Prognosis, Complications and Quality of Life After Fibrinolysis versus PCI Post MI

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ABSTRACT

Acute myocardial infarction (MI) is a major health problem that carries considerable morbidity and mortality. Management of acute MI is carried out through adopting a reperfusion strategy either pharmacological (intravenous fibrinolysis) or mechanical (primary percutaneous coronary intervention (PCI)) to re-open the occluded coronary artery. Many literature studies have compared the efficacy, the complications, and the long-term outcome of both the intravenous fibrinolysis and primary PCI. Despite the superiority and overgrowing popularity of primary PCI in management of acute MI, fibrinolysis is still widely utilized. Many factors play a role in choice of the reperfusion strategy to be adopted, particularly the time from the symptom onset, the time required for preparing for PCI, and patient co-morbidities e.g. risk for bleeding. Primary PCI is generally more efficacious in achieving reperfusion. It is safer with lower mortality rates, and it is associated with lower risk to develop restenosis, re-infarction, heart failure, shock cerebrovascular stroke, or intracerebral haemorrhage. However, the less availability and the variable outcomes with operator experience are the main disadvantages that make PCI not feasible in many situations. This review article aims to compare the efficacy and advantages of intravenous thrombolysis and PCI and their prognosis, complications, and long-term impact on quality of life.

Key words: **acute myocardial infarction, fibrinolysis, PCI**

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Introduction

Coronary heart disease is a major public health problem that carries a considerable morbidity and mortality worldwide. Reports from the heart and stroke statistics note that almost half of the patients suffering from coronary heart disease in 2017 had a history of acute myocardial infarction (MI).[1] Myocardial infarction constitutes 33% of the cases of acute coronary syndrome, and it may present with either non-ST segment elevation MI (NSTEMI) or ST segment-elevation MI (STEMI). STEMI represents an acute occlusion of one of the epicardial coronary arteries due to thrombosis. It is diagnosed via an electrocardiogram and requires a prompt reperfusion.[2]

Reperfusion therapy comprises the immediate restoration of blood flow through or around the occluded coronary artery. It aims not only at addressing and treating the primary cause of occlusion, but also at improving the outcome. [3,4] The main strategies of reperfusion are pharmacological and mechanical approaches. Pharmacological reperfusion includes the use of intravenous fibrinolytic agents to achieve thrombolysis, whilst mechanical reperfusion entails the use of primary percutaneous coronary intervention (primary PCI) or immediate coronary artery bypass grafting.[5,6] This review article aims to compare the efficacy and advantages of intravenous thrombolysis and PCI and their prognosis, complications, and long-term impact on quality of life.

Fibrinolytic Reperfusion Therapy

Fibrinolytic therapy has been known for many decades for reperfusion after acute coronary artery occlusion leading to STEMI. More than 90% of cases of STEMI occur due to thrombus formation and rupture of intra-arterial atherosclerotic plaques.[7] Fibrinolytic agents used for reperfusion act on various points of coagulation pathways to inhibit thrombus formation and enhance the outcome. The main agents currently available for intravenous fibrinolysis are streptokinase, alteplase, reteplase, and tenecteplase.[8]

Streptokinase is the most widely used fibrinolytic agent. It was derived from beta-hemolytic streptococci. It is composed of a single polypeptide chain that binds to plasminogen forming active plasminogen that activates plasmin.[9] The main adverse events of streptokinase are allergic reactions (such as shivering, fever, rash, or rarely hypotension and anaphylaxis), bleeding (often minor bleeding, major bleeding is rare). Alteplase or recombinant tissue plasminogen activator (rtPA) is another fibrinolytic agent that is fibrin-specific and enhances plasminogen activation.[10] It is preferred to streptokinase due to its lower allergic risk. Reteplase or recombinant plasminogen activator (rPA) is a mutant of rtPA that is less-fibrin selective and possesses a longer half-life.[11] Tenecteplase is the last developed fibrinolytic agent. It was genetically-engineered to be very fibrin specific and to have a long half-life.[12]

