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Original Article

Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction: Late is Better Than Not Done at All

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ABSTRACT

Background : For ST-segment elevation myocardial infarction (STEMI) patients, reperfusion through primary percutaneous coronary intervention (PCI) must be done to return the coronary arteries' blood flow. However, a large proportion of patients received late PCI. This study aimed to assess the impact of late PCI on the clinical outcomes of STEMI patients.
Methods : A retrospective cohort study was conducted in Saiful Anwar General Hospital from January 2017 to April 2018. A total of 192 STEMI patients were divided into three groups: (1) on-time PCI; (2) late PCI; and (3) no PCI. The outcome measured included six months and 12 months of cardiovascular mortality and hospital readmission because of worsening heart failure and recurrent myocardial infarction (MI).
Results: At six-month follow-up period, we found that hospital readmission was higher in the no PCI group (9.2% vs. 12.1% vs. 34.8%; $p = 0.009$). The recurrent MI (0% vs. 0% vs. 7.2%; $p = 0.010$) and worsening heart failure (6.2% vs. 8.6% vs. 33.3%; $p < 0.001$) was also higher in the no PCI group. On 12 months follow up period, the mortality (4.6% vs. 13.8% vs. 21.7%; $p = 0.015$) and hospital readmission (15.4% vs. 20.7% vs. 42%; $p = 0.001$) rate was higher in no PCI group. Hospital readmission because of worsening heart failure was also higher in no PCI group (9.2% vs. 17.2% vs. 37.7%; $p = 0.015$).
Conclusion: Not performing revascularization was correlated with higher mortality and hospital readmission rate in STEMI patients. Late PCI was associated with better outcomes than not conducting revascularization.

1. Introduction

STEMI is the most severe manifestation of the acute coronary syndrome (ACS). Generally, STEMI is caused by the rupture of atheromatous plaque, leading to thrombus generation, resulting in acute total occlusion of the coronary artery.[1] Following interrupted coronary blood flow, myocardial damage begins. The more prolonged ischemia occurred, the greater the amount of myocardial damage. Revascularization using primary PCI conducted within 12 hours following onset is the best treatment strategy in STEMI patients.[2,3] Several studies emphasized the strong correlation between the delay in revascularization and mortality in STEMI patients accompanied with out-of-hospital cardiac arrest (OHCA) or cardiogenic shock.[4-6] In STEMI accompanied by cardiogenic shock without OHCA, between 60-180 minutes from the first medical contact, every 10 minutes of treatment delay will produce 3.3 additional deaths per 100 patients treated with PCI.[7]

Previous studies also have shown that STEMI patients received more benefit by primary PCI conducted less than 12 hours from the onset of STEMI symptoms.[8] However, for STEMI patients with onset of more than 12 hours, the evidence to support performing PCI is not strong enough. Occluded Artery Trial (OAT) revealed no benefit of late reperfusion for patients who arrive over three days after the onset.[9,10] However, several studies showed that conducting PCI is still beneficial for myocardial saving, even though it was done late.[11,12] This study aimed to assess the impact of late PCI on the clinical outcomes of STEMI patients.

2. Methods

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2.1. Study Design

It was a retrospective cohort study. We used a consecutive sampling method. This study protocol was recognized and approved by the ethical committee of Saiful Anwar General Hospital.

2.2. Study population

AAll patients admitted to Saiful Anwar General Hospital, Malang, Indonesia, with confirmed STEMI from January 2017 to April 2018, according to the 2017 ESC Guideline for STEMI, were included in this study. We excluded patients with: (1) congenital heart disease; (2) valvular heart disease; (3) pulmonary hypertension; (4) idiopathic cardiomyopathy; (5) severe liver or renal dysfunction; (6) malignancy, (7) autoimmune disease; or (8) uncontrolled systemic diseases (Figure1).

