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Early reperfusion treatment for ST-elevation myocardial infarction: national guidance

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Introduction

It is over 25 years since atheromatous plaque rupture and associated intracoronary thrombosis were identified as the pathophysiologies underlying acute coronary syndromes.[1] At that time the expected in-hospital mortality for ST-elevation myocardial infarction (STEMI) was around 20%, although this figure could be reduced to 17% by the use of coronary care units and prompt defibrillation.[2] Since then the morbidity and mortality associated with STEMI has fallen substantially, due to advances in pharmacotherapy (anti-platelets, antithrombins), the uptake of secondary prevention (beta blockers, angiotensin-converting enzyme inhibitors, statins), rehabilitation and lifestyle changes (smoking cessation, increased exercise, dietary changes) and the increasing emphasis on early coronary reperfusion, using thrombolysis or primary percutaneous intervention (pPCI). This editorial will focus on reperfusion.

'Time is muscle'

Thrombolytic agents were first given via the intracoronary route in the early 1980s and were shown to increase the likelihood of reperfusion in acutely thrombosed coronary arteries, but such administration was impractical, except under selected circumstances, because of the obvious logistical difficulties.[3] Attention turned to intravenous thrombolysis and numerous trials showed their benefit in reducing mortality.[4] The seminal ISIS-2 study showed that the mortality benefit of thrombolytics was still seen at 10 years.[5] These trials also highlighted the importance of time to treatment; mortality and myocardial damage increased with time delay, the most benefit was seen when thrombolysis was given within three hours of symptom onset, and outcomes were best when lytics were given within the first 'golden' hour.[6]

National Service Framework

In 2000, the Department of Health (DH) published a National Service Framework (NSF) aimed at improving the outcome of patients with coronary heart disease.[7] Targets were set for the timely delivery of thrombolysis to patients with STEMI, preferably given pre-hospital, and steadily improving performance was demonstrated in annual reports of the Myocardial Ischaemia National Audit Project (MINAP).[8]

However, a coronary reperfusion strategy based on thrombolysis is not without its problems; the risk of major bleeding and stroke is increased, about 30% of patients are unsuitable for lysis because of contraindications (such as recent surgery or bleeding risk etc), and around 25–40% of patients either fail to reperfuse or have early coronary re-occlusion or ischaemia. Throughout the 1990s a series of trials suggested that pPCI can produce superior outcomes to thrombolysis (less bleeding, fewer strokes, higher rates of successful reperfusion, better myocardial preservation and reduced mortality). Meta-analyses of pPCI (pPCI when used to treat STEMI) supported the superiority of pPCI over thrombolysis, even when transfer between hospitals was required.[9,10]

National Infarct Angioplasty Project

Following a review of reperfusion therapy for STEMI in 2003 the Prime Minister's Delivery Unit recommended that the DH develop a policy for expanding pPCI services. The DH, together with the British Cardiovascular Society and its affiliated specialist group the British Cardiovascular Intervention Society, established an observational study, the National Infarct Angioplasty Project (NIAP), to determine the advisability and feasibility of rolling out pPCI services nationally. Over 2,000 patients were recruited over one year by seven pilot sites in England, and were followed up for a subsequent year, with the results documented in two reports published in 2008.[11,12] The DH concluded that pPCI is the preferred reperfusion strategy for STEMI provided it can be delivered in a timely fashion, whatever time of day or night a patient presents, and that it is cost effective by National Institute for Health and Clinical Excellence criteria, particularly if patients are admitted directly to the catheter laboratory in a pPCI capable hospital.[13]

The delivery of pPCI nationally presents obvious challenges because of the need for 24-hour availability of interventional catheter laboratory staff and facilities, and rapid transport of patients to pPCI centres by ambulance services who could otherwise have potentially administered pre-hospital thrombolysis. The time interval between pPCI being delivered (the so called 'balloon time') and when thrombolysis might have been given is important because an excessive delay giving one reperfusion treatment in order to give a superior treatment later may worsen outcomes. All agree that the faster that coronary reperfusion can be achieved the better the outcome, but the magnitude of the treatment delay beyond which the advantages of pPCI over

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thrombolysis may be lost, remains uncertain, and it probably differs between patients depending on the site and severity of their infarct and their delay to presentation.[14–17] The NIAP report recommended that anticipated treatment delays should not exceed 90 minutes, and that pPCI services should be capable of delivering median call-to-balloon times of <120 minutes (the time from patient calling for help to coronary reperfusion being achieved by PCI) and door-to-balloon times <90 minutes (time from first arrival in hospital to PCI reperfusion), and that these times should be regularly audited to assure quality and promote improvement.

Where we are now

Emerging trial evidence, international guidelines, publication of *Mending hearts and brains* and NIAP reports by the DH have all contributed to a marked national shift from a lytic, to a pPCI-based reperfusion strategy for STEMI in England.[11,12,18,19] In 2009, more patients with STEMI in England and Wales were treated by pPCI than thrombolysis and in-hospital mortality for patients with STEMI treated by pPCI is now around 4–5%.[8] There has been a progressive decline in 30-day mortality for patients with STEMI (12.4% in 2003 to 9.6% in 2008)[8] which is most likely to be due to a combination of factors, including better reperfusion and pharmacological treatments, and the uptake of secondary prevention.

Where pPCI cannot be delivered in a timely fashion, as is the case in some remote areas, pre-hospital lysis is an acceptable alternative and preferred to in-hospital lysis. When lysis is used and there is failure of reperfusion, as judged by ST segment resolution being <50% at 90 minutes, patients should be considered for emergency PCI (which in this context is termed 'rescue PCI').[20] Those who do achieve adequate initial reperfusion by lysis should nevertheless undergo angiography within 24 hours, with a view to revascularisation (PCI or coronary bypass surgery) where appropriate.[21]

The future

The Darzi report *High quality care for all* highlighted the need to improve access to the most clinically and cost-effective treatments.[22] With the continuing support of strategic health authorities, cardiac networks and staff delivering acute cardiac services, it is envisaged that pPCI will become the reperfusion treatment for >90% of the population in England over the next two to three years. Regional planning has resulted in pPCI ('heart attack') centres being established and, as an example, the whole of the Greater London population now has access to pPCI as the preferred reperfusion strategy for STEMI. Obvious challenges face the geographically more remote parts of the UK, and pre-hospital thrombolysis is still likely to be needed in some areas. The place of adjunctive treatment with newer anti-platelets (such as prasugrel) and antithrombins (such as bivalirudin) is yet to be determined but a variety of agents have the potential to improve patient outcome still further.

The incidence of coronary heart disease is falling, but it is still the single most common cause of death in the UK. It varies nationally by region (reflecting inequalities), and compares unfavourably by international comparison.[23] There is still some way to go. Vascular checks in general practice, risk assessment in hospitals, appropriate intervention with primary and secondary prevention strategies, and the prompt management of acute coronary syndromes, will all hopefully build on past encouraging results.[24] However, before past success induces complacency it would be well to consider the potential consequences of the anticipated wave of diabetes, obesity and inactivity that may lead to STEMI, and other acute coronary syndromes, beginning to increase in incidence, particularly in a younger population.

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