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Comparison of PCI and Thrombolytic Effectiveness as Reperfusion Therapy in STEMI

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Abstract
Cardiovascular disease is the leading cause of death worldwide and Acute Coronary Syndrome (ACS) is one of the biggest causes of high mortality in CVD. In Indonesia, according to the Deparment of Health survey in 2008, the mortality rate reached 25% due to heart attack. In ACS patient with STEMI, there are two options for reperfusion therapy: percutaneous coronary intervention (PCI) and fibrinolytic/thrombolytic therapy. The aim of this article review is to discuss reperfusion therapy by comparing PCI and thrombolytic/fibrinolytic therapy of ACS patients with STEMI conditions. The methods in this review are the search of research results and digital data based on Pubmed, Scopus and Google Scholar. From this review, it can be concluded that primary PCI therapy is the preferred therapy in STEMI patients compared with thrombolytic therapy, except in some conditions such as unsupportive facilities and infrastruktur of the hospitals, then thrombolytic therapy can be performed up to 30 minutes after the attack.
Keywords*: ACS, fibrinolytic, PCI, STEMI, thrombolytic*

I. INTRODUCTION

Acute Coronary Syndrome (ACS) is a major cardiovascular problem, its leads on very high hospital care and mortality rate (PERKI, 2015). In Indonesia, according to the household survey done by ministry of Health, in 2008 25% of are related to heart failure). Based on number of patients who diagnosed by a physician, the prevalences are higher in urban areas, but based on symptoms diagnosed by physicians the prevalences are higher in rural areas (Kepmenkes, 2013). ACS is defined as desease of all symptoms related or due to myocardial ischemia (Smith *et al*.,2015). ACS is classified into three groups: unstable angina (UA), non- ST elevation segment myocard infarction (NSTEMI), and ST elevation segment myocard infarction (STEMI) (Kumar & Cannon, 2009; Smith *et al*., 2015). The classification and diagnosis of ACS depends on several clinical aspects found in patients such as ECG and biochemical markers of myocardial necrosis (Smith *et al*., 2015). The term myocard infarction (MI) is used when there is evidence of necrosis in acute myocardial ischaemia conditions. STEMI is distinguished by a persistent increase in ST segment in patients (Smith *et al*., 2015). In patients with STEMI, reperfusion therapy is the main therapy that should be given to patients with symptom onset <12 hours. There are two options for reperfusion action such as percutaneous coronary intervention (PCI) and fibrinolytic therapy (ESC, 2012; ACCF / AHA, 2013).

PCI is the recommended reperfusion therapy when it can be performed in time, with the goal of time from the first medical contact to the tool ≤90 minutes. If the patient does not get PCI within 2 hours, fibrinolytic/thrombolytic therapy should be administered within the first 30 minutes of hospitalization, if there is no contraindication to the patient (Smith *et al*., 2015). Patients who planned for reperfusion should be identifiable by an ER medical team, starting with emergency medical services to reduce delays. Any possibility of a hospital slowdown to reach a 90-minute door-to-balloon time should be avoided since the patient enters the triage. For hospitals that do not have PCI means, rapid referral access can also be performed with an estimated time of less than 120 minutes until PCI is performed. In addition, PCI is preferred in STEMI patients with fibrinolytic contraindications, high risk of bleeding, over 75 years of age, high risk, and cardiogenic shock. While fibrinolytic therapy is recommended in STEMI patients with chest pain onset of less than 3 hours but no PCI means and a history of contrast allergy. Patients who have stents attached to the coronary artery are blocked can reduce the risk of restenosis (narrowed back), recurrent angina and the need for future revascularization actions rather than binding only. This scientific artkel are aimed to discuss those reperfusion therapy by comparing percutaneous coronary intervention (PCI) and administration of thrombolytic therapy (fibrinolytic) in ACS patients with STEMI condition.

