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RISK FACTOR ANALYSIS OF RECURRENT ACUTE CORONARY SYNDROME

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ABSTRACT

Background: Acute coronary syndrome (ACS) is a form of life-threatening coronary heart disease. Interestingly, this entity has the possibility to recurrence with prevalence reaches 21-30% in a year. **Purpose:** This study aims to analyse risk factors associated with recurrent ACS incident. **Methods:** The analytic observation research with the case-control design was applied in this present study. Furthermore, this research was conducted at the Dr. Mohamad Soewandhie General Hospital, Surabaya. This study carried from February to July 2018. The samples used in this study cover 43 cases and 43 controls in the consecutive admission to the ACS patients who came to the cardiac clinic of the Dr. Mohamad Soewandhie General Hospital, Surabaya that meets the research criteria. On the other hand, bivariable analysis was performed using simple logistic regression and multivariable analysis was performed using multiple logistic regression. This study showed that the most influential risk factor for ACS recurrent. **Results:** incident were including control of Low-Density Lipoprotein Cholesterol (LDL-C) ⩾ 100 mg/dL (p= 0.03; adjusted OR= 3.35; 95% CI= 1.16 < OR < 9.68), irregular exercise schedule (p < 0.01; adjusted OR= 9.15; 95% CI= 2.83 <OR <29.58), and smoking history (p= 0.02; adjusted OR= 4.07; 95% CI= 1.29 <OR <12.84). **Conclusion:** The control of LDL Cholesterol levels below 100 mg/dL, regular exercise, and avoid smoking are beneficial for people with ACS to reduce the risk of recurrent ACS incident.

INTRODUCTION

Cardiovascular disease is the top cause of death globally every year. It is estimated there are 17.5 million deaths due to cardiovascular disease in 2012. From this incident, 80% are caused by heart attacks and strokes, interestingly about 75% incidence occur in low-middle income countries. Surprisingly, the annual mortality rate from cardiovascular disease is projected to increase from 17.5 million in 2012 to 22.2 million in 2030. Furthermore, about 34% of deaths from cardiovascular disease occur under the age of 70 years. This causes a high premature death due to cardiovascular disease. Not to mention, coronary heart disease ranked at second place after stroke as the leading cause of death in 2012 with the number of deaths approximately 128.4 thousand people in Indonesia (WHO, 2014; WHO, 2015).

Additionally, acute coronary syndrome (ACS) is an acute syndrome due to blockage of atheroma

plaques in the coronary arteries, so that the heart becomes ischemic and even infarcts (AHA, 2015). The ACS in the Asia Pacific region has a prevalence about 5% (Chan et al., 2016). The ACS can recur with the prevalence about 11.65 to 19.5% (Abu-Assi et al., 2016; Chinwong et al., 2015). The fatality rate in recurrent ACS patients is 31.1% (313/945) (Abu-Assi et al., 2016). Ironically, the increased risk of recurrent ACS will promote the risk of death (Bueno & Asenjo, 2016).

To the greater extent, the main risk factors associated with recurrent ACS can be divided into two, namely non-modifiable risk factors and modifiable risk factors. Ageing and gender are risk factors that cannot be modified. Moreover, the modifiable risk factors include behavior (behavior patterns, unhealthy diets, lack of physical activity, smoking history, alcohol consumption, and consumption of non-compliant drugs), cardiovascular disease (congestive heart failure, stroke, and peripheral arterial disease), comorbidities (diabetes mellitus, hypertension, dyslipidemia, impaired renal function), and treatment history (type of management of ACS and type of ACS) (Chinwong et al., 2015; Lu et al., 2014; WHO, 2014; Yudi et al., 2016).

Risk factors for people who have had ACS must be assessed and controlled properly because the mortality and complications increase in patients with recurrent ACS (Bueno & Asenjo, 2016). The purpose of this study was to analyze the risk factors for recurrent ACS to determine the risk factors that most influence the incidence of recurrent ACS.

METHODS

This research is the observational analytic type with case-control as research design. The research was conducted at the Dr. Mohamad Soewandhie General Hospital, Surabaya. This study started from February to July 2018.

The study population was hospital-based population. The case population is recurrent ACS patients. The affordable population is a recurrent ACS patient who enters the cardiac clinic of the Dr. Mohamad Soewandhie General Hospital, Surabaya from April 2018 until the research was completed. The control population is non-recurrent ACS patients. Equally important, the affordable population for control in this study is ACS patients who do not experience recurrent ACS that goes to the cardiac clinic of Dr. Mohamad Soewandhie General Hospital, Surabaya from April 2018 until the research is completed.

