



ANZCOR Guideline 14.3 – Acute Coronary Syndromes: Reperfusion Strategy

Guideline

Who does this guideline apply to?

This guideline applies to adult victims.

Who is the audience for this guideline?

This guideline is for use by health professionals.

1 Introduction

STEMI occurs in the majority of the patients due to the acute thrombotic occlusion of a major epicardial artery¹⁻³. This is part of a spectrum of acute syndromes that are the result of disruption or erosion of typically lipid rich atherosclerotic plaque which leads to thrombus formation that occludes the vessel. Myocardial necrosis ensues in a time dependent fashion. Therefore strategies aimed at restoring myocardial perfusion at the earliest possible moment are an important part of the management of these patients. The longer the vessel remains occluded the higher the mortality for this patient group. Restoring coronary blood flow and myocardial reperfusion either by percutaneous coronary intervention (PCI) or fibrinolytic therapy has been demonstrated to improve outcomes in patients presenting within 12 hours of symptom onset^{4,5}. It has also been shown to be beneficial in other patient groups beyond 12 hours of symptom onset such as those with cardiogenic shock^{1,3,6,7}.

In general the creation of cardiac clinical networks including emergency and medical providers, non capable and capable PCI hospitals is important to facilitate a regional strategy for the delivery of timely revascularisation^{3,6-13}. The development of these networks has allowed timely institution of reperfusion therapy and reduced mortality from STEMI over the last decade¹⁴.

Related to the issue of STEMI systems of care is a growing body of observational data suggesting out of hospital cardiac arrest (OHCA) patients should be considered for transport to a specialist cardiac arrest centre as part of wider regional system of care for management of patients with OHCA. Such centre would need to have capacity to undertake Primary PCI¹⁵.

1.1 Primary PCI

Primary PCI (PPCI) is the preferred perfusion strategy with the best outcomes demonstrated in a number of large meta-analyses provided it is performed in a timely manner by an experienced team^{16,17}. The benefit is mostly driven by reduced rates of recurrent myocardial infarction and reduced rates of intracranial haemorrhage (ICH) in the PPCI treated patients compared to those receiving fibrinolysis. (LOE I).

Hence where immediate PCI is available the combination of routine administration of fibrinolysis in conjunction with PPCI is without benefit and is associated with increased risk of ICH. It is not recommended (CoSTR 2015, strong recommendation, moderate-quality evidence)¹⁴.

In many parts of Australia and New Zealand, PPCI is not widely available. PPCI is limited by accessibility to a catheterisation laboratory facility, access to appropriate skilled clinician and delays related to the time taken to obtain reperfusion¹⁸.

For PPCI to maintain superiorly over fibrinolytic therapy the PCI related delay must be between 45 and 180 minutes depending on the patient's condition e.g. patient age, site of infarction and duration of symptoms¹⁹⁻²¹. (LOE II).

The Cardiac Society of Australia and New Zealand recommends in general, the maximum acceptable delay from presentation to balloon inflation is²²:

- 60 minutes if a patient presents within 1 hour of symptom onset; or
- 90 minutes if a patient presents later.

(LOE II)

There are a number of strategies that can be undertaken to reduce the time delay to PPCI¹¹. These are strategies to improve the systems of care arising from and they include pre-hospital 12 lead ECGs to facilitate earlier diagnosis, advanced notification of the results of the 12 lead ECG at the receiving institute for rapid reperfusion on arrival of the STEMI patient. Techniques that have evidence to support implementation include²³⁻²⁹ (LOE III-2):

- Arranging suitable activation of the catheter laboratory
- Requiring the catheter laboratory to be ready in 20 minutes
- Having the interventional cardiologist immediately available at the hospital
- Providing real time data feedback
- Support for the treatment strategy by senior medical clincians
- Encouraging a team based approach.

Where PPCI capable facilities are available as part of a system of care, direct triage and transport to those centres for PCI is preferred (CoSTR 2015, weak recommendation, low-quality evidence)¹⁴.

In addition to patients with contraindications for fibrinolysis, PCI should be pursued even if there is a delay rather than opting for a no treatment strategy^{3,6}.

For patients with STEMI presenting with shock, primary PCI or coronary artery bypass is clearly a preferred treatment option. Treatment with fibrinolysis should only be considered if there is a substantial delay to PCI^{30,31}. (LOE II).