II. ACUTE CORONARY SYNDROME (ACS)

A. Anatomy and Physiology of the Heart

The heart is a very complex organ that functions as a blood pumper to the lungs and to the systemic circulation. The heart is divided into 4 parts of the right atrium and left and right ventricle and left. There are various valves that separate between the chambers in the heart. The tricuspid valve separates the right atrium and right ventricle. The mitral / bicuspid valve separates between the left atrium and the left ventricle. The aortic valve separates the left ventricle from the aorta. The blood supply from the aorta to the heart through the coronary

arteries. The coronary artery consists of three major vessel components: left anterior descending, left circumflex, and right coronary arteries (McPhee and Ganong, 2005).

B. Acute Coronary Syndrome (ACS)

ACS is a term used for a collection of symptoms that arise from acute myocardial ischaemia. ACS that occurs due to a heart muscle infarction is called myocardial infarction. Included in the ACS are unstable angina pectoris, non ST segment ST (non STEMI), and ST-segment elevation myocardial infarction (STEMI) (Ramrakha, 2006).

C. Pathophysiology of ACS

Blockage or impasse on the coronary arteries will result in reduced blood perfusion to the heart, which can lead to ischemic conditions. Most cases of ischemia are due to atherosclerotic plaque in coronary arteries (Trujillo and Nolan, 2013). Endothelial vascular damage causes some components of blood cholesterol especially LDL into the endothelial layer and accumulates in it. Accumulated cholesterol undergoes oxidation or enzymatic processes. Leukocytes will enter the endothelial region of LDL accumulation, leukocytes will oxidize LDL phagocytosis in the tissue. An unregulated process of phagocytosis can form a foam cell. T lymphocytes and macrophages will be activated and joined with foam cells to perform the process of phagocytosis. The smooth muscle cells will also be activated and migrated, these cells will secrete extracellular matrices such as collagen to stabilize the formed plaques. Phagocytic cells that perform the phagocytic process will produce several inflammatory mediators such as cytokines. Cytokines induce the secretion of proteolytic enzymes that can break down or melisis extracellular matrix causing the plaque fragile and easy to experience rupture (Trujillo and Nolan, 2013). The ruptured plaque component will be exposed to the blood component, some thrombogenic plaque components such as collagen factor factor will activate platelets and induce the formation of thrombus or blood clots in the coronary vessels (Page and Nappi, 2013).

D. ACS Classification

ACS is classified into three groups: unstable angina (UA), non-ST elevation segment myocard infarction (NSTEMI), and ST elevation segment myocard infarction (STEMI). The three classifications are different in the formation of clots / blood clots in the coronary region, in which the blood clot is still in minimal size, the NSTEMI blood clot is formed in large size and almost mostly covers the coronary vessel lumen, whereas in the STEMI blood clot formed closing all the lumen of blood vessels (Page and Nappi, 2013).

E. STEMI Therapy

Reperfusion action is the preferred choice of therapy in STEMI patients when the period between attacks and therapy is within 12 hours. Reperfusion action becomes an important choice because of STEMI patients, the blood clot that forms closes the coronary vein lumen thoroughly so that the blood supply to the heart is completely inhibited. The reperfusion action aims to remove the clot formed and free the lumen from the clot so that blood perfusion to the heart can occur. There are two options for reperfusion action: percutaneous coronary intervention (PCI) and fibrinolytic therapy. Pharmacological therapy prior to reperfusion action may be given eg antiplatelet, anti-coagulant, nitrate preparation, morphine analgesics, and administration of O2 (ESC, 2012; ACCF / AHA, 2013).

