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The Effect of Door to Wire Crossing and the Incidence of Acute Kidney Injury in ST Segment Elevation Myocardial Infarction Patients Underwent Primary Percutaneous Coronary Intervention at H. Adam Malik Hospital Medan

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ABSTRACT

Backgroud: ST segment elevation myocardial infarction (STEMI) causes hemodynamic changes and an increase in endogenous vasoconstrictor release leads to renal arteriolar vasoconstriction and decreases renal perfusion and may causes acute kidney injury (AKI). Door to wire crossing is a very important prognostic marker in STEMI patients.

Aims: To assess the effect of door to wire crossing and the incidence of AKI in STEMI patients with onset <12 hours undergoing primary percutaneous coronary intervention (PCI) at H. Adam Malik General Hospital Medan.

Methods: This study is a cohort study conducted from October 2018 to July 2019 with study subjects of STEMI patients with onset <12 hours who underwent primary PCI that met the inclusion and exclusion criteria. Creatinine levels will be checked before and 48-72 hours after the primary PCI as well as the door to wire crossing will be recorded and compared.

Result: The incidence of AKI was found around 14% in the group with a door to wire crossing <140 minutes and by 39% in the group with a door to wire crossing> 140 minutes. It was found that the final urea (p = 0.03), creatinine (p = 0.01), CrCl (p = 0.004) and changes in creatinine (p = 0.008) were statistically significant, while the contrast volume was not. In addition, the door to wire cossing >140 minutes (OR: 4.6; p = 0.032), hypertension (OR: 5.96; p = 0.018) and STEMI onset >6 hours (OR: 7.3; p = 0.019) emerged as independent predictors of AKI.

Conclusion: STEMI patients with onset <12 hours who underwent primary PCI with the door to wire cossing >140 minutes have 4.6 times likelihood to develop AKI rather than those with door to wire cossing <140 minutes. The incidence of AKI ranges from 14% -39%. The independent predictors of AKI besides door to wire crossing are hypertension and STEMI's onset.

INTISARI

Latar Belakang: Infark Miokard Akut dengan Elevasi Segmen ST (IMAEST), menyebabkan perubahan hemodinamik dan peningkatan pelepasan vasokonstriktor endogen yang menyebabkan vasokonstriksi arteriolar ginjal dan menurunkan perfusi ke ginjal dan dapat menyebabkan acute kidney injury (AKI). Door to wire crossing merupakan penanda prognostik yang sangat penting pada pasien IMAEST.

Tujuan: Menilai pengaruh door to wire crossing dan kejadian AKI pada pasien IMAEST dengan onset <12 jam yang menjalani tindakan reperfusi berupa intervensi koroner perkutan primer (IKPP) di RSUP H. Adam Malik Medan.

Metode: Penelitian ini merupakan penelitian kohort yang dilakukan mulai Oktober 2018 hingga Juli 2019 dengan subjek studi pasien IMAEST dengan onset <12 jam yang menjalani IKPP yang memenuhi kriteria inklusi dan eksklusi. Pemeriksaan kadar kreatinin serum dilakukan sebelum dan 48-72 jam sesudah dilakukkannya IKPP dan door to wire crossing akan dicatat dan dibandingkan.

Hasil: Dijumpai insidensi AKI sebesar 14% pada kelompok dengan door to wire crossing<140 menit dan sebesar 39% pada kelompok dengan door to wire crossing>140 menit. Dijumpai bahwa kadar ureum akhir (p=0.03), kreatinin akhir (p=0.01), CrCl akhir (p=0.004) dan perubahan kadar kreatinin (p=0.008) signifikan secara statistik, sedangkan volume kontras tidak bermakna secara statistik. Selain itu, parameter door to wire cossing>140 menit (OR: 4.6; p=0.032), hipertensi (OR: 5.96; p=0.018) dan onset IMAEST > 6 jam (OR: 7.3; p=0.019) merupakan prediktor independen kejadian AKI.

Kesimpulan: Pasien IMAEST dengan onset <12 jam yang menjalani IKPP dengan door to wire crossing di atas 140 menit cenderung mengalami kejadian AKI sebanyak 4.6 kali dibandingkan pasien dengan door to wire crossing di bawah 140 menit. Angka kejadian AKI berkisar antara 14%-39%. Prediktor independen kejadian AKI selain door to wire crossing yakni hipertensi dan onset IMAEST.

