RELATIONSHIP BETWEEN FIBRINOLYSIS AND IN-HOSPITAL-DEATH IN PATIENT WITH ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Abstract

Background

Cardiovascular disease cause most death among other non-communicable disease. There are many cases of coronary heart disease in Indonesia, one of them is acute myocardial infarction. The treatment that must be delivered as soon as possible is coronary artery reperfusion using PCI or Fibrinolysis. Fibrinolytic agent is one kind of treatment that recommended by most cardiologist worldwide to treat acute myocardial infarction.

Objective

This study objective was to find the relationship between fibrinolysis and in-hospital death in patients with acute ST-segment elevation myocardial infarction.

Method

This study used observational method and retrospective cohort design, comparing the outcome of treatment in patients with and without fibrinolysis using medical records as the data source. The subject were patients of Dr. Soedono Regional Hospital in Madiun from the year 2013-2016. The data was analyzed using Chi-square.

Result

There're 32 patients who used fibrinolytic and 40 patients without fibrinolytic. Patients who suffered in-hospital death, 10 (40%) were using fibrinolytic and 15 (60%) were not using it. Among patients who used fibrinolytic and who did not, in-hospital-death did not differ significantly statistically (p: 0,761; RR : 1,1, 95% CI : 0,787-1,538).

Conclusion

There's no relationship between fibrinolysis and in-hospital death. But, in-hospital death percentage was higher in patients without fibrinolytic use.

Keyword: STEMI, Fibrinolytic, Mortality, AMI

PENDAHULUAN

Cardiovascular disease is the highest cause of death in the world compared to other non-communicable diseases, which is 17.5 million deaths. Of these, an estimated 7.4 million were due to a heart attack. Although there are fewer risk factors, the number of deaths is greater in developing countries.[1] In Indonesia there are 2,650,340 peoples have coronary heart disease, while in East Java there are 375,127 people with coronary heart disease (CHD)[2]. One type of CHD is acute myocardial infarction (AMI) with symptoms of discomfort in the chest that spread and abnormalities in ECG[3]. Coronary thrombosis is the cause of the incidence of acute myocardial infarction and fibrinolytic agents play an important role in IMA therapy and may may reduce mortality[4]. The use of thrombolysis may produce effective reperfusion in STEMI patients, but thrombolysis also increases the risk of hemorrhage[5]. The aim of this study was to determine the association of fibrinolytic therapy with the incidence of death in patients with acute myocardial infarction of STEMI. We hypothesize that there is a relationship between the provision of fibrinolytic therapy with decreased incidence of death .

METHOD

This study used an observational method with a retrospective cohort study design. This research was conducted in RSUD Dr. Soedono Madiun in November-December 2016. The research subjects were inpatients in RSUD Dr. Soedono Madiun who has been diagnosed with acute myocardial infarction (STEMI) in 2013-2016 with patient's medical records as the data source. Independent variable in this research is the provision of fibrinolytic treatment with depedent variable is the presence or absence of death caused by cardiovascular events.

From the calculation of sample needed for unpaired categorical data analysis, this study needs of 40 samples per group. The subject inclusion criteria are inpatients of RSUD Dr Soedono diagnosed AMI (STEMI type) by doctors in the period of 2013-2016 and the exclusion criteria is incident death with comorbids of noncardiovascular disease and incomplete medical record. The data is retrieved using the prepared worksheet. Patients are

followed up by seeing their progress in the medical record. For patients who passed the criteria, data were taken in the form of sex, age, location of infarct from ECG, Killip score, TIMI score, fibrinolytic usage status. After going through several processes, the sample was divided into 2 groups: groups of patients using fibrinolysis therapy and groups of patients who did not use fibrinolysis therapy.

The data obtained was initially tested univariat to know the distribution and frequency of patient data, then data is processed by using bivariate analysis of *chi-square* from SPSS Software to know the relation between independent variable with dependent. This research has passed the study of ethics by the Medical and Medical Research Ethics Committee of UII Medical Faculty and has been authorized by the Committee of Ethics and Medical Committee of RSUD Dr Soedono Madiun.

RESULT

From the medical records of 2013-2016, data obtained for the group with fibrinolitic were 32 samples and groups without fibrinolitic were 40 samples. The number of patients using fibrinolysis therapy is not much in the hospital. Male patients dominated the frequency of fibrinolytic user by 24 people (75%), as well as for non-fibrinolytic group data frequency of 31 persons (77.5%). The age of patients ranges from 30 years to over 100 years and the mean age of patients is 59.79 years. In patients who using fibrinolytics, the most patients aged 50-59 years (53.1%) whereas in patients without fibrinolytics, most aged 60-69 years (35%). The type of anterior STEMI predominates in both groups. Patients who used fibrinolytics have a greater improvement ratio than patients who did not use fibrinolytics. Patients who did not use fibrinolytics had a greater death-to-patient ratio than fibrinolytic patients. Characteristics and distribution of patient data based on fibrinolytic use can be seen in **Table 1**.