1.2 PCI in patients with ROSC

We recommend performing immediate angiography and if necessary PCI in patients with ST elevation or new left bundle branch block on the standard 12 lead electrocardiograph who respond to cardio-pulmonary resuscitation with spontaneous return of circulation after cardiac arrest^{32,35} (LOE II) (CoSTR 2015, strong recommendation, low-quality evidence)¹⁴. Coma is common and should not be a contraindication to angiography and PCI. We suggest immediate angiography and if necessary PCI in selected patients who do not have evidence of ST elevation on their ECG nor prior clinical features such as chest pain, if coronary ischaemia is considered the likely cause on clinical grounds . (LOE III-1) (CoSTR 2015, weak recommendation, very-low-quality evidence)¹⁴.

Targeted temperature management is recommended in combination with PCI and can be commenced as part of the initial treatment preferably prior to PCI³⁶. Angiography and PCI can be incorporated as part of a standardised post cardiac arrest protocol³⁷. (LOE III-3).

Immediate angiography implies these patients should be managed to minimize door-to-reperfusion times in a manner similar to the general STEMI patient population. However, the complexity and heterogeneity of this patient group may delay their resuscitation, management and time to angiography¹⁴.

A number of complex clinical factors may influence the decision to proceed to angiography and intervention. These include patient age, the presenting rhythm, whether the arrest was witnessed, the requirement for haemodynamic support and the known presence of co morbidities such diabetes mellitus, renal failure, and chronic heart failure¹⁴.

1.3 Fibrinolytic Therapy

Fibrinolytic therapy is more widely available and is beneficial in a wider range of patients who may not have access to PPCI³⁸⁻⁴⁰. Fibrinolytic therapy can be safely given by a trained paramedic, nurse or physician using established protocols⁴¹⁻⁴⁵. (LOE I) The efficacy is greatest given the first three hours of the onset of symptoms. Without timely access to primary PPCI, patients with symptoms of ACS and ECG evidence of ST elevation infarction or true new bundle branch block or true posterior infarction should be treated with fibrinolytic therapy as soon as possible.

In patients presenting early after the onset of chest pain (<1-2 hours) and in certain clinical subsets (<65 years-of-age, anterior STEMI), prehospital fibrinolysis may offer similar outcomes compared to PPCI^{20,46,47}. (LOE II)

There are a number of contraindications to fibrinolysis that health care practitioners need to be well aware of (see Table 1)^{1,48}. In addition, the older patients are a difficult patient group. They have a high absolute risk of death from their STEMI, have an increased absolute benefit from fibrinolytic therapy but the risk of intracranial bleeding from fibrinolysis is also higher. This is increased in the presence of systolic hypertension of over 180 mmHg. The benefits of fibrinolytic therapy are less impressive in areas of infarction other than an anterior STEMI location.

2 Table 1

Contraindications for fibrinolysis⁴⁸

2.1 Absolute contraindications

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in the preceding 6 months
- Central nervous system damage, neoplasms or structural vascular lesions (e.g. ateriovenous malformation)
- Recent major trauma/surgery/head injury (within the preceding 3 weeks)
- Gastro-intestinal bleeding within the last month
- Known bleeding disorder (excluding menses)
- Aortic dissection

2.2 Relative contraindications

- Transient ischaemic attack in preceding 6 months, dementia
- Oral anticoagulant therapy
- Pregnancy within 1-week post-partum
- Non-compressible punctures

- Traumatic resuscitation
- Refractory hypertension (systole. blood pressure >180mmHg
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

In patients with STEMI diagnosed in the pre-hospital setting, reperfusion can be achieved by the administration of fibrinolytics by health care providers in the field. If fibrinolysis is chosen as a reperfusion strategy and transport to hospital estimated to be greater than 30 min from first medical contact, we recommend prehospital fibrinolysis if this capability exists (CoSTR 2015, strong recommendation, moderate-quality evidence)¹⁴. This requires paramedics, nurses or doctors to use well established protocols, have competency based training programs, a quality assurance program and be under medical oversight^{43,49,50}. (LOE II).

This strategy may be particularly important in rural areas where there are long transit times to hospital^{44,51-53}.

2.3 Triage and inter facility transfer for PPCI

It is reasonable to consider direct transport to PCI capable facilities for PPCI for patients diagnosed with STEMI by emergency medical services in the prehospital setting, bypassing closer hospitals as necessary, in systems where time intervals between first medical contact and balloon time are brief (<2 hours) ^{4,26,54-56}.