Introduction

Acute coronary syndrome (ACS) is one of the main problems in the cardiovascular field. This is mainly because it has a high rate of hospitalization, high mortality rate, and the cost of treatment is quite high. According to the World Health Organization (WHO) in 2013, as many as 17.5 million people died or around 31% of total deaths each year were caused by cardiovascular disease. And about 80% of them were caused by heart attacks and strokes.[1]

Acute coronary syndrome refers to a spectrum of clinical presentations ranging from ST segment elevation myocardial infarction (STEMI), Non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris (UAP). The mortality in STEMI patients influenced by various factor,including age, Killip class, duration of treatment, the presence of an emergency medical system based on the STEMI network, treatment strategies, history of infarction, diabetes mellitus, kidney failure, number of coronary arteries involved, and left ventricular ejection fraction (LVEF).[2]

In STEMI, hemodynamic changes and increased release of endogenous vasoconstrictors such as norepinephrin, renin-angiotensin, vasopressin and endothelin causes renal arteriolar vasoconstriction and decreases perfusion to the kidneys and disrupts the kidney function.[2,3]

Acute kidney injury (AKI) frequently complicates the course of STEMI and is associated with adverse outcomes. AKI is a complex disorders characterized by early deterioration of renal function (in hours or days) with clinical manifestations ranging from minimal increase in serum creatinine to renal failure requiring renal replacement therapy.[4] The reported incidence of AKI among STEMI patients ranging between 12% -36.6%.3 Tsai in his study reported the incidence of AKI post Primary PCI from 3% -9%.[5] While Shacham in his study reported the incidence of AKI in STEMI patients around 3-13%.[6]

The sudden myocardial insult in STEMI often results in an acute reduction of cardiac output. This early hemodynamic deterioration may theoretically lead to reduced renal perfusion and consequently to kidney injury. Worsening of kidney function in STEMI patients is a strong independent predictor of mortality during treatment and 1 year afterwards. Worsening kidney function during hospitalization can be caused by various factors such as contrast nephropathy, haemodynamic conditions, drugs (especially renin-angiotensin-aldosterone blockers), bleeding, acute hyperglycemia and so on.[1,3]

Door to wire crossing is a very important prognostic marker among STEMI patients and many attempts were made to minimize the duration of ischemia so that survival is getting better.[7,8,9] In his research, Shacham found worsening of creatinine serum along with increasing time of coronary reperfusion in STEMI patients who underwent primary PCI, and the time of coronary reperfusion acts as a predictor of the incidence of AKI.[6]

The incidence of AKI post primary PCI in H. Adam Malik General Hospital Medan is not yet available. Therefore, researchers wanted to assess the effect of door to wire crossing and the incidence of AKI in STEMI patients with onset <12 hours who underwent reperfusion in the form of primary PCI at H. Adam Malik General Hospital Medan.

Methods

This study is a cohort study with STEMI patients admitted from October 2018 to July 2019. Study subjects were 56 STEMI patients with onset <12 hours who underwent primary PCI that met the inclusion and exclusion criteria. Patients will be excluded if they underwent fibrinolytic,

died within the first 24 hours of treatment, with chronic kidney disease (GFR <60 ml/min/1.73 m^2) or require routine dialysis and patients with cardiogenic shock.

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara and H. Adam Malik General Hospital Medan.

Research subjects with persistent ST segment elevation myocardial Infarction who agreed to undergo primary PCI will be examined for serum creatinine levels at admission prior to primary PCI and will be re-examined and compared 48-72 hours after primary PCI. In addition, the time from the patient's arrival and meets the medical staff with complaints of chest pain till the wire crossing will be recorded and compared. Furthermore, the incidence of AKI in patients will be assessed as well as other parameters. Data processing was done using SPSS software.

All data in this study were processed using SPSS software version 23. The Kolmogorov-Smirnov and Saphiro-Wilk tests were used to determine the normality of data distribution. Categorical variables ware presented as percentages (%) while the numerical variables with normal distribution presented in the form of mean±SD, and median, minimum-maximum if the data were randomly distributed. Bivariate analysis between categorical and categorical variables was performed using the Chi-Square test. Bivariate analysis between categorical and numerical variables was performed using the Independent T test (T-test) and the Mann Whitney test. The cut off for door to wire crossing was determined based on ROC curve analysis. Bivariate analysis was continued to multivariate studies. Multivariate analysis with logistic regression studies was used to assess predictors of AKI events among STEMI patients. A p value of <0.05 was considered significant.

Result

Fifty six patients were enrolled in this study then divided into two group based on its door to wire crossing either it was below 140 minutes or above 140 minutes. Groups with door to wire crossing below 140 minutes, predominantly were male around 25 patients (90%), with an mean age was 57 years, and the median body mass index was 25.7 kg/m^2. The cardiovascular risk in this group such as hypertension was found in 15 patients (53%), 8 patients with diabetes (28%), and 17 patients were smokers (60%). The coronary stenosis mostly located in the non anterior around 20 patients (72%). The mean ejection fraction in this group was 48%. The onset of STEMI in this group varies between 1 to 11 hours (table 1).