Table 1 Characteristics and distribution of patient data based on fibrinolytic use

	Using fibrinolytic		Not using fibrino-lytics	
	Amount (N)	Percentage (%)	Amount (N)	Percentage (%)
	N= 32		N=40	
Sex				
Male	24	75%	31	77,5%

Female	8	25%	9	22,5%
Age				
≤30	0		0	-
30-39	3	9,4%	2	5%
40-49	3	9,4%	2	5%
50-59	17	53,1%	8	20%
60-69	8	25%	14	35%
70-79	1	3,1%	13	32,5%
80-89	0	-	0	-
≥90	0	-	1	2,5%
STEMI type				
Anterior	16	50%	25	62,5%
Inferior	9	28,1%	11	27,5%
Posterior	1	3,1%	0	-
Anteroseptal	2	6,3%	0	-
Inferior +Posterior	1	3,1%	2	5%
Anterior+ Inferior	2	6,3%	2	5%
Anterior+Posterior	1	3,1%	0	-
Outcome				
Improvement	22	68,8%	25	62,5%
Death	10	31,2%	15	37,5%
Killip Classification				
1	19	59,3%	23	57,5%
2	3	9,4%	6	15%
3	3	9,4%	6	15%
4	7	21,9%	5	12,5%
TIMI Score				
Low risk	22	68,8%	20	50%
High risk	10	31,2%	20	50%

The proportion of patients who died from a group that did not use fibrinolytics (60%) was higher than those who using fibrinolytics (40%). The proportion of patients with higher improvement came from the group of patients who did not use fibrinolytics with 57.7% (30 patients) than the group of patients using fibrinolytics ie 42.3% (22 patients). Patients who experienced improvement, 72.3% were included in Killip Classification 1, while 36% of patients who died were included in Killip Classification 4. In patients with improvement, viewed from TIMI Score, 66% of those had a low risk. In patients who died, when viewed from the TIMI Score, 55% of them had a high risk of death. Characteristics of data based on the results of therapy can be seen in Table 2

Table 2 Characteristics of data based on the results of therapy

	Improvement		Death	
	Amount (n) N= 47	Percentage (%)	Amount (n) N=25	Percentage (%)
Sex				
Male	39	83%	16	64%
Female	8	17%	9	36%
Age				
≤30	0	-	0	-
30-39	4	8,5%	1	4%
40-49	4	8,5%	1	4%
50-59	18	38,3%	7	28%
60-69	12	25,5%	10	40%
70-79	8	17%	6	24%
80-89	0		0	-
≥90	1	2,1%	0	-
STEMI type				
Anterior	27	57,4%	14	56%
Inferior	11	23,4%	9	36%
Posterior	1	2,1%	0	-
Anteroseptal	1	2,1%	1	4%
Inferior +Posterior	3	6,4%	0	-
Anterior+ Inferior	3	6,4%	1	4%

Anterior+Posterior	1	2,1%	0	-
Fibrinolytic				
Using	22	42,3%	10	40%
Not using	30	57,7%	15	60%
Killip Classification				
1	34	72,3%	8	32%
2	6	12,8%	3	12%
3	4	8,5%	5	20%
4	3	6,4%	9	36%
TIMI Score				
Low risk	31	66%	11	44%
High risk	16	34%	14	55%

The results of the analysis are presented in the form of cross-row tables and columns. The results of analysis with Chi square shows the significance value of 0.580 and Relative Risk (RR) of 1.100 (95% CI: 0.787-1.538). Thus, since $p > 0.05$, there is no statistically significant relationship between fibrinolytic administration and mortality. However, the difference in the proportion of deaths between patients with fibrinolytics and without fibrinolytics was 20%. The results of the analysis can be seen in **Table 3.**

DISCUSSION

From the results of the study, we found that there is no statistically significant relationship between the incidence of death with the use of fibrinolitic. obtained Chi-square test results that show the significance value of 0.580 ($p > 0.05$) and RR 1.100 (95% CI: 0.787-1.538). The percentage of patients on fibrinolytic users who experienced a higher improvement than those who experience death (46.8%: 40%). Patients without fibrinolytics who experienced deaths higher percentages than those of improvement (60%: 53.2%). Previously, it has been established in the large sample calculation that the significant difference in proportion is 10%. Based on the results of statistical calculations,

	Improvement		Death		Nilai P	RR
	N	%	n	%		
Using fibrinolytic	22	46,8%	10	40%		
					0,580	1,100 (95% CI : 0,787-1,538)
Not using fibrinolytic	25	53,2%	15	60%		
Total	47	65%	25	34%		

40% of the patients died were fibrinolytic users and 60% of the patients died were patients without fibrinolytics, so the difference in proportion in patients who died was 20% (> 10%), clinically there was a relationship between fibrinolytic use and the incidence of death. If clinically significant but not statistically significant, it is because the power of the research is lacking. Power is less due to the number of subjects under study smaller than should be[6].