F. Percutaneus Coronary Intervention (PCI)

Percutaneous Coronary intervention (angioplasty or stenting) without fibrinolytic precursor is called primary PCI. Primary PCI is effective in restoring perfusion in STEMI if performed within the first few hours of acute myocardial infarction. Primary PCI is more effective than fibrinolytics in opening up blocked coronary arteries and is associated with short-term and long-term clinical outcomes. Primary PCI is preferred when there is cardiogenic shock (especially in patients <75 years), the risk of bleeding increases, or symptoms have been present for at least 2 or 3 hours if the blood clot is more mature and easily destroyed with fibrinolytic drugs.
PCI is recommended at presentation> 3 hours, PCI facilities available, contact time between patients arrives with balloon inflation <90 minutes, contact time between patients arrives with reduced inflated balloon (time between patients arriving up to fibrinolytic process) <1 hour, there is contra indication fibrinolytic, high risk (congestive heart failure, grade 3 killip).

G. Trombolytics (Fibrinolytics)

The class of thrombolytic drugs is a class of drugs that can break down thrombus. A group of thrombolytic drugs (fibrinolytics) work by converting plasminogen proenzymes, into plasmin and active enzymes. Plasmin will degrade fibrin in the thrombus and will result in the soluble degradation of fibrin products. Plasmin regulation is affected by plasmin inhibitors (one of them α2-antiplasmin) and activation of plasminogen. Plasminogen inhibitors, especially type 1 (PAI-1), prevent plasminogen activation by regulating the activity of

t-PA (tissue plasminogen activator) and u-PA (urokinase-type plasminogen activator). Plasminogen plasma concentrations are twice as large as α2-antiplasmin. Therefore, at a given plasminogen activator dose, the resulting plasmin concentration may exceed the α2-antiplasmin concentration. In addition to degrading fibrin, unregulated plasmin can also degrade fibrinogen and other clot formation factors. This process is referred to as systemic lytic state, a condition in which there is a reduction in the potential for hemostasis and increases the risk of bleeding (Longo 2010).

Plasminogen and t-PA will bind to fibrin to form a complex that will cause the activation of plasminogen into fibrin. In contrast to free plasmin, plasmin bound to fibrin is not regulated by α2-antiplasmin. In addition, the residual lysine C-terminal will open when plasmin degrades the fibrin that forms the bond for additional plasminogen and t-PA molecules. This will provide positive feedback thereby increasing the production of plasmin (Longo 2010).

The use of thrombolytic therapy can reduce mortality by 25-50%. Studies have shown that thrombolytics are particularly good for patients with ECG changes, including ST segment elevation (especially in patients with aterior infarction) and in patients with bundle branch block (Royal Pharmaceutical Society, 2011). The greatest benefit is obtained if the patient gets therapy within the first few hours. In an RCT study, it was concluded that the use of thrombolytics within the first 12 hours after symptom onset and with ECG showing bundle branch block or ST segment elevation characteristics greater than 1 mm in limb leads or 2 mm in chest leads could reduce mortality in the short term at patients (Fibrinolytic Therapy Trialists' (FTT) Collaborative Group, Lancet 1994; 343: 311-322 Collins R. N Engl J Med 1997; 336: 847-860 in Davidson's). Studies have shown that thrombolytics are particularly good for patients with ECG changes, including ST segment elevation (especially in patients with anterior infarction) and in patients with bundle branch block (Royal Pharmaceutical Society, 2011).