The number of male subjects in groups with door to wire crossing above 140 minutes was 23 patients (83%) with an mean age was 60 years, and the median body mass index was 24.04 kg/m^2. Fifteen patients were found hypertensive (53%), 13 patients with diabetes (46%), and 21 were smokers (75%). Most of the coronary stenosis in this group was located in the anterior around 19 patients (67%). While the mean ejection fraction in this group was 45%. The STEMI's onset ranges from 1.5-11 hours (table 1).

Table 1. Baseline Characteristic

Variable	Door to wire crossing		p-value
	<140 minutes (n=28)	>140 minutes (n=28)	
Male, n(%)	25(90)	23(83)	0.445
Age, years (min-max)	57(34-73)	60(44-69)	0.332+
BMI, kg/m^2 (min-max)	25.70 (20.8-35.7)	24.04 (21.4-31.5)	0.922+
Hypertension, n(%)	15(53)	15(53)	0.812
Diabetes, n(%)	8(28)	13(46)	0.168
Smoker, n(%)	17 (60)	21(75)	0.763
Coronary Stenosis:	8(28)	19(67)	0.168
Anterior	20(72)	9(32)	
Non-Anterior			
LVEF, %±SD	48±2.3	45±1.6	0.645#
Onset, hours(min-max)	7.5(1-11)	6.0(1.5-11)	0.397+

LVEF (Left Ventricular Ejection Fraction),
#Independen T-test, + Mann Whitney test

Kidney Function in STEMI patients Underwent Primary PCI

In group with door to wire crossing below 140, the incidence of AKI was found in 4 patients (14%), with median levels of urem and creatinine at admission was, 19 mg/dL and 0.81 mg/dL respectively and creatinine clearance (CrCl) was 98.6 ml/min/1.73 m^2.

The ureum and creatinine was measured 48-72 hours post primary PCI with median of 29 mg/dL and 0.96 mg/dL, while the CrCl was 83.6 mL/min/1.73 m^2 and the median creatinine change was 0.12. The contrast volume in this group was 129.3 mL. Whereas in the group with door to wire crossing above 140, the incidence of AKI was found in 11 patients (39%), with median levels of initial ureum and creatinine at admission was 23 mg/dL and 0.92 mg/dL while the creatinin clearance (CrCl) was 89.1 mL/min/1.73 m^2. The ureum and creatinine post primary PCI were found with medians of 35.5 mg/dL and 1.1 mg/dL respectively. While the CrCl was 68.8 mL/min/1.73 m^2 and the median changes in serum creatinine was 0.23. The amount of contrast in this group was 127.8 mL. Mann-Whitney test was performed and it was found that the ureum, creatinine, CrCl and serum creatinine changes post primary PCI were statistically significant (table 2).

Table 2.
Kidney Function Characteristics Before and After Primary PCI

Variable	Door to wire crossing		p-value
	<140 minutes (n=28)	>140 minutes (n=28)	
AKI, n(%)	4 (14)	11 (39)	0.276
Admission Ureum, mg/dL (min-max)	19 (15-50)	23 (15-44)	0.235
Admission Creatinine, mg/dL (min-max)	0.81 (0.64-1.30)	0.92 (0.5-1.2)	0.293
Admission CrCl, ml/i (min-max)	98.6 (60-130)	89.1 (60-110)	0.138
Discharge Ureum mg/dL (min-max)	29 (15-78)	35.5 (22-85)	0.030*
Discharge Creatinine mg/dL (min-max)	0.96 (0.68-1.72)	1.1 (0.81-1.98)	0.010*
Discharge CrCl, ml/i (min-max)	83.6 (30-110)	68.8 (38-94)	0.004*
Creatinin changes	0.12 (-0.11-0.62)	0.23 (0.13-0.98)	0.008*
Contrast volume, ml±SD	129.3±3.6	127.8±3.9	0.392

+ Mann Whitney test *Significant

The AKI Predictors

Bivariate analysis was performed with chi-square test comparing the possible predictors in the AKI and non AKI group as presented in table 3. Among fifteen patients, 6 of them experienced AKI in this study. Hypertension (p = 0.016), STEMIS's onset (p = 0.004), and door to wire crossing (p = 0.035) were statistically significant. While variables such as diabetes (p = 0.391), smoking (p = 0.503) and location of stenosis (p = 0.815) were not significant in this study. The significant variables from the bivariate study were continued to multivariate studies to assess which variables were more accurate in predicting the incidence of AKI (table 4).

Table 3.
Bivariate Analysis of AKI Predictors

Variables	AKI (n=15)	Non AKI (n=41)	p value
Diabetes	7	14	0.391
Hypertension	12	18	0.016
Smoker	10	31	0.503
STEMI's Onset >6 jam	14	24	0.004
Anterior stenosis	6	15	0.815
Non anterior stenosis	9	26	0.815
Door to Wire Crossing >140 menit	11	17	0.035

The STEMI's onset was divided into two groups below and above 6 hours based on the ROC curve analysis. The multivariate logistic regression results are in line with the bivariate test results, in which door to wire cossing (OR: 4.6; p = 0.032), hypertension (OR: 5.96; p = 0.018), STEMI's onset > 6 hours (OR: 7.3; p = 0.019) are independent predictors of AKI events.