In another study, 11 of the 23 patients with steming recurrence and cardiogenic shock. [7] Large-scale cohort studies in Sweden show that the proportion of deaths in fibrinolytic users was 27, 3% while the proportion of deaths in patients without fibrinolytics was 32.5%. The mortality rate of patients not on reperfusion therapy was 42% (P <0.001) while the mortality rate of users of fibrinolytic therapy was 31% (P <0.001). The results showed fibrinolytic therapy associated with decreased mortality after 1 year (P = 0,001 CI 95%). [8] However, there was no significant difference in the proportion of deaths between thrombolysis and PCI therapy, only the incidence of heart failure was more common in thrombolytic users than in PCI users. [9]

Reperfusion therapy such as fibrinolysis is based on the concept that after coronary vessel occlusion, myocardial cell death starts from the endocardium to the epicardium. The faster the myocardium gets access to oxygen, the higher the likelihood of a persistent myocardium. [10] The use of fusion reper therapy for STEMI provides the advantage of limiting infarct size, increasing myocardial function, altering infarct zone healing patterns, and decreasing mortality resulting in standard therapy for STEMI. However,

in certain circumstances, there are side effects of reperfusion therapy that is *reperfusion injury.* [11]

Reperfusion injury can produce lethal symptoms such as arrhythmia (*reperfusion arhytmia)* , "freezing" myocardium, or more severe myocardial damage that may lead to heart failure or cardiac arrest.Many things can cause *reperfusion injury* like the emergence of ROS due to the large influx of oxygen, calcium imbalance, and blood-carrying imbalance . [12] So the use of fibrinolytic therapy also has a risk for the occurrence of death in patients.

One of the complications of acute myocardial infarction is heart failure. Killip Classification aims to predict the risk of death in patients with acute myocardial infarction based on clinical symptoms of heart failure . The higher the Killip Classification rate , the higher the risk of death of the patient. [13] Killip Classification of patients at diagnosis affects the outcome of therapy. In patients who, from the outset, have a poor prognosis, the possibility of fibrinolytic use is no longer of significant benefit as there is a failure of cardiac function. In addition to Killip, TIMI *Risk Score* for STEMI can be used to predict the incidence of hospitalized mortality or grouping of patients at high risk. The higher the TIMI score , the more likely it is for the patient to die . Patients who termasu k high-risk group (TIMI> 5) have a high incidence of side effects and mortality is higher than in the low-risk group (TIMI 0-4). [14] In patients who from the beginning have severity, the possibility of fibrinolytic use has little effect. In addition to fibrinolytic use, the severity of the patient before the use of fibrinolytics also affects the outcomes.

As for some limitation of this research. The number of samples that are less than appropriate (40) causes the power of this study to decrease to about 70% where the initial estimate is 80%. In addition, the lack of control over intruder factors such as the incompleteness of medical record data, especially onset and weight, variation in patient severity when given therapy (assessed from Killip or TIMI Score), symptom osnet symptom of each patient and time difference between onset of symptoms and administration therapy.

CONCLUSION

This study showed no statistically significant association between fibrinolytic therapy and decreased incidence of mortality in STEMI type IMA patients, but the percentage of death incidence was higher in those who did not use fibrinolytic therapy than those who used it.

SUGGESTION

For further research it is suggested that the sample be multiplied and the duration of the study is extended and multivariate analysis is performed for several variables. It is also recommended research conducted hospital with Integrated Heart Center so that the data more complete. The saki house should provide immediate fibrinolytic therapy in patients suspected of having IMA STEMI and establish a SOP of fibrinolytic therapy so that the patient's recovery rate is higher.

In another study, 11 of the 23 patients with STEMI were given fibrinolytic therapy and the results did not show any incidence of death in the hospital, but there were still occurrences of ischemic recurrence and cardiogenic shock.[7] Large-scale cohort studies in Sweden showed that the proportion of deaths in fibrinolytic users was 27, 3% while the proportion of deaths in patients without fibrinolytics was 32.5%. The mortality rate of patients not on reperfusion therapy was 42% (P <0.001) while the mortality rate of users terapi fibrinolitik adalah 31 % (P<0,001). Hasil analisis menunjukkan terapi fibrinolisis berhubungan dengan penurunan tingkat kematian setelah 1 tahun (P=0,001 CI 95%).[8] Namun, tidak terdapat perbedaan proporsi kematian yang signifikan antara terapi trombolisis dan PCI, hanya insidensi gagal jantung lebih banyak ditemukan di pengguna trombolitik daripada pengguna PCI. [9]

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