2.3. Baseline Data Collection

All information about the patient, including demographic data, payment status, Killip class, and risk stratification using Thrombolysis in Myocardial Infarction (TIMI) risk score and Global Registry of Acute Coronary Events (GRACE) score were collected using a standard case-report form. The TIMI score is classified into two categories, the score <5 is classified as low risk, while the score> 5 is high risk.[13] We used the GRACE score to estimate mortality within six months in STEMI patients. The GRACE score is classified into three groups: (1) GRACE score of <109 (low risk); (2) GRACE score 109 to 140 (moderate risk); and (3) GRACE score of >140 (high risk).[2,14,15]

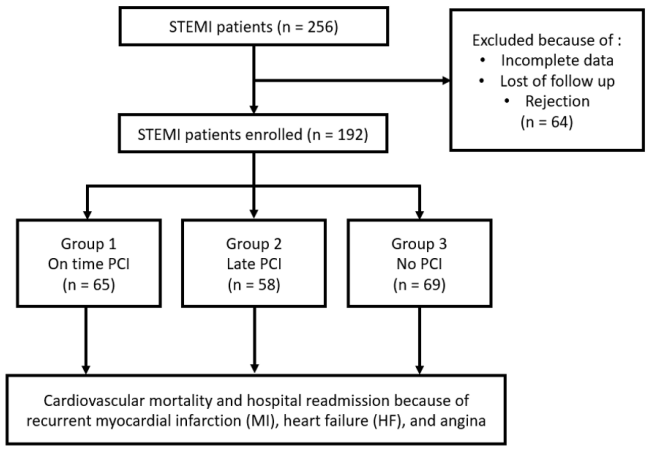

Figure 1. Study flowchart

2.4. Exposure and Outcome

The exposure was the reperfusion strategy. STEMI Patients were divided into three separate groups based on the reperfusion strategy: on-time PCI group, late PCI group, and no PCI group. On-time PCI was defined as PCI that was performed within the time frames according to the 2017 ESC Guidelines for STEMI management. PCI that performed beyond the time frames determined by the 2017 ESC Guidelines for STEMI management was Late PCI.[2] The late PCI criteria included PCI performed beyond 12 hours from the onset of chest pain symptoms in STEMI patients with stable hemodynamic or rescue PCI in >90 minutes after failed fibrinolytic therapy. STEMI patients who received optimal medical treatment but did not receive any reperfusion or failed to undergo PCI (due to abnormal anatomical morphology of coronary artery, passed away before PCI, and refused PCI because of financial problems or not covered by insurance) were classified as no PCI.

The outcome measured was six months and 12 months of mortality and hospital readmission. Readmission data were obtained from medical records or interview questionnaires on phone calls about hospital readmission after discharge due to recurrent MI and worsening heart failure. Mortality data were obtained from family member information declared dead from phone call interviews or medical records that showed mortality during hospitalization. The study flowchart is summarized in Figure 1.

2.5. Statistical analysis

IBM SPSS version 22 software was used to conduct statistical analysis. Number and percentages were used to show categorical data. Mean and standard deviation were used to present numeric data. Statistical analysis for numeric data with normal distribution was performed using the analysis of variance (ANOVA). However, if the data abnormally distributed, the Kruskal Wallis test was used to conduct statistical analysis of numerical data. Statistical analysis for categorical data was conducted using the Chi-square test. A p-value of <0.005 is considered significant statistically.

3. Results

3.1. Patients basic characteristics

We collected the data from 256 STEMI patients. However, about 64 STEMI patients were excluded because of incomplete data, lost follow-up, and refused participation. Finally, a total of 192 patients were involved in the analysis process. The patients' mean age was 57.7 ± 10.2 years, and 81.3% of them were male. The one-year readmission and mortality rates were 26.6% and 13.5%, respectively. The most common cause of readmission is worsening heart failure (62%). Table 1 is summarizing patients' baseline characteristics.

Among the three groups of patients, from baseline characteristics, no significant differences in the proportion of age, sex, chest pain onset, TIMI risk score, GRACE score, Killip class, and medication adherence, except payment status, were found. Coronary angiographic characteristics data in groups of STEMI patients receiving PCI treatment were not significantly different in terms of the number of coronary lesions, the infarct-related artery (IRA), and TIMI flow. A total of 123 (64%) patients were treated by PCI, while 69 (36%) received only optimal medical therapy.