Primary Percutaneous Coronary Intervention

Primary percutaneous coronary intervention (PCI) was first performed in 1977, and has undergone multiple developmental stages for better outcome.[13] Currently, primary PCI is considered the strategy of choice for patients with acute STEMI if performed in a timely fashion[14]. It is also preferred for patients with posterior myocardial infarction or myocardial infarction with left bundle branch block.[15] The technique used for primary PCI comprises the introduction of a wire via femoral or radial arteries to the coronary artery. Intravascular sonography and optic coherence tomography are used during PCI procedure to measure the intracoronary artery pressure and to assess the size, burden, and characteristics of the atheromatous plaque occluding the coronary arteries. Thrombectomy devices are used to mechanically remove the atheroma, and intra-arterial stents are inserted to keep the lumen patent or balloon angioplasty is carried out to prevent re-occlusion. Anti-thrombotic agents, antiplatelet drugs, and glycoprotein-inhibitor therapy are co-utilized to inhibit thrombosis[16]. Primary PCI was reported to have high success rates with more than 90% of patients achieving a thrombolysis in myocardial infarction (TIMI) 3 flow.[4] Primary PCI has lower risk of bleeding and stroke in comparison to intravenous fibrinolysis.[17] Therefore, they have largely replaced the sole use of IV fibrinolysis except in certain situations as will be discussed in the next section.

Fibrinolysis Versus PCI

Many studies have been conducted to compare the safety, efficacy, and outcome of intravenous fibrinolysis and primary PCI. Randomized controlled trails have explored the superiority of primary PCI with stents versus fibrinolysis and primary PCI with balloon angioplasty versus fibrinolysis. Results from these studies clarified certain indications for each of these approaches.

Indications of PCI versus fibrinolysis

The choice of reperfusion approach in patients presenting with acute myocardial infarction depends on a number of factors. These factors include the time from the onset of MI symptoms, the time expected for transport to a well-equipped PCI la boratory, the risk of STEMI, and the bleeding risk.

Primary PCI is currently the approach of choice for most of the patients with acute myocardial infarction who present to the hospital within 90 minutes of their presentation. However, it requires the availability of a skilled PCI laboratory with experienced surgeons. The medical contact-to-balloon or door-to-balloon time must be less than 90 minutes or the door to needle time is more time is more than one hour.(14) Other indications for primary PCI include the presence of cardiogenic shock, increased risk of bleeding or intracranial hemorrhage (ICH), high risk for STEMI, or late presentation to the hospital after three hours from the onset of manifestations (Table 1).[18]

Advantages and disadvantages of PCI and fibrinolysis

The main advantages of fibrinolysis include the ease of its administration, its availability in the vast majority of emergency departments in different hospitals, and its high efficacy particularly when administered during the first 60 minutes of symptom onset.[14] On the other side, intravenous fibrinolysis is less effective than primary PCI when given during the first three hours. The rate of achievement of TIMI 3 flow is about 40-50% with fibrinolysis versus around 90% with primary

Table 1: Comparison between intravenous fibrinolysis and primary PCI

	Fibrinolysis	PCI
Indications	• Presentation <1 hr from symptom onset • Presentation ≤ 3 hrs from symptom onset and delay to PCI>90 min • Prolonged transport • Door-to-balloon time - door-to-needle time > 1 hr • Medical contact-to-balloon or door-to-balloon > 90 min	• Late presentation >3 hrs from symptom onset • Presentation 2-3 hrs from onset with available well-equipped PCI lab and surgical backup • Door-to-balloon time - door-to-needle time < 1 hr • Medical contact-to-balloon or door-to-balloon < 90 min • Doubt or High risk for STEMI • Cardiogenic shock
Advantages	• Easy administration • Wide availability in most EDs • High efficacy especially in the first hour	• Higher efficacy (90% TIMI 3 flow rates) • More safe • Less re-infarction/restenosis • Less cerebrovascular stroke • Less bleeding/intracranial haemorrhage • Effective up to 18 hours from symptom onset
Disadvantages	• Less efficacy than PCY (40-50% TIMI 3 flow rates) • Risk of bleeding and intracranial haemorrhage • Risk of cerebrovascular stroke • Not effective after 3-6 hours	• Not available in all hospitals • Variable outcomes (operator-dependent) • Not feasible in all conditions • Higher cost
Efficacy	Lower	Higher
Mortality rate	Higher	Lower
Risk of stroke	Higher	Lower
Risk of ICH	Higher	Lower
Restenosis	Higher	Lower
Heart failure	Higher	Lower
Cardiac arrest	Higher	Lower
Long-term outcome	Worse	Better

