Characteristics, management, and major adverse cardiac events of ST-elevation myocardial infarction (STEMI) patients in rural area: a Jember acute coronary syndrome medical records study

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ABSTRACT

The mortality and morbidity of ST-elevation myocardial infarction (STEMI) remain high, and it is still the leading cause of death worldwide. Timely reperfusion lowers the risk of MACE and improves survival. However, reperfusion delay is still a significant issue in developing countries, particularly rural area. This study aimed to determine the characteristics, management, and major adverse cardiac events of STEMI patients in Jember Distric to enhance reperfusion therapy in rural areas. It was an analytical observational cross-sectional study with a quantitative method. A total of 108 medical records of STEMI patients of the Dr. Soebandi District Hospital, Jember in period of 2019 to 2020 were included using the consecutive sampling technique. As much as 78 (62%) of the patients did not receive reperfusion therapy while the remaining patients (41 or 38%) received the therapy, namely percutaneous coronary intervention (20 or 18.5%), fibrinolytic therapy (19 or 17.6%), and both (2 or 1.9%). Multivariate analysis for reperfusion was statistically significant ($p=0.016$; OR 3.688 95% CI: 1.274-10.679). The level of education, health funding, and distance to the hospital did not affect the delay of the reperfusion therapy. Reperfusion was highly associated with the incidence of MACE and this study discovered a threefold benefit of reperfusion in lowering the occurrence of MACE ($p=0.016$). In conclusion, the majority of STEMI patients does not get reperfusion therapy. Delays in reperfusion treatment are not related to the patient's level of education, health funding, or distance to the hospital. Nonetheless, the delay my be attributed to the Jember community's lack of awareness of STEMI symptoms.

ABSTRAK

Mortalitas dan morbiditas *ST-elevation myocardial infarction* (STEMI) masih tinggi, dan menjadi penyebab kematian tertinggi di dunia. Reperfusi yang tepat waktu menurunkan risiko MACE dan meningkatkan kelangsungan hidup. Namun, keterlambatan reperfusi masih menjadi masalah nyata di negara-negara berkembang, khususnya di daerah pedesaan. Penelitian ini bertujuan untuk mengetahui karakteristik, penatalaksanaan, dan kejadian jantung buruk mayor pasien STEMI di Kabupaten Jember untuk meningkatkan terapi reperfusi di daerah pedesaan. Penelitian ini merupakan penelitian analitik *observasional cross-sectional* dengan metode kuantitatif. Sebanyak 108 rekam medis pasien STEMI tahun 2019-2020 diikutsertakan dengan menggunakan teknik sampling konsekutif. Sebanyak 78 (62%) pasien tidak mendapatkan terapi reperfusi sedangkan pasien lainnya (41 atau 38%) mendapatkan terapi, yaitu: intervensi koroner perkutan (20 atau 18,5%), terapi fibrinolitik (19 atau 17,6%), dan keduanya (2 atau 1,9%). Analisis multivariat untuk reperfusi secara statistik signifikan ($p=0,016$; OR 3,688; 95% CI: 1,274-10,679). Tingkat pendidikan, dana kesehatan, dan jarak ke rumah sakit tidak mempengaruhi keterlambatan terapi reperfusi. Reperfusi sangat terkait dengan kejadian MACE dan penelitian ini menemukan manfaat tiga kali lipat reperfusi dalam menurunkan kejadian MACE ($p=0,016$). Dapat disimpulkan bahwa mayoritas pasien STEMI tidak mendapatkan terapi reperfusi. Keterlambatan perawatan reperfusi tidak berhubungan dengan tingkat pendidikan pasien, dana kesehatan, atau jarak ke rumah sakit. Meskipun demikian, keterlambatan tersebut mungkin disebabkan oleh kurangnya kesadaran masyarakat Jember terhadap gejala STEMI.

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INTRODUCTION

Cardiovascular disease is a global health issue, accounting for 31% of both morbidity and mortality. In 2025, the mortality rate of coronary heart disease (CHD) was 20 million, and it is expected to rise to 23.6 million by 2030.[1] Acute myocardial infarction (AMI) is one of the CHD is still the leading cause of mortality worldwide, with a prevalence of 12.2 % or around 7.2 million individuals. The prevalence of acute myocardial infarction with ST elevation has jumped from 25 to 40%. According to the Basic Research Data statistics from 2018, the STEMI mortality rate is also the primary cause of cardiovascular death in Indonesia.[2]