3.1. Clinical outcome

During the six-month follow-up period, we found that hospital readmission was higher in the no PCI group (9.2% vs 12.1% vs 34.8%; p = 0.009). We also conducted a subgroup analysis of the cause of hospital readmission. Higher percentage of recurrent MI was found in the no PCI group (0% vs. 0% vs. 7.2%; p = 0.010). A higher percentage of worsening heart failure was also found in the no PCI group (6.2% vs 8.6% vs 33.3%; p < 0.001). The mortality rate among the three groups was not significantly different (3.1% vs 5.2% vs 10.1%; p = 0.221).

During the follow-up period of 30 days following hospital discharge, three patients in suboptimal dose of ACEI group were passed away. Two patients passed away because of cardiogenic shock, while one patient passed away because of sudden cardiac death. Data analysis

During the 12 months follow up period, the mortality (4.6% vs. 13.8% vs. 21.7%; p = 0.015). and hospital readmission (15.4% vs. 20.7% vs. 42%; p = 0.001) rate was higher in no PCI group

From subgroup analysis, we found that worsening heart failure causing hospital readmission was higher in no PCI group (9.2% vs 17.2% vs 37.7%; p = 0.015). However, recurrent MI among the three groups (4.6% vs 1.7% vs 7.2%; p = 0.340) was not significantly different. The clinical outcomes were summarized in table 2. Kaplan-Meier curve showing survival from hospital readmission and mortality during 12 months follow-up period is shown in figure 2.

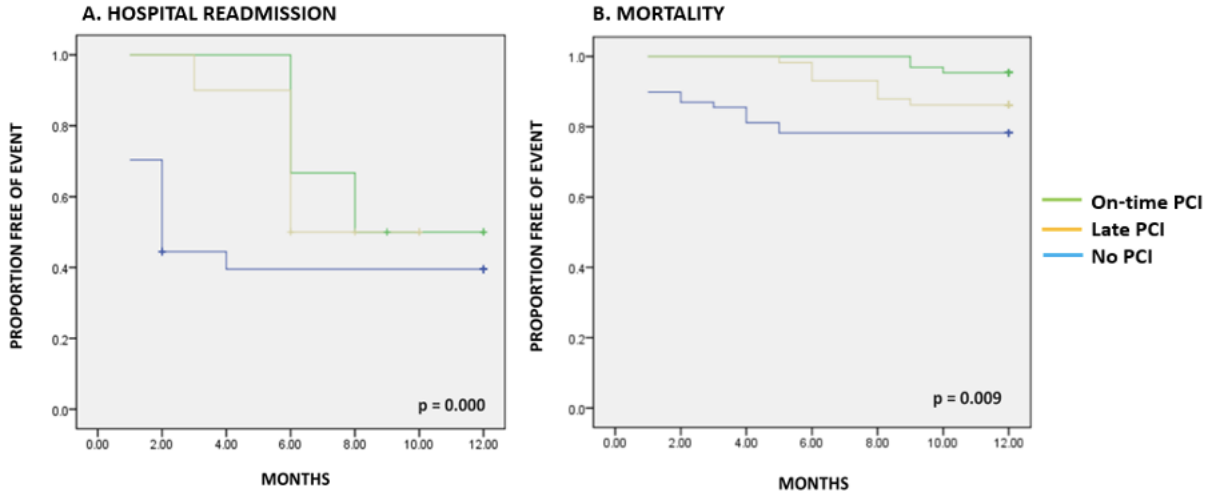

Figure 2. Kaplan-Maier curves for hospital readmission (B) and mortality (B)

