“Time is muscle” in reperfusing occluded coronary arteries in acute myocardial infarction

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There is still room for improvement, both in decreasing delays in, and deciding who is eligible for, reperfusion therapy

In patients with acute ST-segment-elevation myocardial infarction (STEMI), early coronary reperfusion — within 1 to 2 hours of symptom onset — by either thrombolysis or primary percutaneous coronary intervention (PCI) reduces the mortality rate by half. However, this benefit quickly dissipates with further delay in treatment. As “time is muscle”, it is the time from symptom onset to reperfusion (or total ischaemic time), rather than the mode of reperfusion, that is the critical determinant of outcome. Hence the imperative to minimise: (i) delay by patients in recognising symptoms as possible myocardial infarction (MI) and seeking medical help; (ii) delay in ambulances responding to calls; (iii) delays in diagnosing STEMI on first medical contact; and (iv) omissions or delays in administering the most appropriate means of reperfusion in eligible patients. In this issue of the Journal (page 496), Huynh and colleagues, using data from a prospective Australian registry, report on processes of care and outcomes of 755 patients presenting with suspected STEMI.

There is good and bad news in this report. The good news is that the median time from symptom onset to first medical contact in this cohort was 105 minutes (1.75 hours) compared with 3.2 hours for patients with undifferentiated chest pain, reported in 2005. If the sample in the study by Huynh and colleagues is representative of most patients with MI, this suggests that public recognition of warning symptoms and the need to seek medical help urgently has improved over the past 15 years in response to public education campaigns that target individuals at high risk and behavioural barriers to action. Reperfusion reduced mortality at 12 months (adjusted for baseline risk as calculated using the Global Registry of Acute Coronary Events [GRACE] risk score) by 65% (and by 78% if administered in a timely fashion), similar to results noted in recent overseas observational studies that used similar risk-adjustment methods. Finally, there was no difference between metropolitan and rural patients in the time to presentation or the proportions of patients who received reperfusion therapy, or who received it in a timely manner, and the same applied to inhospital and 12-month mortality rates. This suggests the “city–bush” gap in coronary care noted in past studies is being closed, although more rural patients (74%) received thrombolysis, while more metropolitan patients (68%) received primary PCI.

The bad news is that one in three patients did not receive any form of reperfusion — a figure common to other countries and which has proven resistant to change. Unfortunately, contraindications to either form of reperfusion in individual patients were not reported, but contraindications and patient refusal have been
reported to account for no more than 10% of all patients with STEMI. This means just over one in five patients were likely to have been eligible for reperfusion therapy but failed to receive it. Factors associated with not receiving reperfusion therapy on regression analysis included a past history of diabetes or documented coronary stenoses on angiography, acute pulmonary oedema on presentation, left bundle branch block on electrocardiogram (ECG), and a non-cardiologist as the treating doctor. In other studies of patients eligible for reperfusion therapy, additional factors have included older age, admission to a facility not capable of performing PCI, increasing time to presentation, renal insufficiency, prior stroke or coronary artery bypass grafting, being female, and presentation without chest pain or with an equivocal ECG. Some of these associations reflect diagnostic uncertainty in patients with atypical clinical presentations and non-diagnostic ECGs or clinician concern about the risk of bleeding in older patients (especially underweight women) and those with renal failure or prior stroke. However, registry data show that in this patient group at relatively high risk, early reperfusion therapy compared with no reperfusion reduces inhospital mortality by 38%, with primary PCI being more effective than thrombolysis. Clinicians may need to recalibrate their perceptions of benefit and risk in groups of patients who have often been excluded from clinical trials.

The other bad news is that among patients receiving reperfusion therapy in the study by Huynh and colleagues (61%, primary PCI; 37%, thrombolysis), only one in three received it within an optimal time frame. The median door-to-needle time (D2N) for thrombolysis was 43 minutes (versus a 30-minute standard) and door-to-balloon time (D2B) for primary PCI was 102 minutes (versus a 90-minute standard). These times are longer than those reported in contemporary cohorts in other developed countries, such as 33 minutes D2N and 83 minutes D2B in a Canadian cohort, and 30 minutes D2N and 86 minutes D2B in the GRACE international registry. Attention has recently shifted to reducing total system delay, defined as the time from first contact with the health care system (ie, ambulance) to initiation of reperfusion therapy, which now appears to be more strongly associated with mortality than patient delay in seeking care.

In reducing system delay, the timing of PCI (immediate v delayed v rescue) and its relation to thrombolysis in patients presenting to non-PCI-capable hospitals becomes a pivotal issue. Current Australian and New Zealand guidelines state that fibrinolysis is preferred to primary PCI in patients presenting within 1 hour of symptom onset unless balloon insufflation can occur within 60 minutes after first medical contact (in most cases, this is patient pick-up by ambulance). In patients presenting between 1 and 3 hours after symptom onset, fibrinolysis is preferred unless primary PCI can occur within 90 minutes of first medical contact. Studies show that in patients with symptom onset of less than 3 hours and for whom transfer to PCI-capable hospitals would delay primary PCI for more than 90 minutes, the combination of early
lysis and aggressive use of rescue PCI (in the third of patients with persistent ST-segment elevation, cardiogenic shock, severe heart failure or serious ventricular arrhythmias) confers comparable outcomes with that achieved with primary PCI. In this regard, prehospital thrombolysis undertaken by ambulance paramedics, combined with early PCI where appropriate, seems to be an underused strategy in reducing system delay.

Another issue is the role of risk stratification in deciding who should receive which form of reperfusion. A treatment-risk paradox is often seen whereby eligible patients at high absolute risk of death or recurrent MI are less likely to receive reperfusion therapy (for reasons already mentioned) than those at lower risk and in whom treatment delays attenuate the absolute benefit of reperfusion to a greater degree. In considering transferring patients presenting within 6 hours of symptom onset for primary PCI, the higher the risk profile, the larger the reduction in mortality benefit with primary PCI compared with thrombolysis for each 10-minute increase in PCI-related time delay. Delays must be minimised in high-risk patients, rather than simply working to a 60-minute or 90-minute D2B rule. The equipoint between primary PCI and fibrinolysis (the PCI-related time delay at which primary PCI loses the 90-minute D2B rule. The equipoint between primary PCI and fibrinolysis (the PCI-related time delay at which primary PCI loses the 90-minute D2B rule.

Several strategies have been shown in both Australian and overseas studies to be effective in reducing total ischaemic time (Box) and these need to become mainstream care. This will require a multifaceted approach involving educating both patients and doctors; coordinating ambulance, emergency department and cardiac catheterisation laboratory components of care; establishing integrated networks of non-PCI and PCI-capable hospitals with decision support and transfer processes that take patient risk and time to presentation into account; and ongoing data collection and feedback within clinical registries.

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References