ST-elevation myocardial infarction (STEMI) is one of the spectra of acute coronary syndromes due to the sudden decrease of coronary artery blood flow by thrombus occlusion following a rupture of pre-existing atherosclerotic plaque. The American College of Cardiology/American Heart Association and the European Society of Cardiology recommend reperfusion therapy as the first-line therapy of STEMI, either fibrinolytic therapy or percutaneous coronary intervention (PCI). The therapy of PCI has a success rate of 99 %, while fibrinolytic therapy has a success rate of 20-30 %.[3] Those patients who do not have reperfusion therapy are more likely to have complications. Late-onset presentation (> 12 hr), the patient's source of financing, low education level, psychosocial factors, and other relative contraindications are possible reasons for not conducting reperfusion treatment.[3] Major adverse cardiovascular events (MACE) are the term for complications of the reperfusion treatment. This includes heart failure, cardiogenic shock, arrhythmias, and death.[4]

Very few data regarding the characteristics, management, and MACE in STEMI patients in Jember, East Java, Indonesia. Therefore, registry data study is required in order to improve reperfusion treatment. This study aimed to determine the characteristics, management, and major adverse cardiac events of STEMI patients in Jember to enhance reperfusion therapy in the rural area.

MATERIAL AND METHODS

Design of study

It was an analytical observational cross-sectional study using the quantitative method conducted at Dr. Soebandi General Hospital, Jember, East Java, Indonesia from February until March 2021 after ethical clearance approval by the Ethics Committee of the Faculty of Medicine, University of Jember, Number /H25.1.11/KE/2021/456.

Procedure

The study used secondary data from STEMI patient's medical records. All subjects were recruited using the consecutive sampling technique. A total of 119 STEMI patients at Dr. Soebandi General Hospital, Jember in period of 2019 to 2020 were selected in this study. As much as 108 patients met the inclusion and exclusion criteria, while 11 others were excluded. The inclusion criteria of the study were the following: 1) STEMI patients both receiving and not receiving reperfusion therapy for 5 d of evaluation in 2019-2020; 2) Complete medical record data. The following data were also obtained from the medical records: age, sex, the onset of chest pain, comorbidities, level of education, health funding, distance to hospital, and evaluation length. Patients with incomplete data were excluded.

Data analysis

Data were presented as frequency or percentage and analyzed by descriptive, bivariate, and multivariate analysis. Univariate analysis (descriptive analysis) was aimed to describe the characteristics

of each study variable. The Chi-square test was used to compare categorical parameters to evaluate the association between each parameter and MACE (bivariate analysis) in STEMI patients followed by a multivariate analysis logistic regression test with a 95% confidence interval (95%CI). A p value of < 0.05 was defined as statistically significant.

RESULTS

Among 119 STEMI patients who were selected in this study, 108 patients who met the inclusion criteria, while eleven others were excluded. The characteristics, management, and major adverse cardiac events of STEMI patients are presented in TABLE 1.

TABLE 1. Distribution of study parameters variables

Characteristic	[n (%)]
Reperfusion therapy	
Yes	41 (38.0)
PCI	20 (18.5)
Fibrinolytic	19 (17.6)
Both	2 (1.9)
No	78 (62.0)
MACE	
Yes	70 (64.8)
None	38 (35.2)
Age	
<50 y.o.	20 (18.5)
≥50 y.o.	88 (81.5)
Sex	
Males	83 (76.9)
Females	25 (23.1)
Chest pain onset	
<12 hr	51 (47.2)
>12 hr	57 (52.8)
Comorbidities	
Yes	72 (66.7)
None	36 (33.3)
Level of education	
Complete compulsory education	52 (48.1)
Incomplete compulsory education	56 (51.9)
Health funding	
Universal health coverage	0 (0.0)
Dues assistance recipients (PBI)	31 (28.7)
Premium paid	74 (68.5)
Personal funding	3 (2.8)
Distance to the hospital	
Near	14 (13.0)
Far	94 (87.0)

A significant relationship between reperfusion therapy and the occurrence of MACE (p=0.008; OR = 3.345) was observed (TABLE 2). It was demonstrated that STEMI patients who does not get reperfusion treatment has a 3.345 times higher risk of MACE than those who does. TABLE 2 also revealed a significant relationship between MACE with age (p = 0.010; OR=3.577), gender (p=0.022; OR=3.643), onset of pain (p=0.004; OR=3.254), comorbidities (p=0.046; OR 2.5), and level of education (p=0.033; OR 2.419), however no significant relationship with health funding (p=0.946; OR= 0.919).