Transfer of STEMI patients for PPCI from community hospitals is reasonable for those presenting more than 3 h but less than 12 h after the onset of symptoms, provided that the transfer can be achieved rapidly (<2 hrs). The risk of death, reinfarction or stroke is reduced if patients with STEMI are transferred promptly from community hospitals to tertiary care facilities for PPCI⁵⁵⁻⁵⁷. (LOE I) (CoSTR 2015, strong recommendation, moderate-quality evidence)¹⁴.

When long delays to PPCI are anticipated (more than 120 minutes), a strategy of immediate fibrinolysis followed by routine early (within 3–24 hours) angiography and PCI, if indicated, is reasonable (CoSTR 2015, weak recommendation, very-low-quality evidence)¹⁴

2.4 Rescue PCI

It is reasonable to perform coronary angiography and PCI in patients who have failed fibrinolysis according to clinical signs and insufficient ST segment resolution⁵⁸⁻⁶³. (LOE I).

2.5 Pharmaco-Invasive Strategy

Patients with successful fibrinolysis but are not treated at a PCI capable centre should be encouraged to be routinely transferred for angiography and PCI performed within 3-24 hours after fibrinolysis. The optimal timing has not been determined but intervention in under 24 hours has been shown to reduce re-infarction rates. It is recognised that there may be situations and geography where transfer within 24 hours may be difficult or not available.⁶⁴⁻⁶⁸ (LOE II) (CoSTR 2015, weak recommendation, very-low-quality evidence)¹⁴.

2.6 Facilitated PCI

Facilitated PCI refers to the routine use of fibrinolysis prior to PPCI. The strategy of facilitated PCI compared with PPCI is not recommended in STEMI.

A number of studies have examined the strategy of facilitated PCI and they have shown no benefit of PPCI and some studies have shown poor outcomes with routine PCI shortly after fibrinolysis^{69,70}. (LOE II) (strong recommendation, moderate-quality evidence)¹⁴

2.7 Cardiac Arrest Centres

A cardiac arrest centre is a hospital that has the facilities to provide a comprehensive package of post resuscitation care including percutaneous coronary intervention and targeted temperature management. There is evidence from observational studies that such centres appear to have better survival and better neurologically intact survival. The evidence supporting triaging to such centres is however weak with an absence of randomised studies supporting such a strategy. It is reasonable to consider transport patients with OHCA directly to a cardiac arrest centre. This would need to take into account geographic, population and resource factors. (CoSTR 2015, weak recommendation, low level of evidence)¹⁵

References

- Antman EM, Hand M, Armstrong PW, et al. 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines: developed in collaboration With the Canadian Cardiovascular Society endorsed by the American Academy of Family Physicians: 2007 Writing Group to Review New Evidence and Update the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction, Writing on Behalf of the 2004 Writing Committee. Circulation 2008;117:296-329.
- 2. Guidelines for the management of acute coronary syndromes 2006. Med J Aust 2006;184:S9-29.
- O'Connor RE, Brady W, Brooks SC, et al. Part 10: acute coronary syndromes: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2010;122:S787-817.
- 4. Andersen HR, Nielsen TT, Rasmussen K, et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. The New England journal of medicine 2003;349:733-42.
- 5. Grines CL, Browne KF, Marco J, et al. A comparison of immediate angioplasty with thrombolytic therapy for acute myocardial infarction. The Primary Angioplasty in Myocardial Infarction Study Group. The New England journal of medicine 1993;328:673-9.
- O'Connor RE, Bossaert L, Arntz HR, et al. Part 9: acute coronary syndromes: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation 2010;122:S422-65.
- Arntz HR, Bossaert LL, Danchin N, Nikolaou NI. European Resuscitation Council Guidelines for Resuscitation 2010 Section 5. Initial management of acute coronary syndromes. Resuscitation 2010;81:1353-63.
- 8. Bradley EH, Herrin J, Elbel B, et al. Hospital Quality for Acute Myocardial Infarction: Correlation Among Process Measures and Relationship With Short-term Mortality. Jama 2006;296:72-8.

