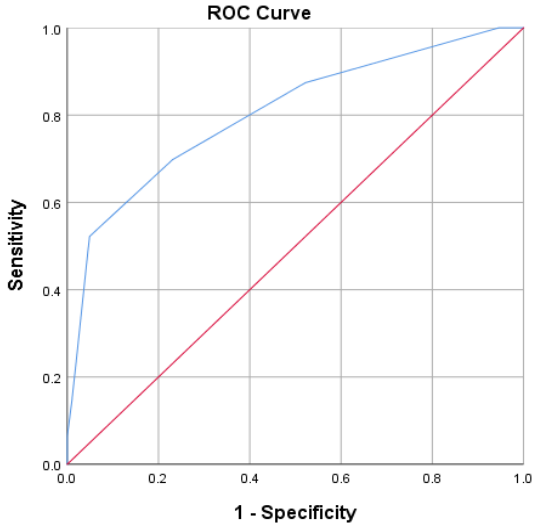
3.2. The Association between CHA2DS2-VASC score and risk of increased SCr level among ACS patients undergoing PCI

Our study revealed that the group of patients who increased SCr exhibited significantly higher CHA_2DS_2-VASc scores compared to those who did not increased SCr level, with a statistically significant difference ($p<0.01$). The ROC curve analysis demonstrated the significant predictive ability of the CHA_2DS_2-VASc score for increased SCr level following PCI, with an area under the curve (AUC) of 0.805 (95% CI 0.762-0.848; $p<0.01$). Based on the significance of the cutoff value, the CHA_2DS_2-VASc score was further evaluated in the study population. Notably, a CHA_2DS_2-VASc score 3 exhibited the best sensitivity (69.8%) and specificity (76.9%) (Figure 1).

Table 1. Clinical characteristics of patients included in our study

Characteristic	Serum Creatinine Level		P Value
	Increased SCr level (n=159)	Normal SCr level (n=368)	
Age	57.96 ± 11.551	56.91 ± 9.869	0.291
Male Sex	130 (81.8)	255 (69.3)	<0.01
Hypertension	87 (54.7)	154 (41.8)	0.02
CHF	73 (45.9)	53 (14.4)	<0.01
DM	55 (34.6)	74 (20.1)	<0.01
Cinical presentation			
NSTEMI	30 (18.9)	73 (19.8)	0.664
STEMI	111 (69.8)	241 (65.5)	
UAP	18 (11.3)	53 (14.4)	
Stroke / TIA	9 (5.7)	2 (0.5)	<0.01
Vascular Disease	73 (45.9)	53 (14.4)	<0.01
Killip			<0.01
1	10 (6.3)	260 (70.7)	
2	99 (62.3)	57 (15.5)	
3	50 (31.4)	51 (13.9)	
Statin	158 (99.4)	365 (99.2)	0.821
ACEI	138 (86.8)	319 (86.7)	0.973
ARB	61 (38.4)	136 (37)	0.759
B-Blocker	62 (39)	164 (44.6)	0.236
SBP	130.8 ± 28.4	126.1 ± 31.4	0.113
DBP	78.5 ± 16.8	77.5 ± 18.4	0.549
HR	82.8 ± 21.1	85.7 ± 23.3	0.169
CHA_2DS_2-VASc	3.3522 ± 1.48894	1.7 ± 1.0	<0.01

Note, SCr, Serum Creatinine; DM, diabetes mellitus; STEMI, ST-elevation myocardial infarction; NSTEMI, Non-ST-segment Elevation Myocardial Infarction; UAP, Unstable angina pectoris; TIA, Transient ischaemic attack; ACEI, Angiotensin-converting enzyme inhibitor; ARB, Angiotensin receptor blocker; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; CHA_2DS_2-VASc, congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category.



Area Under Curve: 0.805 (95% CI 0.762-0.848), P Value: <0.01

Figure 1. The ROC of CHA_2DS_2-VASc score and the incidence of increased SCr level. Note, CHA_2DS_2-VASc, congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category.

Among the patients, 15.7% had a CHA_2DS_2-VASc score > 3, while 14.4% had a CHA_2DS_2-VASc score < 3. The findings of this study suggested that patients with a CHA_2DS_2-VASc score > 3 have a 1.09 times higher risk of increase SCr following PCI procedures compared to patients with a CHA_2DS_2-VASc score < 3. (Table 2)

Table 2. A summary of the association between CHA_2DS_2-VASc score and the risk of increased creatinine serum level among ACS patients who underwent PCI

Score parameter	Increased SCr Level		MD / RR	95% CI	p-value
	Increased SCr level (n=159)	Normal SCr level (n=368)			
CHA_2DS_2-VASc	3.35 ± 1.48	1.75 ± 1.00	-0.30	(-0.53)-(0.06)	<0.01
CHA_2DS_2-VASc < 3	70 (47.8)	356 (95.1)	0.73	0.72 – 0.96	<0.01
CHA_2DS_2-VASc > 3	83 (52.2)	18 (4.9)	1.09	1.1 – 1.73	<0.01