Table 1. Baseline charaterictic of the patients

Variables		Group			p
		On-time PCI (n=65)	Late PCI (n=58)	No PCI (n=69)	
Age	Student	56 + 10.4	57 + 8.9	59 + 11.17	0.450
Sex					0.336
Male		52 (80.0)	51 (87.9)	54 (78.3)	
Female		13(20.0)	7 (12.1)	15 (21.7)	
Payment status					0.000
Insurance		64 (98.5)	50 (86.2)	41 (59.4)	
Regular		1 (1.5)	8 (13.8)	28 (40.6)	
Symptom onset					0.930
<12 hours		44 (67.7)	28 (48.3)	40 (58.0)	
>12 hours		21 (32.2)	30 (51.7)	29 (42.0)	
TIMI score					0.389
<5		55 (84.6)	44 (24.1)	51 (73.9)	
>5		10 (15.4)	14 (24.1)	18 (26.1)	
GRACE score					0.518
Low		31 (47.7)	23 (39.7)	28 (40.6)	
Intermediate		20 (30.8)	18 (31.0)	17 (24.6)	
High		14 (21.5)	17 (29.3)	24 (34.8)	

Killip				0.556
I	48 (73.8)	40 (69.0)	48 (69.6)	
II	2 (3.1)	5 (8.6)	3 (4.3)	
III	0 (0.0)	2 (3.4)	1(1.4)	
IV	15 (23.1)	11 (19.0)	17 (24.6)	
Medication adherence	51(82.3)	55 (94.8)	61 (89.7)	0.080
Infarct related artery				0.155
Left main	0 (0.0)	0 (0.0)	-	
Left anterior descending artery	28 (43.1)	35 (60.3)	-	
Left circumflex artery	4 (6.2)	3 (5.2)	-	
Right coronary artery	33 (50.8)	20 (34.5)	-	
Number of lesions				0.520
1	8 (12.3)	7 (12.5)	-	
2	14 (21.5)	17 (30.4)	-	
3	43 (66.2)	32 (57.1)	-	
TIMI flow				0.203
0-1	1 (1.5)	3 (5.2)	-	
2	13 (20.0)	9 (15.5)	-	
3	51 (78.5)	46 (79.3)	-	

Note, data were presented in mean ± SD or n(%); GRACE = Global Registry of Acute Coronary Events; PCI = percutaneous coronary intervention; TIMI = Thrombolysis in Myocardial Infarction

Table 2. Outcomes

Variables	**Group**			**p**
	On-time PCI (n=65)	**Late PCI (n=58)**	**No PCI (n=69)**	
6 months of follow up	56 + 10.4	57 + 8.9	59 + 11.17	0.450
Mortality Student				0.336
Readmission	52 (80.0)	51 (87.9)	54 (78.3)	
Cause of readmission	13(20.0)	7 (12.1)	15 (21.7)	
Recurrent myocardial infarction				0.000
Heart failure	64 (98.5)	50 (86.2)	41 (59.4)	
Angina	1 (1.5)	8 (13.8)	28 (40.6)	
12 months of follow up				0.930
Mortality	44 (67.7)	28 (48.3)	40 (58.0)	
Readmission	21 (32.2)	30 (51.7)	29 (42.0)	
Cause of readmission				0.389

Recurrent myocardial infarction	3 (4.6)	1 (1.7)	5 (7.2)	0.340
Heart Failure	6 (9.2)	10 (17.2)	26 (37.7)	<0.001
Angina	3 (4.6)	3 (5.2)	9 (13)	0.128

Note, data were presented in mean ± SD or n(%); PCI = percutaneous coronary intervention.

4. Discussion

The hospital readmission rate for six months and twelve months follow-up was higher in no PCI group. From the subgroup analysis, there were essential variations causes of hospital admission. Recurrent MI contributed to hospital readmission for six months follow-up period. However, worsening heart failure contributed to hospital readmission for six months and twelve months follow-up period. From the subgroup analysis, it was found that the most common reason behind hospital readmission was the worsening of heart failure. It was significantly different between the on-time PCI and no PCI groups ($p < 0.001$) and between the late PCI and no PCI groups ($p = 0.019$).