III. COMPARISON PCI AND TROMBOLITIC ON STEMI

Tabel 1. Several Studies Comparing PCI and Thrombolytic Therapy

NO	RESEARCHERS	METHOD	RESEARCH SUBJECT	RESEARCH RESULT
1.	**Comparison of long survival by location of infarction**			
1)	Henriquez *et al*.,2006	Retrospective longitudinal cohort analysis of prospectively entered data.	Zwolle trial 395 patients with acute STEMI were randomly assigned to intravenous streptokinase or PCI.	- Mortality was higher in the streptokinase group than PCI RR 1.6 (95% CI 1.0-2.6) - In anterior STEMI patients, higher mortality in PCI streptokinase RR 2.7 (95% CI 1.4-5.5) - In non-anterior STEMI patients there was no difference in mortality of RR 1.1 (95% CI 0.6-2.1) but streptokinase had MACE incidence of RR 2.1 (95% CI 1.2-3.6)
2.	**Decrease in mortality rate , reinfarction and stroke**			
1)	Mehta *et al*., 2004	Evaluate patient data with STEMI	2975 patients STEMI ≥70 years, 365 underwent PCI and 769 received TT	- PCI showed lower reinfarction and mortality of OR 0.15 (95% CI 0.05-0.44) and OR 0.62 (95% CI 0.39 to 0.96) - There was no difference in the incidence of cardiogenic shock, bleeding and stroke
2)	Keely, Boura&Grines, 2003	Quantitative review of 23 randomized trial	7739 patientseligible to PTCA or TT	Primary PTCA is better than TT in reducing short-term mortality (7% vs 9%p = 0.0002), non-fatal reinfarction (3% vs. 7% p <0.0001), stroke (1% vs 2% p = 0.0004) as well as the combined number of deaths, non-fatal reinfarction and stroke (8% vs. 14% p <0.0001)
3)	Dalby *et al*., 2003	Meta analisys of all data randomized trials	6 clinical trials involving 3750 patients	PCI decreased reinfarction, stroke and mortality rates compared to TT by 68% (95% CI, 34% -84%, P <0.001), 56% (95% CI, -15% -77%; P = 0.015) and 19% (95% CI, -3% to 36%; p= 0.08). The combination of all indicators showed a decrease of 42% (95% CI 29% -53%, P <0.001)

4)	Aversano *et al.* , 2002	Prospective randomized trial	451 patientseligible to thrombolytics	Output levels in the PCI and TT groups after 6 months showed mortality 6.2% vs 7.1% (P = 0.72), reinfarction 5.3% vs. 10.6% (P = .004), and stroke output 2.2% vs 4.0% (P = 0.28). The median LOS values were also lower in the PCI group (4.5 vs 6.0 days, P = 0.02).
5)	Hyunh *et al.* , 2009	Bayesian hierarchical random-effect meta-analyzes against 23 RCT and 32 observational studies	194,040 patients with STEMI	PCI is associated with short-term mortality of OR 0.66 CI 95% 0.51 to 0.82) in RCT and OR 0.77; 95% CI 0.62-0.95 in observational studies. PCI was associated with a 63% reduction in the incidence of stroke in RCTs and 61% in observational studies. After> 1 year, PCI was associated with short-term mortality of OR 0.76;95% CI, 0.58 to 0.95) and decreased reinfarctionof OR 0.49; 95% CI 0.32-0.66 on RCT
3. Decreased Lenght of Stay and accelerated neurological improvement				
1)	Ying-Qing *et al*,2013	Meta-analysis of clinical trials	17 studies comparing PCI and TT	The rate of hospital discharge improved in patients using PCI (p <0.001) maup un TT (p <0.001). Cardiac arrest patientswith STEMI who received TT after spontaneous circulatory restoration did not decrease hospital discharge (p = 0.543) or neurologic recovery rate (p = 0.165) than patients undergoing PCI

This is several previous studies comparing the use of pci with thrombolytics:

1. Differences in Survival by Location of Infarction *(Henriques et al., 2006)*
A study by Henriques *et al* performed an analysis to patients with acute STEMI (ST-Elevation Myocardial Infarctio who received Primary PCI (Primary Percutaneous Coronary Intervention) or thrombolytic therapy. This study was designed as a longitudinal retrospective cohort study. Aim of this study are to determine the survival difference of those treatment based on the location of infarction and longterm outcome after 8 years. This study used MACE (Major Adverse Cardiac Event) to measure outcome indicator for assessing the survival difference. This study was conducted on 395 patients who then performed random allocations, 194 patients received PCI and 201 patients received streptokinase. A total of 105 patients died; 63 patients in the streptokinase group and 42 patients in the PCI group (RR 1.6; 95% CI 1.0 - 2.6; P = 0.03).