- 9. Bradley EH, Herrin J, Elbel B, et al. Hospital quality for acute myocardial infarction: correlation among process measures and relationship with short-term mortality. Jama 2006;296:72-8.
- 10. Bradley EH, Herrin J, Wang Y, et al. Door-to-drug and door-to-balloon times: where can we improve? Time to reperfusion therapy in patients with ST-segment elevation myocardial infarction (STEMI). Am Heart J 2006;151:1281-7.
- 11. Bradley EH, Nallamothu BK, Herrin J, et al. National efforts to improve door-to-balloon time results from the Door-to-Balloon Alliance. J Am Coll Cardiol 2009;54:2423-9.
- 12. McNamara RL, Wang Y, Herrin J, et al. Effect of door-to-balloon time on mortality in patients with ST-segment elevation myocardial infarction. J Am Coll Cardiol 2006;47:2180-6.
- 13. Nallamothu BK, Wang Y, Magid DJ, et al. Relation between hospital specialization with primary percutaneous coronary intervention and clinical outcomes in ST-segment elevation myocardial infarction: National Registry of Myocardial Infarction-4 analysis. Circulation 2006;113:222-9.
- Nikolaou NI, Welsford M, Beygui F, et al. Part 5: Acute coronary syndromes: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Resuscitation. 2015;95:e121-46
- 15. Finn JC, Bhanji F, Lockey A, et al. Part 8: Education, implementation, and teams: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. Resuscitation. 2015;95:e203-24..
- 16. Addo T, Grines CL, Keeley EC. Primary PTCA versus thrombolytic therapy for acute MI. Cardiology Review 2003;20:12-7.
- 17. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003;361:13-20.
- Walters DL, Aroney CN, Chew DP, et al. Variations in the application of cardiac care in Australia. Med J Aust 2008;188:218-23.
- Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation 2005;111:761-7.
- Pinto DS, Kirtane AJ, Nallamothu BK, et al. Hospital Delays in Reperfusion for ST-Elevation Myocardial Infarction: Implications When Selecting a Reperfusion Strategy. Circulation 2006;114:2019-25.
- 21. Steg PG, Bonnefoy E, Chabaud S, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. Circulation 2003;108:2851-6.

- 22. Aroney CN, Aylward P, Chew DP, et al. 2007 addendum to the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand Guidelines for the management of acute coronary syndromes 2006. Med J Aust 2008;188:302-3.
- 23. Aguirre FV, Varghese JJ, Kelley MP, et al. Rural interhospital transfer of ST-elevation myocardial infarction patients for percutaneous coronary revascularization: the Stat Heart Program. Circulation 2008;117:1145-52.
- 24. Bradley EH, Herrin J, Wang Y, et al. Strategies for reducing the door-to-balloon time in acute myocardial infarction. The New England journal of medicine 2006;355:2308-20.
- 25. Le May MR, Davies RF, Dionne R, et al. Comparison of early mortality of paramedic-diagnosed ST-segment elevation myocardial infarction with immediate transport to a designated primary percutaneous coronary intervention center to that of similar patients transported to the nearest hospital. Am J Cardiol 2006;98:1329-33.
- 26. Le May MR, So DY, Dionne R, et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. The New England journal of medicine 2008;358:231-40.
- 27. van de Loo A, Saurbier B, Kalbhenn J, Koberne F, Zehender M. Primary percutaneous coronary intervention in acute myocardial infarction: direct transportation to catheterization laboratory by emergency teams reduces door-to-balloon time. Clin Cardiol 2006;29:112-6.
- 28. van 't Hof AW, Rasoul S, van de Wetering H, et al. Feasibility and benefit of prehospital diagnosis, triage, and therapy by paramedics only in patients who are candidates for primary angioplasty for acute myocardial infarction. Am Heart J 2006;151:1255.
- 29. Dorsch MF, Greenwood JP, Priestley C, et al. Direct ambulance admission to the cardiac catheterization laboratory significantly reduces door-to-balloon times in primary percutaneous coronary intervention. Am Heart J 2008;155:1054-8.
- Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK Investigators. Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock. The New England journal of medicine 1999;341:625-34.
- 31. Hochman JS, Sleeper LA, White HD, et al. One-year survival following early revascularization for cardiogenic shock. JAMA 2001;285:190-2.
- 32. Spaulding CM, Joly LM, Rosenberg A, et al. Immediate coronary angiography in survivors of outof-hospital cardiac arrest. The New England journal of medicine 1997;336:1629-33.
- Dumas F, Cariou A, Manzo-Silberman S, et al. Immediate percutaneous coronary intervention is associated with better survival after out-of-hospital cardiac arrest: insights from the PROCAT (Parisian Region Out of hospital Cardiac ArresT) registry. Circ Cardiovasc Interv 2010;3:200-7.
- 34. Noc M. Urgent coronary angiography and percutaneous coronary intervention as a part of postresuscitation management. Crit Care Med 2008;36:S454-7.