TABLE 2. Bivariate analysis between reperfusion & parameters with MACE

Variable	MACE [n (%)]		Total	OR	95%CI	p
	Yes	No				
Reperfusion therapy						
Yes	33 (30.6)	8 (7.4)	41 (38.0)	3.345	1.346-8.311	0.008
No	37 (34.3)	30 (27.8)	67 (62.0)			
Total	70 (64.8)	38 (35.2)	108 (100)			
Age						
<50 y.o.	8 (7.4)	12 (11.1)	20 (18.5)	3.577	1.309-9.772	0.010
≥50 y.o.	62 (57.4)	26 (24.1)	88 (81.5)			
Total	70 (64.8)	38 (35.2)	108 (100)			
Sex						
Males	49 (45.4)	34 (31.5)	83 (76.9)	3.643	1.147-11.566	0.022
Females	21 (19.4)	4 (3.7)	25 (23.1)			
Total	70 (64.8)	38 (35.2)	108 (100)			
Onset pain						
<12 hr	26 (24.1)	25 (23.1)	51 (47.2)	3.254	1.423-7.442	0.004
>12 hr	44 (40.7)	13 (12.0)	57 (52.8)			
Total	70 (64.8)	38 (35.2)	108 (100)			
Comorbidities						
Yes	42 (38.9)	30 (27.8)	72 (66.7)	2.500	1.001-6.241	0.046
None	28 (25.9)	8 (7.4)	36 (33.3)			
Total	70 (64.8)	38 (35.2)	108 (100)			
Level of education						
Complete compulsory	39 (36.1)	13 (12.0)	52 (48.1)	2.419	1.066-5.490	0.033
Incomplete compulsory	31 (28.7)	25 (23.1)	56 (51.9)			
Total	70 (64.8)	38 (35.2)	108 (100)			
Health funding						
Universal health coverage	68 (63.0)	37 (34.3)	105 (97.2)	0.919	0.081-10.476	0.946
Personal funding	2 (1.9)	1 (0.9)	3 (2.8)			
Total	70 (64.8)	38 (35.2)	108 (100)			

TABLE 3. Bivariate analysis between distance to the hospital and reperfusion therapy

Distance to hospital	Reperfusion therapy [n (%)		Total	OR	95% CI	p
	Yes	No				
Near	7 (6.5)	7 (6.5)	14 (13.0)	0.567	0.183-1.752	0.320
Far	34 (31.5)	60 (55.6)	94 (87.0)			
Total	41 (38.0)	67 (62.0)	108 (100)			

TABLE 4. Multivariate analysis of the incidence of MACE

Variable	Coefficient	OR	95% CI	p
Reperfusion therapy	1.305	3.688	1.274-10.679	0.016
Age	1.271	3.564	1.115-11.393	0.032
Sex	1.420	4.136	1.154-14.816	0.029
Pain onset	1.021	2.776	1.068-7.218	0.036
Comorbidities	-0.268	0.765	0.593-0.987	0.039
Constant	-5.724	0.003	-	0.001

TABLE 3 presented no significant relationship between the distance to the hospital and reperfusion (p=0.320; OR=0.567). Multivariate analysis using logistic regression test (TABLE 4) confirmed these variables to be significantly associated with MACE: reperfusion (p=0.016), age (p=0.032), sex (p=0.029), onset since pain (p=0.036), and comorbidities (p=0.039) (TABLE 4). The overall percentage value in this study was 77.8%. Education level was not significantly related with p = 0.301.

DISCUSSION

The delay in reperfusion treatment was unaffected by the level of education, health funding, or distance to the hospital. Patients did not receive reperfusion treatment for a variety of reasons, including presenting late pain onset (>12 hr), declined reperfusion therapy, and poor level of education (38%) that might fuel the inadequacy of knowledge on STEMI symptoms. Nonetheless, multivariate studies indicated they were not statistically significant. The lack of funding (no universal health coverage), as well as contraindications in some patients, such as a history of stroke (0.9%) and post cardiopulmonary resuscitation (2.8%), and decreased consciousness, patient's fear, and the lack of understanding of the indications and symptoms of STEMI were the reasons of not receiving therapy. Moreover, the referral mechanism was ineffective. The distance to Dr. Soebandi General Hospital, Jember also did not affect reperfusion therapy.