Note, CHA_2DS_2-VASc, congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category; ACS, Acute coronary syndrome; PCI, Percutaneous coronary intervention; MD, mean difference; RR, relative risk

4. Discussion

Our study revealed a positive association between a CHA_2DS_2-VASc score and the incidence of increased SCr level in ACS patients following PCI procedures. The findings from our analysis indicated that the relationship between the CHA_2DS_2-VASc score and the outcome is notably stronger. However, it was crucial to emphasize that these results needed to be confirmed through a more extensive sample size. Diverging from earlier study, Kurtul et al. established that among patients with ACS undergoing PCI, a CHA_2DS_2-VASc score of 4 was determined as the most effective cutoff point for predicting the occurrence of renal impairment.[7]

The precise mechanism underlying the findings in this study remained unknown. However, several possible mechanisms might be considered. Based on previous study, it was suggested that renal vasoconstriction, endothelial dysfunction, and endothelial cell damage are primary factors contributing to the development of renal impairment. This is subsequently followed by renal tubular injury and hypoxia in the renal medulla. Advanced age, diabetes mellitus, female, CHF, and renal impairment have been recognized as risk factors for renal injury, and these factors are components of the CHA_2DS_2-VASc score.[8,9,10] Therefore, it was reasonable that our study findings demonstrated the utility of the CHA_2DS_2-VASc score in predicting renal impairment events.

This study also revealed a noteworthy association between SBP and the risk of renal impairment. Previous studies have indicated that persistent elevation of arterial blood pressure could contribute to the development of arteriosclerosis and impair the renal vasculature's ability to regulate blood pressure. This may lead to thickening of the renal arterioles, hypertension, increased glomerular capillary filtration, and subsequent ischemia and glomerular sclerosis.[14] Consistent with these findings, the study conducted by Modi et al. demonstrated a significantly higher prevalence of hypertension in the group of patients with renal impairment compared to the normal group. The presence of hypertension was considered a risk factor for renal impairment, particularly in elderly individuals undergoing coronary angiography and PCI procedures.[19]

This study no found statistically significant differences between the increased SCr level group and normal SCr level groups in terms of baseline characteristics, such as clinical presentation, diastolic blood pressure and heart rate. These findings suggested that the baseline characteristics evaluated in this study were not confounding factors.

This study carried several clinical implications that might contribute to patient care and research in the future. Firstly, by identifying the CHA_2DS_2-VASc score association with renal impairment in patients undergoing PCI, clinicians may utilize this score as a simple and practical tool for risk assessment. This may aid in early identification and intervention strategies to prevent or minimize renal impairment. Secondly, the findings highlighted the importance of considering specific risk factors, such as advanced age, diabetes mellitus, and congestive heart failure, in patients undergoing PCI to mitigate the risk of renal impairment. This knowledge might guide personalized treatment decisions and optimize patient outcomes. Lastly, the study emphasized the need for further research in larger and more diverse populations to validate and refine the predictive capacity of the CHA_2DS_2-VASc score for renal impairment. Future studies should also explore additional risk factors and investigate potential interventions to reduce the incidence of renal impairment in this patient population.

This study had certain limitations that should be acknowledged. Firstly, our study was conducted at a single center, which may limit the generalizability of the findings. Additionally, the sample size employed in this study was relatively small, potentially affecting the statistical power and precision of the results. Secondly, the specific type and amount of contrast media utilized and fluid hydration volume were not thoroughly assessed, which might have an impact on the outcomes. Lastly, the study did not investigate other important outcomes such as major cardiovascular events, which could provide a more comprehensive understanding of the overall impact.

5. Conclusion

Based on the findings of this study, the CHA_2DS_2-VASc score may serve as a straightforward indicator for estimating the occurrence of increased serum creatinine level in patients undergoing PCI procedures. In PCI patients, an elevation in the CHA_2DS_2-VASc score beyond 3 is associated with a higher incidence of increased serum creatinine level.

6. Declaration

6.1 Ethics Approval and Consent to participate

The subjects in this study are humans, so ethical rules must be followed. This research has passed the ethical due diligence, approved based on the Certificate of Ethical Eligibility No. 400/098/K.3/102.7/2023 issued by the Health Research Ethics Committee at Dr. Saiful Anwar Malang.

6.2. Consent for publication

Not applicable.

6.3 Availibility of data and materials

Data used in our study were presented in the main text.

6.4 Competing interests

Not applicable.

6.5 Funding Source

Not applicable.

6.6 Authors contributions

Idea/concept: EF. Design: EF. Control/supervision: SW, SA, BS, VY. Data collection/processing: EF. Analysis/interpretation: EF. Literature review: EF, SW. Writing the article: EF. Critical review: SW, SA, BS, VY. All authors have critically reviewed and approved the final draft and are possible for the content and similarity index of the manuscript.

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