- 35. Nolan JP, Neumar RW, Adrie C, et al. Post-cardiac arrest syndrome: epidemiology, pathophysiology, treatment, and prognostication: a scientific statement from the International Liaison Committee on Resuscitation; the American Heart Association Emergency Cardiovascular Care Committee; the Council on Cardiovascular Surgery and Anesthesia; the Council on Cardiopulmonary, Perioperative, and Critical Care; the Council on Clinical Cardiology; the Council on Stroke (Part II). Int Emerg Nurs 2010;18:8-28.
- 36. Wolfrum S, Radke PW, Pischon T, Willich SN, Schunkert H, Kurowski V. Mild therapeutic hypothermia after cardiac arrest a nationwide survey on the implementation of the ILCOR guidelines in German intensive care units. Resuscitation 2007;72:207-13.
- 37. Sunde K, Pytte M, Jacobsen D, et al. Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest. Resuscitation 2007;73:29-39.
- 38. A comparison of reteplase with alteplase for acute myocardial infarction. The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. The New England journal of medicine 1997;337:1118-23.
- 39. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. Assessment of the Safety and Efficacy of a New Thrombolytic Investigators. Lancet 1999;354:716-22.
- 40. Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI). Lancet 1986;1:397-402.
- 41. Weaver W, Cerqueira M, Hallstrom A, et al. Prehospital-initiated vs hospital-initiated thrombolytic therapy: the Myocardial Infaction Triage and Intervention Trial (MITI). JAMA 1993;270:1203-10.
- 42. Gatenby R, Lyons K, Stewart T, et al. Feasibility, safety, and efficacy of domiciliary thrombolysis by general practitioners: Grampian region early anistreplase trial. BMJ 1992;305:548-53.
- 43. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and prehospital thrombolysis for acute myocardial infarction: A meta-analysis. JAMA 2000;283:2686-92.
- 44. Doherty DT, Dowling J, Wright P, Murphy AW, Bury G, Bannan L. The potential use of prehospital thrombolysis in a rural community. Resuscitation 2004;61:303-7.
- Pedley DK, Bissett K, Connolly EM, et al. Prospective observational cohort study of time saved by prehospital thrombolysis for ST elevation myocardial infarction delivered by paramedics. BMJ 2003;327:22-6.
- 46. Steg PG, Bonnefoy E, Chabaud S, et al. Impact of Time to Treatment on Mortality After Prehospital Fibrinolysis or Primary Angioplasty: Data From the CAPTIM Randomized Clinical Trial. Circulation 2003;108:2851-6.
- 47. Bonnefoy E, Steg PG, Boutitie F, et al. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (CAPTIM) trial: a 5-year follow-up. Eur Heart J 2009;30:1598-606.

- 48. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction--executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). J Am Coll Cardiol 2004;44:671-719.
- 49. Arntz HR, Wenzel V, Dissmann R, Marschalk A, Breckwoldt J, Muller D. Out-of-hospital thrombolysis during cardiopulmonary resuscitation in patients with high likelihood of ST-elevation myocardial infarction. Resuscitation 2008;76:180-4.
- 50. Welsh RC, Travers A, Senaratne M, Williams R, Armstrong PW. Feasibility and applicability of paramedic-based prehospital fibrinolysis in a large North American center. Am Heart J 2006;152:1007-14.
- 51. Coccolini S, Berti G, Bosi S, Pretolani M, Tumiotto G. Prehospital thrombolysis in rural emergency room and subsequent transport to a coronary care unit: Ravenna Myocardial Infarction (RaMI) trial. Int J Cardiol 1995;49 (suppl):S47-S58.
- 52. Foster DB, Dufendach JH, Barkdoll CM, Mitchell BK. Prehospital recognition of AMI using independent nurse/paramedic 12-lead ECG evaluation: impact on in-hospital times to thrombolysis in a rural community hospital. Am J Emerg Med 1994;12:25-31.
- 53. Gonzalez ER, Jones LA, Ornato JP, Bleecker GC, Strauss MJ. Hospital delays and problems with thrombolytic administration in patients receiving thrombolytic therapy: a multicenter prospective assessment. Virginia Thrombolytic Study Group. Ann Emerg Med 1992;21:1215-21.
- 54. Dalby M, Bouzamondo A, Lechat P, Montalescot G. Transfer for primary angioplasty versus immediate thrombolysis in acute myocardial infarction: a meta-analysis. Circulation 2003;108:1809-14.
- 55. De Luca G, Biondi-Zoccai G, Marino P. Transferring patients with ST-segment elevation myocardial infarction for mechanical reperfusion: a meta-regression analysis of randomized trials. Ann Emerg Med 2008;52:665-76.
- 56. Widimsky P, Groch L, Zelizko M, Aschermann M, Bednar F, Suryapranata H. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur Heart J 2000;21:823-31.
- 57. Andersen HR, Nielsen TT, Vesterlund T, et al. Danish multicenter randomized study on fibrinolytic therapy versus acute coronary angioplasty in acute myocardial infarction: rationale and design of the DANish trial in Acute Myocardial Infarction-2 (DANAMI-2). Am Heart J 2003;146:234-41.
- 58. Arntz HR. Reperfusion strategies in ST-elevation myocardial infarction--current status and perspectives for early and pre-hospital treatment. Resuscitation 2008;77:296-305.
- 59. Edmond JJ, Juergens CP, French JK. The pharmaco-invasive approach to STEMI: when should fibrinolytic-treated patients go to the "cath lab"? Postgrad Med J 2009;85:331-4.

