

Prehospital thrombolysis followed by early angiography and percutaneous coronary intervention where appropriate — an underused strategy for the management of STEMI

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ST-elevation myocardial infarction (STEMI) comprises about 30% of acute coronary syndromes¹ and is a medical emergency. Prompt and efficient treatment can substantially reduce mortality and morbidity resulting from this condition.²⁻⁶ Health services in Australia need to be organised in ways that maximise the chances of patients with STEMI receiving such treatment no matter where they live.

The most effective treatment of STEMI is timely restoration of blood flow to the infarcting myocardium (reperfusion). The earlier this is achieved, the greater will be the amount of myocardium saved, improving short- and long-term clinical outcomes.²⁻⁶ For example, reperfusion within the first hour of the onset of symptoms may completely abort a heart attack;⁷ reperfusion within the first 2 hours converts, in most circumstances, a potentially large heart attack to a small heart attack.³ Reperfusion after 6 hours is likely to result in minimal or no myocardial salvage.⁸

Unfortunately, in Australia, only a minority of patients with STEMI receive timely reperfusion (within 2 hours of the onset of symptoms). Most receive reperfusion more than 3 to 4 hours after the onset of symptoms,^{9,10} that is, when only minimal myocardial salvage is possible. The main barrier to early reperfusion is delay by patients in summoning medical assistance after the onset of symptoms. Australian data indicate that patients wait on average 1 to 2 hours before seeking help.⁹⁻¹²

Methods of reperfusion

Reperfusion can be achieved either by intravenous administration of a powerful blood clot-dissolving agent (thrombolysis) or by primary percutaneous coronary intervention (PCI). The latter procedure usually involves balloon angioplasty to open the occluded artery and insertion of a stent to maintain patency.

Advantages and disadvantages of thrombolysis

The main advantage of thrombolysis is that it is relatively simple to administer and therefore can be given early — either in the emergency department (ED) or outside the hospital setting by appropriately trained paramedical staff (prehospital thrombolysis [PHT]). The main disadvantages of thrombolysis are that it achieves reperfusion in only 60% to 80% of cases¹³⁻¹⁶ (the effectiveness being greater if given early in the course of STEMI^{3,14}); and it is associated with a small risk of intracranial haemorrhage (approximately 1%), particularly in older people.

Advantages and disadvantages of primary PCI

The main advantage of primary PCI is that it achieves effective reperfusion in over 90% to 95% of cases. Furthermore, it is a more definitive treatment in that it deals with the underlying atherosclerotic plaque (usually by stenting), thereby stabilising the plaque and reducing the chances of reinfarction or continuing ischaemia. The main disadvantages of primary PCI are that it is available in

ABSTRACT

- Prompt myocardial reperfusion, particularly if achieved within 2 hours of the onset of symptoms, improves outcomes in patients with ST-elevation myocardial infarction (STEMI).
- Recent data suggest that ambulance-administered prehospital thrombolysis, if given within 2 hours of the onset of STEMI, produces superior outcomes to primary percutaneous coronary intervention (PCI); if given within 4 hours, the outcomes are similar.
- For optimal results after thrombolysis, patients require angiography (and PCI where appropriate) within 24 hours of the event.
- These developments have major implications for the practice of cardiology and for the organisation of health services in Australia.

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only a minority of hospitals as a 24-hour service; and it usually takes a significant amount of time to organise and perform after patient arrival at the hospital. Because of the inherent delays in providing primary PCI, reperfusion is rarely achieved within the optimal time of 2 hours after the onset of symptoms.

Which is better — thrombolysis or primary PCI?

Meta-analysis of randomised trials of in-hospital thrombolysis versus primary PCI shows that primary PCI is the more effective treatment for patients with STEMI,¹⁷ but its advantage is dissipated if the time from arrival at the hospital to angioplasty (door-to-balloon inflation [DTBI]) is unduly delayed. The guidelines of the National Heart Foundation of Australia (NHFA) and the Cardiac Society of Australia and New Zealand (CSANZ) suggest that, for patients presenting within 6 hours of the onset of symptoms, primary PCI is the preferred option providing the estimated DTBI time is <90 minutes.¹⁸ These time guidelines presume that thrombolysis can be given within 30 minutes of arrival at hospital; that is, they presume a door-to-needle (DTN) time of <30 minutes. The limited data that are available suggest that DTBI times of <90 minutes and DTN times of <30 minutes are achieved only in a minority of cases.¹⁹ This mirrors the experience in the United States.²⁰