Tabel 4.
Multivariate Analysis Predictors of AKI

Variables	OR (CI: 95%)	p value
Hypertension	5.96	0.018
Door to wire crossing	4.60	0.032
STEMI's Onset	7.30	0.019

Discussion

This study aims to assess the effect of door to wire crossing and the incidence of AKI in STEMI patients with onset <12 hours undergoing primary PCI. In addition, this study also aims to seek other variables that contribute to the incidence of AKI.

In this study, patients' door to wire crossing ranged from 82 minutes to 456 minutes. It was divided into 2 groups, door to wire crossing below 140 and above140 minutes. The majority of patients in the group with door to wire crossing above 140 minutes were male, with a median age slightly higher than the other group. In addition, patients in this group were also found to have higher comorbid rates such as diabetes mellitus and a higher number of smokers. The location of coronary stenosis also tends to be more anterior in the group with door to wire crossing above 140 minutes. Other variables such as the left ventricular ejection fraction and the onset of STEMI were not much different between the two groups.

The incidence of AKI was more prevalent in patients with door to wire crossing above 140 minutes which was around 39%. In addition, the median ureum and initial creatinine in this group were slightly higher. The results of the non-parametric test found that the ureum, creatinine, and CrCl post primary PCI as well as changes in creatinine level were statistically significant, whereas the contrast volume was not.

Tsai in his study reported the incidence of AKI post primary PCI ranging from 3%-9%. The incidence of AKI reported in STEMI patients was estimated between 12%-36.6 and associated with highermortality and morbidity.3,5 In this study, the incidence of AKI was found around 14% in the group with a door to wire crossing below 140 minutes and 39% in the group with a door to wire crossing above 140 minutes. Marenzi in his study showed the effect of contrast amount on the incidence of AKI in post primary PCI patients. But in this study, the contrast volume was not much different between the two groups so that no significant effect was found.10 Brinker in his study stated the definition of contrast nephropathy events, commonly known as contrast induced nephropathy or CIN as an increase in serum creatinine > 0.5 mg/dL or > 25% from baseline within 24 hours after contrast exposure.[11]

The CIN incident itself was found in both groups. In the group with door to wire crossing below 140 minutes, there were 1 incidents while in the group with door to wire crossing above 140 minutes there were 3 CIN incidents. Based on a study by Andra that assessed the incidence of CIN after elective PCI in patients with hypertension and without hypertension, it was found that

the incidence of CIN was more often in patients with hypertension but no difference in contrast between the two groups was found.[12]

Based on STEMI's guidelines from the European Society of Cardiology, the expected door to wire crossing is less than 60 minutes at hospitals with Primary PCI facilities and less than 90 minutes for patients referred from other hospitals to the primary PCI center and at the latest the decision to perform primary PCI is less than 120 minutes.[13] In this study the cut-off point for door to wire crossing was 140 minutes. This is mainly due to the delay in the family's decision to declare the willingness to undergo the primary PCI.

From bivariate analysis, it was found that variables such as hypertension, STEMI's onset, and door to wire crossing were statistically significant and could predict the incidence of AKI. The multivariate logistic regression showed that variables such as door to wire cossing (OR: 4.6; p = 0.032), hypertension (OR: 5.96; p = 0.018), and STEMI's onset (OR: 7.3; p = 0.019) were independent predictors AKI incident.

The results of this study are in line with studies by Shacham mentioned patients having longer door to wire crossing had higher serum creatinine and more AKI complicating the course of STEMI. The presence of comorbidities such as hypertension and diabetes mellitus also influences the incidence of AKI.[6,8,9] In this study hypertension itself appears as a significant predictor of AKI events.

The results of this study are in line with previous studies by Shacham and Queiroz who found the influence of door to wire crossing with the incidence of AKI in STEMI patients undergoing primary PCI.[6,14] Similar results were also apparent from Bates's study which showed lower door to wire crossing time as a protective factor for AKI incident.[7]

Limitation

The number of study subjects is smaller compared to other studies. In addition,a follow up studies can be made in order to observe the major cardiovascular events such as re-hospitalization.

Conclusion

STEMI patients with onset less than 12 hours who underwent primary PCI with the door to wire crossing above 140 minutes have 4.6 times likelihood to develop AKI rather than those with door to wire crossing below 140 minutes. The incidence of AKI among STEMI patients with onset <12 hours undergoing primary PCI ranges from 14%-39%. The influential variables to predict AKI events besides door to wire crossing are hypertension and STEMI's onset.

Disclosures

The authors have no conflicts of interest to disclose.

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