PCI.[15] Furthermore, intravenous fibrinolysis carries a high risk for bleeding and intracerebral hemorrhage, and it is significantly less effective than primary PCI if administered within 3 to 6 hours from symptom onset.[17]

Primary PCI, on the other hand, is the strategy of choice in patients with acute STEMI. It is highly superior to IV fibrinolysis (with more than 90% restoration of TIMI 3 flow rate) and markedly lower risk for bleeding or intracranial hemorrhage.[20] It is also superior as regards the long-term outcome with considerably low risk for restenosis or re-infarction.[21] Moreover, primary PCI is less affected by patient-related factors such as the time of symptom onset, and its efficacy is established over up to 18 hours from clinical presentation.[22] The main disadvantages, however, are being less available, not often feasible, and being operator-dependent. So the, the outcome would vary from one center and one interventionist to another.[23]

Prognosis, complications, and long-term outcome of PCI versus fibrinolysis

The long-term outcome after primary PCI is generally better than fibrinolysis. Various literature studies approved the superiority of PCI over intravenous fibrinolysis as regards the mortality rates, risk for restenosis or re-infarction, and risk for bleeding and intracranial hemorrhage. Despite the multiplicity of studies supporting the general superiority of primary PCI to fibrinolysis, data from other researchers are conflicting.

Primary PCI was proven to have lower 30-day mortality rates (4.4% versus 6.5% mortality rate in fibrinolysis). Higher rates were reported among the CAMI study.(17) The mortality rate was 15% and 7.7% among patients undergoing fibrinolysis and PCI, respectively ($P<0.05$). Despite the superiority of PCI in the vast majority of the studies, many trials (such as FAST-MI, STREAM, and WEST) reported no significant difference in mortality rates between PCI and fibrinolysis-treated

groups.[15,24,25] In disagreement with this, Westerhout et al. reported that the mortality rates are lower among patients who undergo fibrinolysis within two hours of symptom onset in comparison to primary PCI.[26]

One of the main contraindications for intravenous fibrinolysis is bleeding tendency and risk for intracranial hemorrhage.[15] Thus, primary PCI is considered the approach of choice in these conditions. However, researchers from the STREAM trial reported no statistically significant difference between fibrinolysis using tenecteplase as regards the hemorrhagic complications particularly intracranial hemorrhage.[5] Similarly, results from the CAMI study reported no significant difference between primary PCI and fibrinolysis as regards hemorrhagic stroke and major bleeding.[17] Hemorrhagic stroke occurred in 0.6% and 0.3% of patients who underwent fibrinolysis and primary PCI, respectively ($p>0.05$). Major bleeding occurred in 5% of the fibrinolysis-treated cases and 3% of PCI-treated patients ($p>0.05$).