Samples were taken from affordable populations that fit the research criteria. The inclusion criteria for the case were ACS patients who experienced repeated attacks after leaving hospital treatment for more than 30 days. Control inclusion criteria were new ACS patients who did not experience a recurrence of ACS after more than a year. Exclusion criteria were respondents who were unwilling, respondents who could not communicate well, and respondents who had conditions related to memory disorders.

The sample size was calculated using software "sample size determination in health" studies using a confidence level of 95% and test strength of 80%. The Odds Ratio (OR) value was 3.81 and the proportion of exposure in the control group about 10.30% was obtained from the study of Chinwong et al (2015) for the variable impaired renal function. By using a case-control ratio of 1:1, a sample size of 43 cases and 43 controls were obtained. The case and control sampling were carried out by consecutive admission, namely patients who came to the Cardiac clinic of the Dr. Mohamad Soewandhie General Hospital, Surabaya during the research period that fulfilled the criteria will be taken as a sample in sequence.

In this study, data sources were from primary data and secondary data. Primary data is obtained through direct interviews with respondents using the questionnaire. Primary data included age (years) at the time of previous ACS exposure, history of stroke (yes/no), exercise (routine/not), smoking history (smoking/not), and medication adherence (yes/no). Secondary data comes from medical records that will be recorded on the data collection sheet. Secondary data included the previous type of ACS (STEMI/NSTE-ACS), history of congestive heart failure (yes/no), DM status (hyperglycemic DM/normoglycemic DM/non-DM), hypertensive status (uncontrolled hypertension/controlled hypertension/not hypertension), control of Low-Density Lipoprotein cholesterol (LDL-C) ($\geqslant$100 mg/dL/<100 mg/dL), renal function disorders (yes/no), and recurrent ACS events (yes/no). DM status, hypertension status, and control of LDL-C levels were measured by taking the average value of the last two visitations including the visitation of the patient before experiencing recurrent ACS and the control patients. The hyperglycemic diabetes is defined if the average fasting blood sugar is more than 130 mg/dL (ADA, 2017). The uncontrolled hypertension is defined if the average systolic blood pressure is more than 130 mmHg or average blood pressure is more than 80 mmHg (Whelton et

al., 2018). Impaired renal function if estimated glomerular filtration rate (eGFR) less than 60 mL/minute/1.73 m^2.

Data were analyzed using simple logistic regression analysis techniques for bivariable analysis and multiple logistic regression for multivariable analysis. The independent variable with a value of p< 0.25 in bivariable analysis will be included in the multivariable analysis. Interpretation of the influence is expressed in the form of an OR with a 95% confidence interval (CI).

RESULTS

In this present study we found that the average age at the time of experiencing previous ACS in cases or controls group did not significantly different. The proportion of previous ACS types, DM status, and hypertension status between cases and control groups were almost balanced. The proportion of renal function disorders between cases and control groups are balanced. Most respondents did not have a history of stroke or a history of congestive heart failure in both the case or control group. Most respondents adhere to treatment in both the case and control groups. The significant difference in the proportion of exposure was only found in the control of LDL-C levels, exercise, and smoking (Table 1). Multivariable analysis with multiple logistic regression involved four variables, namely control of LDL-C cholesterol levels, exercise, smoking, and medication adherence.

The results of multiple logistic regression found the three variables that mostly influence the incidence of recurrent ASC, namely control of LDL-C cholesterol level ⩾ 100 mg/dL (p= 0.03; adjusted OR= 3.35; 95% CI= 1.16 <OR <9.68), irregular exercise (p< 0.01; adjusted OR= 9.15; 95% CI= 2.83 <OR <29.58), and smoking history (p= 0.02; adjusted OR= 4.07; 95% CI= 1.29 <OR <12.84) (Table 2).

DISCUSSION

In this study we found several risk factors that influence the incidence of recurrent ACS, namely control of LDL cholesterol level ⩾ 100 mg/dL, irregular exercise, and smoking history.

LDL control ⩾ 100 mg/dL.

The results of this study revealed that ACS patients with control of LDL Cholesterol ⩾ 100 mg/dL were more likely to experience recurrent ACS compared to ACS patients with control of LDL Cholesterol levels < 100 mg/dL. The risk for recurrent ACS in people with LDL cholesterol control ⩾ 100 mg/dL is three times compared to people with LDL Cholesterol control <100 mg/dL. This study is in line with previous research which found that LDL Cholesterol levels below 70 mg/dL were able to reduce the risk of recurrent ACS events being twice lower than LDL cholesterol levels> 100 mg/dL (Chinwong et al., 2015).