The total number of patients who did not receive therapy was 62% of patients, while 38% of patients received reperfusion therapy. There were more patients receiving PCI therapy (20 patients or 18.5%) than fibrinolytic therapy (19 patients or 17.6%), while 2 patients received both PCI and fibrinolytic therapy (1.9%). Multivariate analysis indicated that reperfusion therapy significant effected the incidence of MACE with an OR of 3.688 (95%CI: 1.274-10.679). In other words, patients

who did not get reperfusion therapy had an increased risk of MACE 3.688 higher than patients with reperfusion therapy. These results are consistent with the study conducted by Yang *et al.* that reperfusion therapy is associated with decreased risk of MACE than the patients who does not get reperfusion therapy.[5]

Reperfusion aims to fix the myocardial blood flow, saving myocardium, maintaining the function of the left ventricle, and reducing the mortality level.[6] A successful reperfusion therapy greatly relies on the period passing between the symptom appearance and the therapy. Early reperfusion with a short period between "symptom-to-needle" and "door-to-needle" in patients with myocardial infarction is the main goal of reperfusion.

The key factor in STEMI treatment is the ischemic time, or when the symptoms appear until the reperfusion therapy.[7] The longer the artery is exposed to occlusion, the wider the ischemic wave which extends from the endocardium to the epicardium so an immediate reperfusion act must be made.[8] Percutaneous coronary intervention is the treatment of choice in the management of patients with acute STEMI which significantly reduces mortality and morbidity compared to fibrinolytics as a reperfusion strategy.

Clinical outcomes in STEMI patients are influenced by the occurrence of complications known as MACE, which consists of left ventricular dysfunction, recurrent ischemia, early reinfarction, severe coronary disease, stroke and malignant arrhythmias.[5] According to the data and result of studies, reperfusion therapy can lower the risk of MACE.

A study by Parung *et al.* stated that the number of patients who did not get reperfusion treatment was higher than the number of patients who did.[9] The number of STEMI patients who received reperfusion therapy at Dr. Soetomo General Hospital, Surabaya in 2013

was 41%, where 28% of them received PCI while 72% received fibrinolytic therapy. About 59% of STEMI patients did not receive reperfusion therapy. This occurred because the National Health Insurance (Jaminan Kesehatan Nasional/JKN) had yet to begin in 2013, and most patients were still unable to afford reperfusion therapy.[9] This condition increases the incidence of MACE in patients with no reperfusion therapy. As recommended by the European Society of Cardiology, individuals with clinical symptoms of STEMI and persistent ST-segment elevation or new LBBB on the ECG should be treated as soon as possible within 12 hr.[10]

According to Huber *et al.*[11] three factors contributed to the time delay between the onset of chest pain and the start of reperfusion therapy: delayed patient's decision to get to the hospital (1.5 to 3 hr), delayed prehospital transportation (30 to 130 min) and delayed STEMI management. Furthermore, a referral system might lengthen the time it takes for patients to get reperfusion treatment. Another factor affecting the delay was the patient's inaccuracy in perceiving the symptoms of chest pain.[12] About 41% of the patients perceive that the symptoms of chest pain experienced were not heart disease and 64.1% of them had delayed treatment. The patient's ability to correctly perceive the symptoms would determine the patient's response.[13,14]

The patient's level of education has an impact on their knowledge and decision-making. Patients who did not complete obligatory education (low education) had a limited understanding of symptoms and decision-making, whereas patients who completed their compulsory education (higher education) had sufficient information for considering options and clear judgments.[15] Furthermore, as the level of education affected the reperfusion therapy, it might also indirectly affect the

incidence of MACE. Multivariate analysis in this study showed that education level does not influence reperfusion treatment delay. This might be due to other important factors: local cultural and the size of the study's sample. Local culture practice might cloud patient's judgment of STEMI symptoms.[16]

The National Health Insurance covered treatment costs for the majority of STEMI patients in Dr. Soebandi General Hospital. Patients with premium-paid the National Health Insurance participants (non-PBI) presented more STEMI cases than those with dues assistance recipients (PBI) participants. The PBI patients accounted for 31 patients (28.7%), while the non-PBI group consisted of 74 patients (68.5%). The personal decision to whether to receive reperfusion treatment or not was heavily influenced by their health insurance coverage. Patients who received reperfusion therapy were often residents covered by the National Health Insurance, while those who were not covered by the National Health Insurance were found to receive less reperfusion therapy. A total of 19 out of 108 patients (17,6%) received fibrinolytic reperfusion therapy with streptokinase as a fibrinolytic drug. This is due to the low cost of streptokinase.[9,10]

CONCLUSION

In conclusion, reperfusion is proven to be effective in reducing MACE with an OR of 3.688. The delay in reperfusion therapy is not related to the level of education, health funding, and distance to the hospital. Lack of awareness of STEMI is suspected to be the major cause of the delay in reperfusion therapy. This can be seen from late-onset presentation (> 12 hr) and psychosocial factors. Late-onset STEMI patients (>12 hr) have a 3.254 times higher risk of MACE than patients presented with early onset STEMI.