The meta-analysis study by Yang et al., which involved 11 studies reported the incidence of readmission related to myocardial infarction, showed significantly different results ($p = 0.008$). There was a tendency of decreasing rates of recurrent MI in late revascularization groups in all patients. Subgroup analysis showing late reperfusion beyond 12 hours was associated with a significant reduction of the incidence of recurrent MI compared to groups with optimal medical therapy ($p <0.001$), but this difference did not show significant results in 2-60 days late reperfusion ($p = 0.55$). Whereas for readmission related to worsening heart failure, the meta-analysis of Yang et al. reported that late reperfusion of beyond 12 hours was significantly correlated with a reduction in worsening heart failure ($p = 0.004$).16

According to the open artery hypothesis, time-dependent myocardial rescue (early) and a time-independent process (late) are involved in the extended paradigm of acute MI. Late coronary reperfusion seems to disturb the adverse remodelling process of the heart, chamber enlargement, and systolic dysfunction. Late coronary reperfusion seems to disturb the adverse remodelling process of the heart, chamber enlargement, and systolic dysfunction. In the late reperfusion setting through the contraction band necrosis, cellular oedema, and intramyocardial haemorrhage, favourable myocardial stiffening is also believed to take place more readily.[17,18] Moreover, persistent occlusion of the IRA has been related to an increase in the rate of apoptosis in the peri-infarct region markers of ischemia. Left ventricular dilatation, progressive left ventricular systolic dysfunction through apoptosis, gradual cells lost are thought to have a role in the terrible ventricular remodelling.[19,20] Patients with an open IRA significantly had lower 30-day mortality than a not opened IRA ($p <0.001$). This advantage could not be explained by myocardial rescue alone, because it resided following adjustment for left ventricular ejection fraction (LVEF). The coronary artery's patency was also correlated with lower 30-day and 1-year mortality, but not after adjustment for other late mortality variables. Having an open IRA at the first coronary angiography confers a survival benefit that expands beyond the advantages of myocardial rescue from thrombolytic treatment and is not related to LVEF.[21]

Beyond 12 hours Reperfusion AlternatiVe Evaluation (BRAVE-2) trial specifically included STEMI patients with the symptom onset ranging from 12 to 48 hours. They were randomized to conservative strategy and invasive strategy. A total of 365 STEMI patients were involved in the BRAVE-2 trial, revealed a statistically significant decrease in the size of the final infarction in the group receiving invasive strategy with single-photon emission computed tomography (SPECT) imaging at a median of 7.1 days. Clinical outcome results followed on days 30 and 90 did not show differences between both groups.12 Mortality rate was significantly lower in the invasive strategy group (11.1%) than the conservative group (18.9%), at four years follow up, reflecting the absolute risk difference of 7.8%.[22]

Our study aimed to look for the impact of late PCI on the clinical outcome of STEMI patients without seeing the delay based on the division of time frames. Delay >72 hours are considered the same for the period after, while the data obtained for the delay in PCI in opening an IRA starts from 24 hours to 11 months. The research with better design might be warranted. The relatively small number of samples and the high exclusion rate of patients were also the drawbacks of this study besides the limited follow-up period of up to 12 months. Further research with a larger number of samples, a more extended follow-up period, and a more accurate analysis is needed.

5. Conclusion

Not performing revascularization was correlated with higher mortality and hospital readmission rate in STEMI patients. Late PCI was associated with better outcomes than not conducting revascularization. However, conducting on-time PCI based on the guideline recommendation was the best approach for improving STEMI patients' outcomes.

6. Declarations

6.1. Ethics Approval and Consent to participate
This study was approved by local Institutional Review Board, and all participants have provided written informed consent prior to involve in the study.

6.2. Consent for publication
Not applicable.

6.3. Availability 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: H. Design: H. Control/supervision: MSR, CT, SW, BS, YW. Data collection/processing: H, MRF, I. Extraction/Analysis/interpretation: H, MRF, I. Literature review: MSR, CT, SW, BS, YW. Writing the article: H. Critical review: MSR, CT, BS, YW. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

6.7. Acknowledgements
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References.

1. Srikanth S, A Ambrose J. Pathophysiology of coronary thrombus formation and adverse consequences of thrombus during PCI. Current cardiology reviews 2012;8:168-76.

2. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of

acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). European heart journal 2018;39:119-77.

3. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Journal of the American College of Cardiology 2013;61:485-510.

4. Lemkes JS, Janssens GN, van der Hoeven NW, et al. Coronary angiography after cardiac arrest without ST-segment elevation. New England Journal of Medicine 2019;380:1397-407.

5. Miedema MD, Newell MC, Duval S, et al. Causes of delay and associated mortality in patients transferred with ST-segment–elevation myocardial infarction. Circulation 2011;124:1636-44.

6. Scholz KH, Maier SK, Maier LS, et al. Impact of treatment delay on mortality in ST-segment elevation myocardial infarction (STEMI) patients presenting with and without haemodynamic instability: results from the German prospective, multicentre FITT-STEMI trial. European heart journal 2018;39:1065-74.

7. Neumann F-J, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. European heart journal 2019;40:87-165.

8. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. European heart journal 2006;27:779-88.

9. Hochman JS, Lamas GA, Buller CE, et al. Coronary intervention for persistent occlusion after myocardial infarction. New England Journal of Medicine 2006;355:2395-407.

10. Hochman JS, Reynolds HR, Džavík V, et al. Long-term effects of percutaneous coronary intervention of the totally occluded infarct-related artery in the subacute phase after myocardial infarction. Circulation 2011;124:2320-8.

11. Busk M KA, Nielsen SS, et al. Infarct size and myocardial salvage after primary angioplasty in patients presenting with symptoms for< 12h vs 12–72h (Aarhus Univ Hosp, Denmark) Eur Heart J 30: 1322-1330, 2009. Year Book of Cardiology 2010;2010:330-3.

12. Schömig A, Mehilli J, Antoniucci D, et al. Mechanical reperfusion in patients with acute myocardial infarction presenting more than 12 hours from symptom onset: a randomized controlled trial. Jama 2005;293:2865-72.

13. Morrow DA, Antman EM, Charlesworth A, et al. TIMI risk score for ST-elevation myocardial infarction: a convenient, bedside, clinical score for risk assessment at presentation: an intravenous nPA for treatment of infarcting myocardium early II trial substudy. Circulation 2000;102:2031-7.

14. Fox KA, Dabbous OH, Goldberg RJ, et al. Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE). bmj 2006;333:1091.

15. Fox KA, FitzGerald G, Puymirat E, et al. Should patients with acute coronary disease be stratified for management according to their risk? Derivation, external validation and outcomes using the updated GRACE risk score. BMJ open 2014;4.

16. Yang H-T, Xiu W-J, Zheng Y-Y, 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. Cardiology journal 2019;26:333-42.

17. Appleton DL, Biondi-Zoccai G, Abbate A. Benefits of coronary revascularization in stable patients in the short and long term after acute myocardial infarction. Interventional Cardiology 2010;2:67-76.

18. Fan Y, Bai X, Chen Y, et al. Late percutaneous coronary intervention prevents left ventricular remodelling and improves clinical outcomes in patients with ST-elevation myocardial infarction. Clin Cardiol 2015;38:82-91.

19. Abbate A, Bussani R, Biondi-Zoccai GG, et al. Persistent infarct-related artery occlusion is associated with an increased myocardial apoptosis at postmortem examination in humans late after an acute myocardial infarction. Circulation 2002;106:1051-4.

20. Abbate A, Bussani R, Biondi-Zoccai GG, et al. Infarct-related artery occlusion, tissue markers of ischaemia, and increased apoptosis in the peri-infarct viable myocardium. European heart journal 2005;26:2039-45.

21. Puma JA, Sketch MH, Thompson TD, et al. Support for the open-artery hypothesis in survivors of acute myocardial infarction: analysis of 11,228 patients treated with thrombolytic therapy. The American Journal of Cardiology 1999;83:482-7.

22. Ndrepepa G, Kastrati A, Mehilli J, Antoniucci D, Schömig A. Mechanical Reperfusion and Long-term Mortality in Patients With Acute Myocardial Infarction Presenting 12 to 48 Hours From Onset of Symptoms. JAMA 2009;301:487-8