In patients with posterior STEMI, there were no difference in mortality between streptokinase and PCI groups (RR 1.1, 95% CI 0.6 - 2.1, P = 0.68). Major Adverse Cardiac Events (MACE) were more susceptible to patients in the streptokinase group 50 (39%), than the PCI 28 (24%) group (RR 2,1; 95% CI 1.2 - 3.6) and NNT (number needed to treat) to solve one MACE event is four. Patients with anterior STEMI, mortality was higher in the streptokinase group than in the PCI group (RR 2.7; 95% CI 1.4-5.5; P = 0.004). Major Adverse Cardiac Events (MACE) were significantly more in the streptokinase group compared with the PCI group, 44 (59%) in the streptokinase group and 25 (32%) in the PCI group (RR 3.0, 95% CI 1.7 - 5, 9). Number Needed to Treat (NNT) to solve one MACE is five. Acute STEMI patients with anterior infarct location have longer survival when treated with PCI rather than streptokinase. Therapy with PCI reveals a significantly more survival. It could be because PCI is better able to maintain the residual function of the left ventricle.

2. Decrease in mortality rate, reinfarction and stroke
1). Prospective cohort: Decreased risk of reinfarcation and mortality in elderly patients (Mehta, Immad, Robert J, & Joel M, 2004). This study compared the effectiveness of PCI therapy and thrombolytic therapy (TT) in elderly STEMI patients. The study design was a prospective cohort study involving 2975 elderly patients (age ≥70 years) under STEMI conditions and without reperfusion contraindications registered in the GRACE (Global Registry of Acute Coronary Event). The following comparison of research results related to the number of MACE incidence in the study subjects.

MACE type	Type of therapy	
	PCI (n = 365; 12,7%)	**Thrombolytics (n = 769; 26.7%)**
Mortality	13.5%	14.8%
Reinfark	1.1%	5.7%
Cardiogenic shock	11.3%	11.6%
Major bleeding	8.6%	5.9%
Stroke	1.1%	2.8%

Figure 1. MACE Event on Research Subject

Patients with PCI showed lower rates of reinfarction (OR 0.5; 95% CI 0.0 - 0.44); and mortality (OR 0.62; 95% CI 0.39 - 0.96) compared with patients in the TT group. In elderly STEMI patients, the PCI group showed a lower incidence of reinfarction and mortality than the TT group.

2). Systemic Review: Decreased mortality, reinfarction, and stroke (Keely, Judith, & Cindy L., 2003)
This research is a systemic review of 23 randomized trials research data from 1993 to 2002. The aim was to compare the effectiveness of reperfusion therapy between percutaneous transluminal coronary angioplasty (PTCA) with thrombolytic therapy in STEMI patients. Outcome indicators measured included total mortality, reinfarction, ischemic recurrence, total stroke, stroke hemorrhage, and combination of mortality, reinfarction and stroke.

Total of 7739 patients were randomized, 3872 patients received PTCA and 3867 patients received thrombolytic therapy. The thrombolytic agents used were streptokinase in 8 studies (n = 1837) and specific fibrin in 15 studies (n = 5902). Overall, short-term outcomes in patients receiving PTCA are mortality, non-fatal reinfarction, combined mortality, nonfatal reinfarction and stroke outcomes tend to be lower compare to TT. The outcome is not only significantly decreased in short-term outcomes but is also significant in long-term follow-up.

The results showed better PTCA than thrombolytic therapy in reducing incidence of death in the short term (7% (n = 270) vs 9% (n = 360) / OR 0.77, p = 0.0002), death without data SHOCK trial (5% (n = 199) vs 7% (n = 222) / OR 0.71; p = 0.0001), non fatal reinfarction (3% (n = 80) vs 7% (n = 222) / OR 0.43, p <0.0001), stroke (1% (n = 30) vs 2% (n = 64) / OR 0.5; p = 0.0004), and a combination of death outcomes, non-fatal reinfarction and stroke (8% (n = 253) vs. 14% (n = 442) / OR 0.57; p <0.0001). Thus PTCA is more effective than thrombolytic therapy in AMI ST-segment elevation management.