- 60. Kunadian B, Sutton AG, Vijayalakshmi K, et al. Early invasive versus conservative treatment in patients with failed fibrinolysis--no late survival benefit: the final analysis of the Middlesbrough Early Revascularisation to Limit Infarction (MERLIN) randomized trial. Am Heart J 2007;153:763-71.
- 61. Kunadian B, Vijayalakshmi K, Dunning J, Sutton A, de Belder MA. Towards an understanding of the role of rescue angioplasty for failed fibrinolysis: comparison of the MERLIN, RESCUE and REACT trials. J Invasive Cardiol 2007;19:359-68.
- 62. Patel TN, Bavry AA, Kumbhani DJ, Ellis SG. A meta-analysis of randomized trials of rescue percutaneous coronary intervention after failed fibrinolysis. Am J Cardiol 2006;97:1685-90.
- 63. Testa L, van Gaal WJ, Biondi-Zoccai GG, et al. Repeat thrombolysis or conservative therapy vs. rescue percutaneous coronary intervention for failed thrombolysis: systematic review and meta-analysis. QJM 2008;101:387-95.
- 64. Bohmer E, Hoffmann P, Abdelnoor M, Arnesen H, Halvorsen S. Efficacy and safety of immediate angioplasty versus ischemia-guided management after thrombolysis in acute myocardial infarction in areas with very long transfer distances results of the NORDISTEMI (NORwegian study on DIstrict treatment of ST-elevation myocardial infarction). J Am Coll Cardiol 2010;55:102-10.
- 65. Borgia F, Goodman SG, Halvorsen S, et al. Early routine percutaneous coronary intervention after fibrinolysis vs. standard therapy in ST-segment elevation myocardial infarction: a metaanalysis. Eur Heart J 2010;31:2156-69.
- 66. Cantor WJ, Fitchett D, Borgundvaag B, et al. Routine early angioplasty after fibrinolysis for acute myocardial infarction. The New England journal of medicine 2009;360:2705-18.
- 67. Cantor WJ, Fitchett D, Borgundvaag B, et al. Rationale and design of the Trial of Routine ANgioplasty and Stenting After Fibrinolysis to Enhance Reperfusion in Acute Myocardial Infarction (TRANSFER-AMI). Am Heart J 2008;155:19-25.
- 68. Di Mario C, Dudek D, Piscione F, et al. Immediate angioplasty versus standard therapy with rescue angioplasty after thrombolysis in the Combined Abciximab REteplase Stent Study in Acute Myocardial Infarction (CARESS-in-AMI): an open, prospective, randomised, multicentre trial. Lancet 2008;371:559-68.
- 69. Ross AM, Coyne KS, Reiner JS, et al. A randomized trial comparing primary angioplasty with a strategy of short-acting thrombolysis and immediate planned rescue angioplasty in acute myocardial infarction: the PACT trial. PACT investigators. Plasminogen-activator Angioplasty Compatibility Trial. J Am Coll Cardiol 1999;34:1954-62.
- 70. McDonald MA, Fu Y, Zeymer U, et al. Adverse outcomes in fibrinolytic-based facilitated percutaneous coronary intervention: insights from the ASSENT-4 PCI electrocardiographic substudy. Eur Heart J 2008;29:871-9.