After reperfusion, the risk for cerebrovascular stroke is 0.7% among patients who had primary PCI versus 2.0% among patients who had intravenous thrombolysis.[27] The risk of re-infarction was significantly lower among patients undergoing PCI than patients with intravenous fibrinolysis[28]. The superiority of primary PCI is thought to be attributed to the fact that the rate of achievement of TMI 3 flow primary PCI is 90% whereas it ranges from 50-60% only in patients undergoing fibrinolytic therapy.[27,29] Some researchers, on the other hand, noted that there was no statistically significant difference between the efficacies of fibrinolysis versus PCI if performed during the first 3 hours without delay. In contrast, a study conducted in 2008 found that the primary PCI was superior to fibrinolysis even if delayed.[30] Additionally, primary PCI was reported to have lower rates of heart failure, cardiac arrest, and mechanical complications when compared to fibrinolysis ($p <0.05$).[17]

Conclusions

Despite the superiority and overgrowing popularity of primary PCI in management of acute MI, fibrinolysis is still widely utilized. Many factors play a role in choice of the reperfusion strategy to be adopted particularly at the time from the symptom onset, the time required for preparing for PCI, and patient co-morbidities e.g. risk for bleeding. Primary PCI is generally more efficacious in achieving reperfusion. It is safer with lower mortality rates, and it is associated with lower risk to develop restenosis, re-infarction, heart failure, shock cerebrovascular stroke, or intracerebral haemorrhage. However, the less availability and the variable outcomes with operator experience are the main disadvantages that make PCI not feasible in many situations.

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References

1. Subcommittee AHASC and SS. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation. 2017;131(4):e29-322.

2. Puddu PE, Cenko E, Ricci B, Bugiardini R, Ricci B, Bugiardini R. STEMI: Diagnosis. In: Encyclopedia of Cardiovascular Research and Medicine. ; 2018:465-473.

3. Reed GW, Rossi JE, Cannon CP. Acute myocardial infarction. Lancet (London, England). 2017;389(10065):197-210..

4. Boden WE, Eagle K, Granger CB. Reperfusion strategies in acute ST-segment elevation myocardial infarction: a comprehensive review of contemporary management options. Journal of the American College of Cardiology. 2007;50(10):917-29

5. Armstrong PW, Gershlick A, Goldstein P, Wilcox R, Danays T, Bluhmki E, et al. The Strategic Reperfusion Early After Myocardial Infarction (STREAM) study. American Heart Journal. 2010;160(1):30-5.e1.

6. Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, et al. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. European Heart Journal. 2010;31(8):943-57

7. White HD, Chew DP. Acute myocardial infarction. Lancet (London, England). 2008;372(9638):570-84.

8. Menon V, A Harrington R, S Hochman J, P Cannon C, D Goodman S, G Wilcox R, et al. Thrombolysis and adjunctive therapy in acute myocardial infarction: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy 2004. 549S-75S p

9. Banerjee A, Chisti Y, C Banerjee U. Streptokinase - A clinically useful thrombolytic agent 2004. 287-307 p.

10. Goodman SG, Menon V, Cannon CP, Steg G, Ohman EM, Harrington RA. Acute ST-segment elevation myocardial infarction: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008;133(6 Suppl):708s-75s.

11. Kastrati A, Mehilli J, Schlotterbeck K, et al. Early administration of reteplase plus abciximab vs abciximab alone in patients with acute myocardial infarction referred for percutaneous coronary intervention: A randomized controlled trial. JAMA. 2004;291(8):947-54

12. Davydov L, Cheng JW. Tenecteplase: a review. Clin Ther. 2001;23(7):982-97; discussion 1.

13. Somjot S Brar GWS. Decision-making: stenting in acute myocardial infarction. Future Cardiology. 2010;6(3):301-14

14. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Jr., Chung MK, de Lemos JA, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013;127(4):e362-425.

15. Armstrong PW, Gershlick AH, Goldstein P, Wilcox R, Danays T, Lambert Y, et al. Fibrinolysis or Primary PCI in ST-Segment Elevation Myocardial Infarction. New England Journal of Medicine. 2013;368(15):1379-87.

16. Keeley EC, Hillis LD. Primary PCI for Myocardial Infarction with ST-Segment Elevation. New England Journal of Medicine. 2007;356(1):47-54.