3). Meta-Analysis: Reduced mortality, reinfarction, and stroke *(Dalby, Bouzamondo, Lechat, & Montalescot, 2003).* Meta-analysis study comparing clinical effectiveness between PCI and thrombolytics from 6 research journals and total of 3750 patients with acute myocardial infarction from January 1985 to September 2002. Indicator of comparison between PCI and thrombolytic therapy is CC (combine criteria) of death/reinfarction/stroke. Overall, CC significantly decreased by 42% (95% CI 29% - 53%, P <0.0001). If the CC parameters (death/reinfarction/stroke) of PCI and thrombolytics are separated, then PCI is better that thrombolytic in reducing mortality patients by 19% (95% CI, 3% - 36%; P = 0.08); cases of reinfarction were significantly reduced by 68% (95% CI, 34% - 84%, P <0.001) and a 56% reduction in stroke incidence (95% CI -15% -77%;P=0.015).

4). Randomized Control Trial: Decreased mortality, recurrent MI, and stroke *(Aversano, Laynet, Eugene, Michael, David, & Sandra, 2002).* This is a RCT of The Atlantic Cardiovascular Patient Outcomes Research Team (C-PORT) trial, multi center study, which aims to know the level of superiority of PCI to thrombolytic at Hospital without surgical process. The outcome parameters were composite (death, recurent MI, and stroke) measure during 6 months after intervention. A total of 451 patients eligible for thrombolytic administration with acute myocardial infarction within duration less than 12 hours after ST wave elevation in EKG results. Patients with inclusion criteria were then randomized into two intervention groups ie 226 patients receiving accelerated tissue plasminogen activator therapy (bolus dose 15 mg / kg, and infusion 0.75 mg / kg for 30 minutes followed by a dose of 0.5 mg / kg during 60 minutes) and 225 patients received PCI.

Based on intention to treat analysis on outcomes (mortality, recurrent MI, stroke and composite end point), an OR ratio of PCI vs short-term thrombolytic (6 weeks) and long-term (6 months after myocardial infarction) with 0,52 (95% CI 0.30-0.89) and 0.57 (95% CI 0.34-0.95). The incidence of composites (death, recurent MI, and stroke) at the end of the assessment was decreased in the PCI group (10.7% vs 17.7%; P = 0.03) at 6 weeks,

and the final assessment point at 6 months (12,4% vs. 19.9%, P = 0.03). Outcomes after 6 months on PCI vs thrombolytic therapy were 6.2% vs 7.1% (P = 0.72) at mortality, 5.3% vs. 10.6% (P = 0.04) for recurent MI, and 2.2% vs 4.0% for stroke (P = 0.28). Based on these results, PCI give better clinical outcome and reduce the length of hospitalization in patients after 6 months of myocardial infarction.

5). Meta-Analysis from Randomized Controlled Trial and Observational Studies: Decreased mortality, reinfarction, and short-term stroke (<6 weeks) and long-term (> 1 year) (*Thao Hyunh et.al., 2009).* The meta-analysis of this study aimed to compare the effectiveness of PCI intervention with fibrinolytic therapy in STEMI against the short-term and long-term mortality of 23 RCTs with a total of 8140 patients and 32 observational studies with a total of 185,900 patients published until May 1, 2008. The goal is to eliminate the limitations of application RCT to actual clinical practice. In several RCT studies regarding PCI versus Fibrinolytic, there is some information that is not explicitly discussed. For example, the indication of PCI and RCT selection as well as information relating to the effectiveness of primary PCI may not be applicable due to limited facilities and infrastructure.

