Thrombolytic therapy with aspirin saves lives in the management of ST-elevation myocardial infarction (MI). In recent years, emerging data suggest that direct angioplasty is superior to thrombolytic therapy. The results of the Danish Multicenter Randomized Trial on Thrombolytic Therapy vs. Acute Coronary Angioplasty in Acute Myocardial Infarction (DANAMI-2) trial confirm these observations.

The DANAMI-2 trial
DANAMI-2 is the first large randomized control trial to compare the outcomes of treating ST-elevation MI with thrombolytic therapy vs. primary angioplasty (percutaneous coronary intervention [PCI]), with transfer via ambulance within three hours, to an invasive centre when necessary. The trial involved a total of 1,572 patients, 782 of which were randomized to thrombolytic therapy [100 mg of front-loaded tissue plasminogen activator (tPA)] and 790 to primary PCI. The median transport distance for patients presenting to local referral hospitals and randomized to PCI was 56 km, with the maximum transfer distance of 153 km.

Among the participants, 1,129 patients were randomized from referring hospitals to either thrombolytic therapy or direct angioplasty. Patients enrolled were at high risk. They all had ST-elevation on electrocardiogram (ECG) greater than 4 mm with symptoms lasting up to 12 hours from the onset of chest pain at the time of intervention. No upper age limit was set. Approximately 76% of patients were male and just over 50% of patients sustained anterior MIs in each group. The mean age was 63. Patients in cardiogenic shock were excluded.

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Results
The trial was stopped early due to superior outcomes in patients receiving primary PCI. Patients who received thrombolytic therapy with front-loaded tPA had their therapy started, on average at 160 minutes or within three hours of the onset of chest pain.

Those that underwent balloon angioplasty were treated approximately one hour later or 220 minutes from the onset of chest pain. A tremendous infrastructure was put in place, as patients were treated at the invasive centre. Of the 443 patients who originated from invasive centres, most came from outside centres, making up the vast majority of study participants. The extra time taken to get the artery open from transport time was short.

Important observations include a very low event rate in patients being transferred for direct angioplasty. Overall, few complications occurred during transfer. The complications included atrial fibrillation (2.5%), ventricular tachycardia (0.2%), ventricular fibrillation (1.4%), and second- or third-degree heart block (2.3%). There were no deaths and no patient required endotracheal intubation during transfer. Of those randomized to PCI, 99% underwent coronary angiography and 87% went on to receive PCI. A total of 93% of the patients who received primary angioplasty also received stent implantation. There was a low crossover rate in this study, with only 2.5% of patients randomized to thrombolytic therapy undergoing “salvage” angioplasty within the first 24 hours.

Conclusion
The primary end point of the study was the composite of all-cause mortality, reinfarction, or disabling stroke at six months of followup. The PCI treated patients demonstrated a 40% relative risk reduction in the primary composite end point (8.0 vs. 13.7%; \(P = 0.0003\)). While all individual components showed trends in favor of PCI, including death (6.6% vs. 7.6%; \(P = 0.35\)) and stroke (1.2% vs. 2.0%; \(P = 0.15\)), the difference in the composite end point was driven largely by the significant reduction in repeat MI (1.6% vs. 6.34%; \(P < 0.0001\)) in the patients receiving PCI.

Results were good in patients referred in from another institution as well as those who initially enrolled at these specialized centres. The number needed to treat was 18 patients to prevent one adverse event and 100 patients to be treated to save a life. There was a 1% absolute reduction in mortality, which has been hard to demonstrate in more recent trials dealing with acute ischemic syndromes.

Physician’s Perspective
This is a most impressive trial that clearly demonstrates direct angioplasty shows positive benefits compared to thrombolytic therapy if patients with large MIs can have PCI within and up to 12 hours from the onset of their chest pain.

However, what was not presented was extremely important. Patients presenting within 12 hours of onset of chest pain were eligible for the study if transport to the angioplasty suite could be accomplished within three hours. For example, one had up to 15 hours from the onset of chest pain to have the artery opened. What is clear is that within four to six hours from onset of chest pain, PCI was conducted in many patients. What is not known is where the window of opportunity lies and this important subgroup needs to be explored. This leads us to ask...
The question, within what time interval can direct angioplasty reap the best benefits? For instance, if a patient presents at six or eight hours post-onset at your institution, is there enough time and will the patient derive meaningful benefit from PCI? This will be reviewed in light of current studies at a later time.

The implications of this trial are huge. In our own institution, which does direct angioplasties especially after hours, opening up the Cath Lab usually takes at least an hour before the procedure is actually started. Transporting patients across the city and in our geographic location is difficult and our current infrastructure does not permit this to happen on a rapid basis.

The take-home messages are very clear. Patients with chest pain who are suspected of having acute ischemic syndromes must present to hospital early, for example, less than 30 minutes from the onset of chest pain. Patients should not call their physicians nor try to go to their offices. They need to call 9-1-1 or quickly have someone bring them to an emergency room, preferably one that does direct angioplasty.

Emergency rooms need to rapidly triage these patients and an ECG needs to be done within minutes of their presentation. Paramedics are now learning to do ECGs in the field and to interpret them. One may consider transporting patients to selective sites, based on the time from the onset of chest pain and their initial ECG. Physicians need to learn to screen and select patients who are having a large anterior MI, including those with a significant inferior-posterior MI. They should be considered for direct angioplasty.

We need to learn what the best time interval is and when it is too late to try and mobilize these precious resources.

We should not forget that thrombolytic therapy and acetylsalicylic acid (ASA), as well as beta blockers also save lives. Time is muscle. Door-to-needle times need to be steadily improved. Newer thrombolytic therapies allow easier use, administration and the possibility of treatment prior to arrival at the emergency room.

Each community should develop a plan of action. This will also include informing their patients about what is the best thing to do if they get chest pain. It is clear that with the Canadian perspective, the vast majority of patients with ST-elevation and infarction cannot be treated with direct angioplasty, nor should they be. However, patients with large MIs or those with hemodynamic compromise should have rapid access to direct angioplasty. Patients who are having a small MI that are doing well can best be treated with direct angioplasty or early use of thrombolytic therapy. This is, indeed, an exciting new discovery. However, more information from this trial is needed.

References