New strategies for reperfusion therapy

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PCI is the preferred strategy in acute myocardial infarction when performed by an experienced team as soon as possible after first medical contact.Time is essential: for P-PCI there is an 8 percent excess annual mortality for every 30 min delay.A STREAM trial currently underway looks to ascertain whether the best strategy for patients who cannot receive P-PCI is early fibrinolysis together with mandated angiography.

A new trial has begun in order to ascertain once and for all whether the best strategy for patients who cannot receive P-PCI is early fibrinolysis, together with mandated angiography. This is the STREAM trial whose principal investigators are Profs Frans van der Werf, Paul Armstrong and Tony Gershlick.

Acute occlusion of a major coronary artery due to disruption of an atheromatous plaque and the formation of occlusive thrombus has major clinical implications. At the moment of cessation of the blood flow, heart muscle cells start to die. We have known since the mid 1970s that as occlusion time progresses then the possibility of salvage of the myocardial cells diminishes. If significant proportions of the myocardium become irreversibly scarred then this has a major impact on the short medium and longer term prognosis - abnormal heart rhythms, heart failure and sudden death are all the consequence of significant myocardial damage due to irretrievably dying/dead heart muscle cells.

From the early days of treating acute myocardial infarction (now known as "ST segment elevation myocardial infarction"- or- "STEMI") with clot busting (fibrinolytic) drugs it has been clear that time is of the essence in

obtaining optimal reperfusion of the myocardium through dissolution of the clot formed within the coronary artery- the original GISSI studies showed there was benefit of these agents out to 6 hours, later extended to 12 hours following trials such as the "LATE study". Real world, one month mortality fell from ~18% pre fibrinolysis to 9-10% with the use of aspirin and fibrinolysis. In 2002 the European Heart Survey estimated the one month mortality at 8.4%. In the early and mid 1990s, and during an era when angioplasty was becoming increasingly used to treat fixed coronary atheromatous obstruction in patients with angina, angioplasty or PCI (percutaneous coronary intervention) become the subject of research trials to test whether this technique (Primary-PCI) could be used to treat both the clot and the underlying atheromatous narrowing and in many benchmark studies was compared with fibrinolysis. Better flow with P-PCI and treatment of the underlying lesion led to beneficial differences in outcome favouring P-PCI.

Evidence has led the ESC to suggest that P-PCI is the preferred strategy in acute myocardial infarction when performed by an experienced team as soon as possible after first medical contact. Since many patients present to hospitals without PCI facilities and since it can be difficult to establish a P-PCI service around the clock, great efforts have gone into establishing P-PCI optimally in Europe as the reperfusion strategy wherever possible, including the recently launched "Stent for life "project.

Just as time delay to reperfusion has long been established as being important for fibrinolysis, so it is with P-PCI. The Zwolle group have shown that for P-PCI there is an 8% excess annual mortality for every 30 min delay. Such delays are particularly pertinent when a patient presents to a non-PCI hospital and needs transfer for P-PCI. Further there is data to suggest that if the delay between when fibrinolysis can be given and P-PCI is delivered is greater than 100 mins or if the door to balloon time is > 90 mins then the benefits of P-PCI may be attenuated.

Indeed the ESC has recommended the maximum time delay should be from first medical contact to balloon as being no greater than 120 mins. The number of patients outside urban conurbations who can receive P-PCI within these time delays is a matter of contention but in rural areas this may reach 20-30% world-wide. The real research question currently being addressed is how best to manage such patients. The current consideration for such patients (who cannot receive P-PCI within the mandated time lines, and that requires robust testing, is early fibrinolysis (be it pre hospital or within 3 hours of symptoms in those presenting to hospital) together with rescue PCI for those who fail to reperfuse (as per the REACT trial) and angiography within 24- hours even for those who do reperfuse- this is the so-called "pharmaco-invasive strategy" A number of registries have shown that this strategy can be equivalent to P-PCI.

A large French registry, the FAST study, concluded: "When used early after the onset of symptoms, a pharmacoinvasive strategy that combines thrombolysis with a liberal use of PCI yields early and 1-year survival rates that are comparable to those of PPCI" (Danchin N et al Eur Heart J. 2009 Jul;30(13):1598-606).The German PREMIR registry concluded "In patients with STEMI already diagnosed in the prehospital phase the ischemic time is short, accuracy of the diagnosis is high and reperfusion therapy is performed in over 82%. In hospital mortality was not different between prehospital fibrinolysis and primary PCI (Zeymer U Resuscitation. 2009 80(4):402-406) and the CAPTIM trial (which compared pre hospital fibrinolysis with P-PCI has published its 5 year follow up and shown no difference between pre-hopsital lysis and P-PCI Bonnefoy E Eur Heart J. 2009 Jul;30(13):1598-606) Some aspects of this study required further clarification (Rescue and angiography rates) and so a further study has recently been initiated.

Thus to ascertain once and for all whether the best strategy for patients who cannot receive P-PCI is early fibrinolysis together with mandated

angiography the STREAM trial (PIs Frans van der Werf, Paul Armstrong , Tony Gershlick) is being undertaken. This world wide study has currently recruited ~400 patients/2000 and compares a strategy of early fibrinolysis with optimal adjunctive pharmaco-therapy together with rescue PCI for failed lysis and routine angiography for successful lysis (>4

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