The results showed that primary PCI was more effective in reducing short-term mortality risk compared with fibrinolytic therapy, both in RCT and observational studies with 34% (OR: 0.66 , 95%credible interval ; 0.51 - 0.82) and 23% (OR : 0.77 ; 95% credible interval ; 0.62 -0.95). For long-term mortality in RCT, it was found that PCI primary was better than thrombolytic therapy by 24% (OR:0.76 ; 95% credible interval ; 0.58 - 0.95). While in observational studies, there was no significant difference between the use of PCI and thrombolytic therapy to reduce long-term mortality with values (OR: 0.88 , 95% credible interval , 0.60 to 1.18). The use of PCI is also capable of reducing the incidence of short-term reinfarction with a 65% reduction in RCT research and 53% in observational studies. The decrease in long-term reinfarction was only significant in the RCT study with a decline rate of 51%, while in observational studies, there is no significant difference between PCI and thrombolytic therapy. The decrease in absolute risk of mortality, reinfarction and short-term stroke by PCI use in RCT and observational studies was 2.2% (95% CrI, 1.3 to 3.2); 4.5% ; 1.2%) and 1.2% and (1.1% (95% CrI, 0.4 to 1.5); 2.9% ; 0.6%). While for the long term, significant values were obtained only for mortality and reinfarction in RCT studies with a 3.5% reduction (95% CrI, 0.7-6.4) and 3.4% (95% CrI, 1.6-5.9).

Thus, it can be concluded that primary PCI is capable of significantly reducing mortality, reinfarction, and stroke in the short term ($\leq$ 6 weeks). The ability of primary PCI to reduce mortality, reinfarction , and stroke in the long term ($\geq$ 1 year) is currently only obtained significantly in studies conducted by RCT. While in the observational study, there is no significant difference in mortality decrease between primary PCI and fibrinolytic. Effective thrombolytics therapy are given a maximum of 30 minutes after the attack while for effective PCI given a maximum of 90 minutes after the attack.

3. Meta Analysis: Decreased Lenght of Stay and accelerated neurological improvement *(Ying-Qing Li et al., 2013).* This Meta-analysis study aimed to compared the effectiveness of PCI with thrombolytics after ROSC (Restoration of Spontaneous Circulation) in CA patients (Cardiac Arrest with STEMI from 24 cohort study journals published from January 1995 to October 2012. Outcome parameters used to evaluate the effectiveness of both treatments is length of hospital stay / LOS (Length of Stay) and accelerated improvement of neurological function. The results showed that PCI significantly reduced LOS and increased the acceleration of neurologic improvement in patients with ROSC after CA with successive values (OR, 1.92, 95% CI, 1.32-2.78, p, 0.001) and (OR, 6.71; 95 % CI, 2.97-15.15, p, 0.001). Similarly with thrombolytic therapy, the results showed that thrombolytic therapy also significantly reduced LOS and increased acceleration of neurologic function improvement in patients with ROSC after CA with successive values (OR, 2.63, 95% CI, 1.77-3.90, p, 0.001) and (OR, 0.76 , 95% CI, 0.27-2.17, p = 0.309). Meanwhile, when PCI was compared with thrombolytics, the results showed that there was no significant difference between the two therapies in lowering LOS or accelerating the functioning of neurolgis in patients with ROSC after CA with p = 0.543 and p = 0.165 (Figure 20). Thus, it can be concluded that thrombolytics can be used as an alternative therapy when CA attacks due to STEMI if the facilities and infrastructure for PCI are not sufficient.