17. Peiyuan H, Jingang Y, Haiyan X, Xiaojin G, Ying X, Yuan W, et al. The Comparison of the Outcomes between Primary PCI, Fibrinolysis, and No Reperfusion in Patients ≥ 75 Years Old with ST-Segment Elevation Myocardial Infarction: Results from the Chinese Acute Myocardial Infarction (CAMI) Registry. PLOS ONE. 2016;11(11):e0165672.

18. Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, Hughes LO, et al. Randomized Trial of Preventive Angioplasty in Myocardial Infarction. New England Journal of Medicine. 2013;369(12):1115-23.

19. Cantor WJ, Fitchett D, Borgundvaag B, Ducas J, Heffernan M, Cohen EA, et al. Routine Early Angioplasty after Fibrinolysis for Acute Myocardial Infarction. New England Journal of Medicine. 2009;360(26):2705-18.

20. ElGuindy AM. STREAM and FAST-MI – Pharmacoinvasive therapy: A continued role for fibrinolysis in the primary PCI era. Glob Cardiol Sci Pract. 2014. doi:10.5339/gcsp.2014.27

21. Ahmed B, Wael T, Mohammed M, Mohamed S. Primary PCI versus Pharmaco-Invasive Strategy in Patients with ST-Elevation Myocardial Infarction; a Randomized Clinical Study. Journal of Cardiovascular Disease Research. 2018;9(1).

22. Westerhout CM, Bonnefoy E, Welsh RC, Steg PG, Boutitie F, Armstrong PW. The influence of time from symptom onset and reperfusion strategy on 1-year survival in ST-elevation myocardial infarction: a pooled analysis of an early fibrinolytic strategy versus primary percutaneous coronary intervention from CAPTIM and WEST. American Heart Journal. 2011;161(2):283-90.

23. Boden WE, Eagle K, Granger CB. Reperfusion strategies in acute ST-segment elevation myocardial infarction: a comprehensive review of contemporary management options. Journal of the American College of Cardiology. 2007;50(10):917-29..

24. Danchin N, Puymirat E, Steg PG, Goldstein P, Schiele F, Belle L, et al. Five-year survival in patients with ST-segment-elevation myocardial infarction according to modalities of reperfusion therapy: the French Registry on Acute ST-Elevation and Non-ST-Elevation Myocardial Infarction (FAST-MI) 2005 Cohort. Circulation. 2014;129(16):1629-36.

25. Armstrong PW, Committee WS. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. European heart journal. 2006;27(13):1530-8.

26. Gershlick AH, Westerhout CM, Armstrong PW, Huber K, Halvorsen S, Steg PG, et al. Impact of a pharmacoinvasive strategy when delays to primary PCI are prolonged. Heart (British Cardiac Society). 2015

27. Jolly SS, Cairns JA, Yusuf S, Meeks B, Pogue J, Rokoss MJ, et al. Randomized Trial of Primary PCI with or without Routine Manual Thrombectomy. New England Journal of Medicine. 2015;372(15):1389-98.

28. Rebuzzi AG, Niccoli G, Ferrante G. Acute myocardial infarction interventional procedures: primary percutaneous coronary intervention versus facilitated percutaneous coronary intervention, rescue angioplasty, rescue excimer laser. Minerva cardioangiologica. 2007;55(1):73-82.

29. Larson DM, Duval S, Sharkey SW, Garberich RF, Madison JD, Stokman PJ, et al. Safety and efficacy of a pharmaco-invasive reperfusion strategy in rural ST-elevation myocardial infarction patients with expected delays due to long-distance transfers. European Heart Journal. 2012;33(10):1232-40.

30. Busk M, Maeng M, Rasmussen K, Kelbaek H, Thayssen P, Abildgaard U, et al. The Danish multicentre randomized study of fibrinolytic therapy vs. primary angioplasty in acute myocardial infarction (the DANAMI-2 trial): outcome after 3 years follow-up. European Heart Journal. 2008;29(10):1259-66.