Immediate angioplasty for the National Health Service?

In-hospital fatality from acute myocardial infarction remains high. Precisely how high depends on the way data are collected, and on what patients are included. While clinical trials of thrombolysis suggest that the case fatality rate should be around 7%, registry data suggest that the true “real world” rate (which includes many elderly patients) is much more like 20%. Gitt and Senges’ argue that the high death rate results from failure to use thrombolysis, and that as it will be difficult to improve on current thrombolysis rates the way forward is to increase the use of immediate, or primary, angioplasty. If this strategy is correct, the implications for the National Health Service are enormous. There is evidence that hospitals with a higher volume of angioplasty procedures show a lower fatality rate among patients undergoing primary angioplasty, and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines suggest that primary angioplasty should be considered as an alternative to thrombolysis “if performed in a timely fashion (balloon inflation within 90 minutes of admission) by individuals skilled in the procedure (more than 75 procedures per year) and supported by experienced personnel in a laboratory environment (centres performing more than 200 angioplasty procedures per year) that have cardiac surgical capabilities”. Before such facilities are made widely available in the UK we need to think very hard. We must not fall into the trap of assuming that because an “old” treatment is not producing the results we would like, the “new” one will be better.

The theoretical advantages of primary thrombolysis are clear. As well as providing reperfusion—and reperfusion rates are probably better with angioplasty than thrombolysis—angioplasty also deals with the underlying atheromatous plaque and therefore should improve long term outcome. While angioplasty has its own complications, some of these are prevented by the use of stents, and the great advantage of angioplasty is that unlike thrombolysis it does not increase the risk of intracerebral bleeding. However, the clinical trials directly comparing immediate angioplasty and thrombolysis in acute myocardial infarction have not given very clear results; the detailed results have been summarised elsewhere.

Trials of angioplasty versus thrombolysis

The early trials gave the best results: a trial of only 142 patients showed that immediate angioplasty was superior to thrombolysis in the preservation of left ventricular function and in the reduction of subsequent infarction and angina, and another involving 395 patients showed in-hospital fatality rates of 6.5% with tissue plasminogen activator (tPA) and 2.6% with angioplasty. Small trials that showed opposite effects received little attention. Some of the results were difficult to interpret because the findings did not “feel right”—for example, in a trial of supposedly low risk patients the rates at six months of death, non-fatal stroke, and reinfarction were 4% in patients treated with angioplasty but 20% in those treated by thrombolysis. The largest trial was a subset of the GUSTO II study where 1138 patients with myocardial infarction presented within 12 hours were randomly allocated to treatment with primary angioplasty or tPA. The death rates at 30 days were 5.7% and 7.0% respectively in the two treatment groups. The reinfarction rates were 4.5% and 6.5%, and the stroke rates were 0.2% and 0.8%. None of these differences was significant, but taken as a compound end point, angioplasty was associated with an event rate of 9.6% and thrombolysis with a rate of 13.7% (p = 0.033). At six months the difference in this combined end point was no longer significant (angioplasty 14.1%, thrombolysis 16.1%). A systematic review of all the trials suggested that with primary angioplasty the 30 day death rate after myocardial infarction was 4.4% compared with 6.5% among patients treated with thrombolysis, and the rate of death or non-fatal reinfarction was 7.2% compared with 11.9%. Angioplasty was associated with a lower stroke rate at 0.7% compared with 2.0%.

Claims have been made that angioplasty is particularly superior in certain patient subgroups. For example, angioplasty has been shown to reduce mortality at six months, but not at 30 days, in patients with cardiogenic shock. Subset analysis of this rather small (302 patients) trial suggested a major benefit in younger, but not older, patients. A registry of patients not randomised to the trial suggested limited benefit from angioplasty and another small trial showed no benefit.

So do these figures really suggest that direct angioplasty represents an advance over thrombolysis? Clinical trials seldom provide a definitive “evidence base” for practice because of the difficulty of relating their results to patients in the real world. Disease registers describe the “real world” and provide larger patient groups for the comparison of treatments than is possible with clinical trials, but their problem, of course, is that it is never certain whether there has been some systematic difference between treatment groups. Registers therefore have to be seen as an important addition to the evidence base, and must be viewed together with trial results. One has more confidence in the apparent benefit of a treatment when both trial and register evidence point the same way.

Lessons from registers

Lessons can be learnt from thrombolysis. The benefit of thrombolysis to an individual patient with an acute myocardial infarction is possibly not as great as some would like to think. Register data show that patients given thrombolysis outside the confines of a clinical trial have a higher fatality rate than those treated after randomisation within a trial; those not thrombolysed have the highest fatality of all. This suggests that the good results obtained in the trials are at least in part due to the selection of low risk patients. The higher fatality in patients not thrombolysed probably indicates an intrinsically higher risk, as much as a lack of
thrombolysis. The simplest explanation is age: the average age of patients in the thrombolytic trials is about 60 years, whereas the average age of patients admitted to a district general hospital (DGH) with a myocardial infarction is more like 70, and there is some evidence that thrombolysis is less effective in the elderly. A long term observational study in one large DGH in the UK during the 1980s and 1990s showed that the introduction of thrombolysis did not lead to any discernible reduction in hospital fatality, even though some lives were (presumably) saved.16

Register data do not support the superiority of immediate angioplasty over thrombolysis. A comparison of 1050 patients treated by angioplasty with 2095 treated by thrombolysis showed hospital fatality rates of 5.6% and 5.5% in the two groups.17 Another comparison of 4939 patients treated by angioplasty with 24 708 treated by thrombolysis showed in-hospital fatality rates of 5.2% and 5.4%, respectively, though there were less strokes (0.7% v 1.6%) among those treated by angioplasty.18 All these comparisons were, of course, made in patients in whom thrombolysis was an option but it would seem an unjustifiable leap of faith to suppose that immediate angioplasty should be routine in patients who could not be thrombolysed. This trial is waiting to be done. Providing facilities for primary angioplasty would be much more expensive than was the introduction of thrombolysis, and primary angioplasty needs to be subjected to detailed scrutiny before it is allowed to supplant thrombolysis.

So should we be planning for an increase use of immediate angioplasty for UK patients with acute myocardial infarction? In today’s National Health Service there is often a wait of nearly a year for a patient with unstable angina to have his or her symptoms relieved by angioplasty, and unstable patients with acute coronary syndromes can often wait a couple of weeks in a DGH before transfer to a regional centre for angioplasty. There are plenty of obstructions in our service that need dilating before we change our management of occluded arteries in acute myocardial infarction.

JOHN HAMPTON

Cardiovascular Medicine, Queen’s Medical Centre, Nottingham NG7 2UH, UK
John.Hampton@nottingham.ac.uk

STAMPS IN CARDIOLOGY

Conferences

The Third European Conference on Microcirculation was held in Jerusalem on 16 March 1964. Although no specific stamp was produced the illustrated first day cover was issued depicting the coronary vasculature. Cleverly constructed, the grey outline to the upper part of shape of the heart is a map of Europe.

M K DAVIES
A HOLLMAN