4. Pooled Analysis: The influence of selection of reperfusion strategy based on the time period since the onset of symptom to reperfusion to 1 year survival for STEMI *(Westerhoutet.al., 2011)*
Pooled analysis was performed by collecting data from the CAPTIM (Comparison of Primary Angioplasty and Pre-Hospital Fibrinolysis in Acute Myocardial Infarction) (n = 840, 1997-2000) and WEST (Which Early ST-Elevation Myocardial Infarction) (n = 328, 2003- 2005). All patients in CAPTIM were injected with IV bolus Heparin 5000 U and Aspirin 250-500 mg. Patients with pre hospital fibrinolytic (FL) received Alteplase iv bolus followed by infusion for 90 min. While patients assigned to PCI will be sent to the hospital to

undergo coronary anigography and angioplasty. Heparin was continued for at least 48 hours, while patients with stenting were treated with tyenopyridine for 1 month. CAPTIM patient criteria are recognized symptoms within 6 h of onset (typical pain for at least 30 min, not responding with nitrate therapy, ST segment elevation of at least 0.2 mV at adjacent adjacent ≥2 or left bundle branch block). Patients will be excluded if the transfer time to hospital> 60 minutes. While in the WEST trial, patients were divided into 3 groups of therapy (ususal care, early invasive strategy, and primary PCI) with randomization techniques. Abciximab was recommended for all PCI procedures until fibrinolytic therapy was administered within 3 hours. Similar to CAPTIM, the STEMI inclusion criteria are STEMI patients with symptom onset within 6 hours.

The results showed the duration of symptoms to get medical treatment in the WEST shorter than CAPTIM with a median value of 53 vs 78 minutes. However, the time interval between treatments (medical contact) with shorter randomisation of CAPTIM compared to WEST with a value of 26 min vs 38 min. Overall, the time since symptom emergence until getting further treatment, shorter in WEST than CAPTIM. Cardiogenic shock events after 30 days of higher intervention in patients with primary PCI compared with FL patients, but not significant. Intracranial hemorrhage is very rare in this population. From a comparison of fibrinolysis versus PCI to 1 year of mortality associated with increased time since onset of the onset, PCI and FL mortality was found to be 127 min (<127 min, 59.1% of all patients; time, <240 minutes, 91.6%). Patients treated with FL within 2 hours after onset of attack had a higher survival rate than PCI (FL (10/358) 2.8% vs PCI (20/288) 6.9% , P = .021 , HR 0.43 , 95% CI 0.20- 0.91). Whereas the handling is done> 2 hours, there is no significant difference between the 2 treatment strategies (FL (19/274) 6.9 % vs PCI (14/234) 6.0% , P = .529 , HR 1.23 , 95% CI 0.61 -2.46).Thus, it can be concluded that FL shows a decrease in mor talitas for 1 year compared to PCI if handling is done within ≤ 2 hours. The timing of symptom onset until the patient gets treatment should be a major consideration when choosing reperfusion therapy for STEMI.

IV. CONCLUSION

This is the conclusion of research results from several journals related to the preference of primary PCI vs. thrombolytic therapy selection in STEMI patients.

Outcome Therapy Parameters	Preferences Therapeutic Choice	
	***Primary* PCI**	**Thrombolytics**
Length survival based on infarct location	✓	
Decreased mortality, reinfarction, and stroke	✓	
Decreased LOS and accelerated improvement of neurological function *	✓	
Increased survival for 1 year if reperfusion is done ≤ 2 hours **		✓

* The results obtained are based on RCT research. As for the Observational Cohort study, there was no significant difference between PCI and thrombolytics.
** If reperfusion therapy is performed> 2 hours, then there is no significant difference between the two therapeutic strategies.

Based on the results of comparison of outcome therapy in literature study that has been done, it can be concluded that primary PCI therapy is preferred as treatment therapy in STEMI patients compared with thrombolytic therapy. Except in some conditions such as facilities and infrastructure that are not supportive, thrombolytic therapy can be done maximum 30 minutes after the attack. The time lag between symptom onset and treatment of reperfusion therapy should also be an important consideration for choosing an effective reperfusion strategy. Trombolytics are more effective than PCI if the time lag between symptom onset and handling is 2 hours. While if the lag time> 2 hours, then there is no significant difference between the two.

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