Research by De Biase et al (2017) demonstrated a significant difference in the mean level of LDL Cholesterol between non-recurrent ACS patients and recurrent ACS patients. In this study, mean LDL Cholesterol levels in patients with non-recurrent ACS were 99.83 ± 37.70 mg/dL, while mean LDL Cholesterol levels in recurrent ACS patients were 122.87 ± 37.72. This finding indicates that lowering LDL Cholesterol is useful to reduce the risk of recurrent ACS. Decreasing LDL Cholesterol levels below 40 mg/dL can reduce the risk of recurrent ACS (Reddy & Bittner, 2013).

Dyslipidemia is known to be one of the causes of atherogenesis. LDL Cholesterol is the main target in the management of coronary heart disease patients. When LDL Cholesterol has been reached the proper level, an increase in High-Density Lipoprotein Cholesterol (HDL-C) does not reduce the risk of cardiovascular disease (Ceponiene, Zaliaduonyte-Peksiene, Gustiene, Tamosiunas, & Zaliunas, 2014; Erwinanto et al., 2013). The efforts that can be made by ACS patients to maintain LDL Cholesterol levels <100 mg/dL are doing medication checks routinely according to the control schedule so that LDL-C levels can be monitored and controlled with statin drugs. Statin drugs used in ACS patients are high-intensity statins that can reduce LDL-C ⩾ 50% (Raymond, Cho, Rocco, & Hazen, 2015).

Exercise

Exercise affects the incidence of recurrent ACS. Regular exercise definition in this study is if the exercise recommended by the treating doctor is done at least three times a week with a minimum duration of 30 minutes. The type of exercise carried out by all respondents is just by regular walk.

Table 1

Bivariable Analysis of Variables on Repeated SKA Events

Variable	Recurrent ACS				Total		*p*	OR (95% CI)
	Yes		No					
	n	%	n	%	n	%		
Age at Previous ACS (years)								
≥ 57	21	48,80	22	51,20	43	50,00	0,83	0,91 (0,39 < OR < 2,12)
< 57	22	51,20	21	48,80	43	50,00		
ACS Type								
STEMI	23	53,30	25	58,10	48	55,80	0,66	0,83 (0,35 < OR < 1,94)
NSTE-ACS	20	46,50	18	41,90	38	44,20		
Stroke History								
Yes	5	11,60	4	7,00	9	10,47	0,46	1,75 (0,39 < OR < 7,85)
No	38	88,40	40	93,00	78	89,53		
History of Congestive Heart Failure								
Yes	14	32,60	16	37,20	30	34,88	0,65	0,82 (0,33 < OR < 1.98)
No	29	67,40	27	62,80	56	65,12		
DM Status								
DM Hyperglycemic	11	25,60	7	16,30	18	20,93	0,46	1,51 (0,51 < OR < 4,51)
DM Normoglycemic	6	14,00	11	25,60	17	19,77	0,27	0,52 (0,17 < OR < 1,63)
Non-DM	26	60,50	25	58,10	51	59,30		
Hypertension Status								
Uncontrolled Hypertension	20	46,50	20	46,50	40	46,51	0,86	0,91 (0,32 < OR < 2,62)
Controlled Hypertension	12	27,90	13	30,20	25	29,07	0,77	0,84 (0,26 < OR < 2,68)
Not hypertension	11	25,60	10	23,30	21	24,42		
LDL Cholesterol Control (mg/dl)								
≥ 100	26	60,50	16	37,20	42	48,84	0,03	2,58 (1,08 < OR < 6,16)
< 100	17	39,50	27	65,80	44	51,16		
Disorders of Kidney Function								
Yes	14	32,60	14	32,60	28	32,56	1,00	1,00 (0,41 < OR < 2,47)
No	29	67,40	29	67,40	58	67,44		
Exercise								
Not a Routine	35	81,40	18	41,90	53	61,63	< 0,01	6,08 (2,28 < OR < 16,16)
Routine	8	18,60	25	58,10	33	38,37		
Smoking History								
Smoking	28	65,10	15	34,90	43	50,00	0,01	3,48 (1,44 < OR < 8,46)
Not Smoking	15	34,90	28	65,10	43	50,00		

(Continous)

Table 1
Continous

Variable	Recurrent ACS				Total		*p*	OR (95% CI)
	Yes		No					
	n	%	n	%	n	%		
Treatment Compliance								
Not Obedient	13	30,20	7	16,30	20	23,26	0,13	2,23 (0,79 < OR < 2,30)
Obedient	30	69,80	36	83,70	66	76,74		
Total	43	100,00	43	100,00	86	100,00		