REFERENCES

1. World Health Organization. Cardiovascular Diseases (CVDs). World Health Organization 11 June 2021. https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)
2. Badan Penelitian dan Pengembangan Kesehatan. Laporan Nasional Riset Kesehatan Dasar 2018. Jakarta: Kementerian Kesehatan Republik Indonesia, 2018.
3. Bambari HA, Agnes LP, Joseph VFF. Terapi reperfusi pada infark miokard dengan ST-Elevasi. e-CliniC 2021; 9(2):287-98. https://doi.org/10.35790/ecl.9.2.2021.32850
4. Bosco E, Hsueh L, McConeghy KW, Gravenstein S, Saade E. Major adverse cardiovascular event definitions used in observational analysis of administrative databases: a systematic review. BMC Med Res Methodol 2021; 21(1):241. https://doi.org/10.1186/s12874-021-01440-5
5. Yang Y, Hao Y, Liu J, Yang N, Hu D, Sun Z, *et al*. Practice of reperfusion in patients with ST-segment elevation myocardial infarction in China: findings from the Improving Care for Cardiovascular Disease in China-Acute Coronary Syndrome project. Chin Med J (Engl) 2022; 135(23):2821-8. https://10.1097/CM9.0000000000002257
6. Nasution SA, Hendra P, Eka G, Ikhwan R. In-hospital major adverse cardiac events factor predictors on

ST-Elevation myocardial infarction after primary percutaneous coronary intervention at Dr. Cipto Mangunkusumo General Hospital. eJKI 2022; 10:(2):107-113. https://doi.org/10.23886/ejki.10.193.107-13

7. Bohula EA, Morrow DA. ST elevation myocardial infarction: management. In: Zipes D, Libby P, Bonow R, Mann D, Tomaselli G, Braunwald E, editors. Braunwald's Heart Disease: a Textbook of Cardiovascular Medicine (11ᵗʰ ed). Philadelphia: Elsevier Inc, 2020; p 1123-80.

8. Vogel B, Claessen BE, Arnold SV, Chan D, Cohen DJ, Giannitsis E, *et al.* ST-segment elevation myocardial infarction. Nat Rev Dis Primers 2019; 5(1):39. https://doi.org/10.1038/s41572-019-0090-3

9. Parung AA, Liben P, Herwanto B. Tingkat mortalitas terapi reperfusi pada penderita STEMI di RSUD Dr. Soetomo Surabaya. JUXTA J Ilm Mhs Kedokt Univ Airlangga 2016; 8:17-23.

10. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, *et al.* Fourth universal definition of myocardial infarction (2018). J Am Coll Cardiol 2018; 72(18):2231-64. https://doi.org/10.1016/j.jacc.2018.08.1038

11. Huber K, De Caterina R, Kristensen SD, Verheugt FWA, Montalescot G, Maestro LB, *et al.* Pre-hospital reperfusion therapy: a strategy to improve therapeutic outcome in patients with ST-elevation myocardial infarction. Eur Heart J 2005; 26(19):2063-74. https://doi.org/10.1093/eurheartj/ehi413

12. Hendrawati, Rohman MS, Tjahjono CT, Widito S, Satrijo B, Waranugraha Y, *et al.* Percutaneous coronary intervention in ST-segment elevation myocardial infarction: late is better than not done at all. Heart Sci J 2020; 1(3):21-6. https://doi.org/10.21776/ub.hsj.2020.001.03.5

13. Novrianti I, Dhani W, Faizal M, Sari W. Pharmacological therapy for ST-Segment elevation myocardial infarction: a review. J Islamic Pharm 2020; 5(2):9-13.

14. Wong GC, Welsford M, Ainsworth C, Abuzeid W, Fordyce CB, Greene J, *et al.* 2019 Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology Guidelines on the acute management of ST-elevation myocar-dial infarction: focused update on regionalization and reperfusion. Can J Cardiol 2019; 35(2):107-32. https://doi.org/10.1016/j.cjca.2018.11.031

15. Yang HT, Xiu WJ, Zheng YY, Liu F, Gao Y, Ma X, *et al.* Invasive reperfusion after 12 hours of the symptom onset remains beneficial in patients with ST-segment elevation myocardial infarction: evidence from a meta-analysis of published data. Cardiol J 2019; 26(4):333-42. https://doi.org/10.5603/CJ.a2018.0034

16. Guo Q, Jinyu H, Yong S, Guoxin T, Li H, Shasha M. The role of late reperfusion in ST-segment elevation myocardial infarction: a real-world retrospective cohort study. BMC Cardiovas Disord 2020; 20(1):207. https://doi.org/10.1186/s12872-020-01479-0