In the meta-analysis referred to above, the difference in mortality between the two treatments was 9% versus 7% in favour of primary PCI, but if trials in which streptokinase, an inferior thrombolytic agent, were excluded, the absolute mortality difference was only 1%. Furthermore, few patients in the reviewed studies received treatment within 2 hours of the onset of symptoms and none received PHT — a treatment proven to be superior to in-hospital thrombolysis.^{21,22} Importantly, in none of the studies

was it routine policy to perform angiography and PCI within 24 hours of administration of thrombolysis. There is emerging evidence (discussed below) that PHT given within 2 hours of the onset of symptoms and followed by early routine angiography, and PCI where appropriate, results in superior outcomes to primary PCI.

PHT within 2 hours of the onset of symptoms followed by early angiography and PCI where appropriate versus primary PCI

There has been only one randomised study with long-term outcome data comparing PHT to primary PCI in the treatment of STEMI — the Comparison of Angioplasty and Pre-hospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) study.²³ In this French study, 840 patients, who presented with STEMI initially managed by mobile emergency care units, were allocated at random to receive either PHT or primary PCI. The median delay between the onset of symptoms and treatment was 130 minutes in the PHT group and 190 minutes (time to first balloon inflation) in the primary PCI group. All patients, irrespective of randomised status, were taken to a hospital with 24-hour emergency PCI capability. In the PHT group, angiography and PCI were left to the discretion of the treating physician and were performed in 85% and 70% of patients, respectively, during the hospital stay.

The 5-year follow-up of the CAPTIM study showed that mortality was 9.75% in the PHT group compared with 12.6% in the primary PCI group ($P=0.18$).²⁴ For those treated within 2 hours of the onset of symptoms, mortality was 5.8% in the PHT group and 11.1% in the primary PCI group (hazard ratio, 0.50; 95% CI, 0.25–0.97; $P=0.04$). For those treated between 2 and 4 hours, mortality was similar (14.5% v 14.4%). The significantly lower 5-year mortality for patients treated with PHT within 2 hours of the onset of symptoms (5.8%) compared with the mortality for those treated between 2 and 4 hours (14.5%) again emphasises the importance of early reperfusion for STEMI patients. French registry data also support the CAPTIM findings.²⁵ In this registry, PHT was associated with a 0.49 relative risk of death at 1 year compared with primary PCI ($P=0.05$).

It could be argued that improvements in the delivery of primary PCI, such as reduced DTB times and the aspiration of the thrombus immediately before PCI, might improve the results of primary PCI and eliminate, even reverse, the mortality differences between the two strategies. In the CAPTIM study, thrombus aspiration was not performed in the primary PCI arm, but the average time of 82 minutes between randomisation (which occurred in the ambulance setting) and treatment was better than the average DTB times for patients presenting to most Australian EDs;¹⁹ it also compared favourably with the ambulance transport-to-balloon time of 74 minutes in Australia's recent Ambulance Victoria and MonashHeart Acute Myocardial Infarction (MonAMI) study.²⁶ In this study, intensive care ambulance officers transmitted the 12-lead electrocardiogram (ECG) of the patient with suspected heart attack to the ED for confirmation of STEMI. Once confirmation had been received, the hospital "infarct angioplasty team" was activated and the patient was transported directly to the cardiac catheterisation laboratory for primary PCI. This policy resulted in a significant reduction in DTB times compared with DTB times for patients arriving at the ED without this prehospital triage (56 v 98 minutes; $P<0.001$). Outcome results were not presented in that study.

What are the implications of the CAPTIM study for Australian practice?

The results of the CAPTIM study suggest that for patients triaged by a specialised ambulance service within 2 hours of the onset of STEMI, a PHT strategy and subsequent transfer to a hospital with PCI capability is superior to a primary PCI strategy (50% reduction in 5-year mortality). For those treated between 2 and 4 hours, the two strategies were equivalent. The implications of these findings are far reaching. The NHFA and CSANZ guidelines suggest that primary PCI is superior to thrombolysis if the former can be performed within 90 minutes of medical contact.¹⁸ As previously discussed, this recommendation is predominantly based on a meta-analysis comparing in-hospital thrombolysis with primary PCI,¹⁷ but few patients in that series underwent treatment within 2 hours of the onset of symptoms. In the CAPTIM study, the time differential between thrombolysis and PCI was only 60 minutes, yet patients treated within 2 hours of the onset of symptoms did significantly better in the PHT arm than those treated with primary PCI. In light of these findings, the NHFA and CSANZ guidelines concerning the management of STEMI early after the onset of symptoms may need to be revised, particularly if the CAPTIM findings were to be replicated by another randomised study. Furthermore, the current strategy in many metropolitan areas of large Australian cities for ambulance notification of STEMI and patient transport to a PCI-capable hospital (the MonAMI-style protocol) warrants review. This strategy has significantly reduced DTB times, but providing a 24-hour emergency PCI service is very resource-intensive and demanding of the cardiac catheterisation staff. If the CAPTIM findings (that the efficacy of PHT is equal to that of primary PCI if administered within 4 hours of the onset of symptoms and superior if administered within 2 hours) are true, the need for, and cost of, emergency after-hours PCI would be reduced.