Table 2
Double Logistic Regression Analysis of Repeated SKA Events

Variable	*p*	B	OR (95% CI)
Exercise			
Not a Routine	< 0,01	2,23	9,26 (2,91 < OR < 29,45)
Routine (reference)			
Treatment Compliance	0,48	0,44	1,56 (0,46 < OR < 5,28)
Not Obedient			
Obedient			
Smoking History			
Smoking	0,01	1,43	4,18 (1,46 < OR < 11,94)
Not Smoking (reference)			
LDL Cholesterol Control (mg/dl)			
≥ 100	0,03	1,20	3,33 (1,16 < OR < 9,60)
< 100 (reference)			

There was a significant difference between respondents who exercised regularly with respondents who did not routinely exercise toward recurrent ACS events. The risk of recurrent ACS attacks in ACS patients who do not routinely exercise is nine times greater than ACS patients who are routinely doing exercise. The results of this study are in line with the research conducted by Papataxiarchis et al (2016). The study looked at the effect of exercise on the incidence of ACS followed for ten years, it was found that ACS patients who routinely exercised ≥ three times/week have a lower risk for recurrent ACS 1.50 times less than patients who did not exercise regularly. In ACS patients with DM who routinely exercise have greater protective effects, which are twice smaller compared with ACS patients with DM who do not exercise regularly.

In the same way, regular exercise performed every day or almost every day each week with a minimum duration of about 30 minutes and moderate intensity can improve cardiovascular conditions (Notara, Panagiotakos, & Pitsavos, 2014). Exercise can lower blood pressure, control blood sugar levels become better, increase atherosclerosis plaque stability, and lower oxidative stress, so that exercise can reduce the risk of recurrent ACS (Diaz & Shimbo, 2013; Papataxiarchis et al., 2016). Exercise is the most important non-pharmacological therapy in the secondary prevention efforts of ACS.

The type, frequency, and intensity of exercise must be adjusted to the clinical condition of the ACS patient (comorbidities, disability status, cardiac function capacity, preferences, etc.). Excessive exercise or not exercising can be one of the risk factors of recurrent ACS, so ACS patients should undergo a heart rehabilitation program after experiencing ACS (Dunlay, Pack, Thomas, Killian, & Roger, 2014; Thomas et al., 2018).

Smoking.

In this study, we found that smoking affects the incidence of recurrent ACS. Respondents who had a history of smoking more chance to experience recurrent ACS incidents than respondents who never smoked. The results of the multivariable analysis showed that the risk for recurrent ACS in ACS patients with a smoking history was four times greater than ACS patients who had never smoked.

This study is in line with two other previous studies which found an association between smoking and recurrent ACS events (Al Saleh et al., 2017; Zhang et al., 2015). Smoking is known as a traditional risk factor for coronary heart disease. Smoking can damage vascular endothelial and trigger vasoconstriction. The effect can cause hypertension, platelet aggregation, atherosclerosis formation, and ultimately increase the risk of developing ACS (Zhang et al., 2015).

Uniquely, ACS patients who have stopped smoking still have a risk of recurrent ACS, but the risk continues to decline over time. The risk for recurrent ACS after quitting smoking can decrease by almost 50% in 10 years (Notara et al., 2015). Furthermore, ACS patients who have stopped smoking need time so that the risk of recurrent ACS is equivalent to ACS patients who have never smoked. This result indicates that ACS patients who have stopped smoking still have a risk of recurrent ACS, but the risk continues to decline over time. This phenomenon can be caused by damage to blood vessels that have been caused by smoking. Histopathological research found that coronary arteries in patients with acute myocardial infarction with a history of smoking provide a more severe feature of partial narrowing or total occlusion, and involve more coronary arteries (multi vascular) compared to patients with acute non-smoking myocardial infarction (Leone, 2014). Different results were found in the research conducted by Chinwong et al (2015). The study did not get the effect of smoking on recurrent ACS events. The incidence of recurrent ACS did not differ significantly, both among former smoker ACS patients with ACS patients who had never smoked or between active ACS patients who smoked and ACS patients who never smoked. Changes in healthy behaviour by quitting smoking are useful for decreasing the risk of recurrent ACS. Health experts can provide brief advice about quitting smoking and offer counselling and pharmacotherapy services to stop smoking. ACS patients who have stopped smoking are continually evaluated so that they remain obedient to stop smoking (Notara et al., 2015; Verbiest et al., 2017).

Research Limitation

This study did not cover the number of vascular factors involved in previous ACS attacks, the type of action/ treatment carried out in previous ACS attacks, and dietary factors. Clinical data is not examined by the researchers themselves but only uses secondary data.

CONCLUSION

Risk factors that influence the incidence of recurrent ACS are control of LDL cholesterol $\geqslant$ 100 mg/dL, irregular exercise, and smoking history. ACS patients need to be well-educated to routinely control and adhere to statin treatment, counselling and pharmacotherapy services to stop smoking, and be referred to the cardiac rehabilitation program

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