One can argue that the CAPTIM study is but one study and a second independent study is necessary to confirm results. An ideal option would be to conduct a randomised Australian study similar to the CAPTIM study. Patients presenting to intensive care ambulances within 4 hours of the onset of symptoms, with a diagnosis of STEMI confirmed by central interpretation, would be randomly allocated to either immediate transport to a PCI-capable hospital for primary PCI or to receive ambulance-administered PHT, followed by transport to a PCI-capable hospital for routine angiography, and PCI if needed, within 3 to 24 hours after thrombolysis. Patients considered not eligible for PHT on the basis of a pre-specified checklist (non-randomised patients) would also be transported for immediate primary PCI and could form a third comparative group.

How practical is ambulance-administered PHT?

A wealth of experience indicates that suitably trained ambulance officers, backed up by an appropriate central advisory service, can accurately diagnose STEMI on the 12-lead ECG and safely administer PHT.^{27–29} At present, only a minority of ambulance officers in Australia are trained to give PHT, but given the compelling evidence for its benefits, state governments should plan to equip all emergency ambulances with 12-lead ECG capability and train all emergency ambulance officers to administer PHT.

Management of patients after PHT

Following thrombolysis, patients benefit from admission to a PCI-capable hospital for two reasons. First, if reperfusion has failed, rescue PCI is more readily available. Second, on the basis of many recent studies, routine angiography, and PCI where appropriate, overrides a selective ischaemia-driven invasive approach as the recommended management after thrombolysis.³⁰⁻³⁷ Importantly, these studies strongly indicate that angiography, with PCI if needed, is best performed within the first 24 hours.³⁰⁻³⁷ The well known difficulties in arranging prompt transport from one hospital to another make immediate admission to a PCI-capable hospital preferable. For these reasons, patients who have been treated with PHT should be taken to the nearest PCI-capable hospital even when transport distances are long. This strategy was tested in the Norwegian Study on District Treatment of ST-Elevation Myocardial Infarction (NORDISTEMI),³⁶ in which PHT patients in rural Norway were randomly allocated to be taken to either the nearest community hospital or the nearest PCI-capable hospital. The average transport distance in the latter group was 158 km. These patients had shorter hospital stays and significantly improved outcomes compared with the group admitted to community hospitals.

In view of the persuasive evidence of the benefits of routine angiography, and PCI if needed, within the first 24 hours after thrombolysis, health services in Australia need to accommodate this requirement. The more widespread development of PCI facilities in regional Australia, even if available only on a 9 am to 5 pm basis, would enhance the ability to provide this service.

Summary

The optimal treatment for STEMI is reperfusion within 2 hours of the onset of symptoms. Health services in Australia need to be organised to maximise the chances of this occurring. The current NHFA education campaign encouraging patients to call emergency ambulance services as soon as possible after the onset of symptoms warrants strong support. For patients with STEMI who present directly to an ED, the current NHFA and CSANZ guidelines are appropriate. For those who summon an ambulance in rural and regional areas, PHT and transport to the nearest PCI-capable hospital is the treatment of choice, even if the transport distances are long. For patients in the metropolitan areas of large cities who present within 4 hours of the onset of symptoms, either PHT followed by transport to a PCI-capable hospital or immediate transport to a hospital capable of performing primary PCI within 90 minutes of ambulance notification are acceptable options. PHT is the favoured option if the presentation is within 2 hours; primary PCI is preferred if the presentation is beyond 4 hours.

All patients who receive thrombolysis, whether prehospital or in-hospital, should undergo angiography, and PCI if indicated, within 24 hours of their presentation. Development of more regional cardiac catheterisation facilities would facilitate this requirement.

Competing interests

None identified.

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