Primary coronary angioplasty in acute myocardial infarction

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Summary
It is well established that recanalisation of the infarct-related artery is of great benefit in the early hours after acute myocardial infarction. This can be achieved by the use of thrombolytic agents and/or by percutaneous transluminal coronary angioplasty (PTCA). This article reviews data on the role of primary PTCA and summarises current opinion on its use.

Keywords: percutaneous transluminal coronary angioplasty, myocardial infarction

Acute myocardial infarction: methods of recanalisation

- primary PTCA (direct)
- thrombolytic agent

with/without sequential PTCA

 - immediate (on completion of thrombolysis)
 - rescue (for failed thrombolysis after 1–2 h)
 - deferred (1–7 days post thrombolysis)
 - elective (> 1 week post-thrombolysis if continuing ischaemia)

Box 1

In 1980, De Wood *et al* first reported angiographic evidence of a high incidence of totally occluded or critically stenosed infarct-related arteries in the early hours of acute myocardial infarction.¹ Such findings prompted the use of intracoronary and later intravenous streptokinase therapy. It is now well established that after acute myocardial infarction, the earlier the infarct-related artery is recanalised, the greater the benefits to the patient – both in terms of reduced infarct size and improved survival.²

There are presently two methods of achieving recanalisation of the infarct-related artery. The first is the intravenous administration of a thrombolytic agent, resulting in the enzymatic degradation of the occlusive thrombus. The second is primary (or direct) percutaneous transluminal coronary angioplasty (PTCA). This contrasts with sequential PTCA, which may be performed at various times after thrombolytic therapy has been administered (box 1). After the promising results of early thrombolytic trials, there was considerable interest in sequential PTCA. It was observed that following successful thrombolytic recanalisation, a high-grade residual lesion was frequently observed and led Meyer *et al* to use PTCA after intracoronary streptokinase during the same sitting.³ This combination treatment was advocated as a means of avoiding reocclusion and recurrent ischaemia. The rationale for dealing with the flow-limiting potential of the residual plaque has led to many studies which have examined the need to proceed to PTCA at various times but there continue to be unresolved issues about optimal strategies for sequential PTCA and doubts about its efficacy. Results of the major randomised trials involving sequential PTCA have been reviewed elsewhere.⁴ However, primary PTCA may offer patients a better alternative to thrombolytic therapy, providing a superior mode of recanalisation.

The technique of coronary artery recanalisation by primary PTCA was introduced in 1983 by Hartzler *et al*⁵ and its potential advantages over thrombolytic therapy were recognised even in the early experience.^{5,6} Primary PTCA causes mechanical disruption of the occlusive thrombus and the underlying stenosis and results in a rapid restoration of coronary blood flow. Three years ago, three prospective randomised studies from The Netherlands⁷ and the US^{8,9} compared primary PTCA with intravenous streptokinase or tissue plasminogen activator (tPA). PTCA resulted in higher patency rates (93–98%), improved left ventricular ejection fractions,⁷ fewer bleeding complications and less recurrent myocardial ischaemia and re-infarction, than thrombolysis. A few centres in the US and Europe perform this technique routinely, but for logistic reasons it is uncommon practice in the UK.

Advantages of primary PTCA

Primary PTCA using a guidewire and balloon catheter has several advantages over conventional thrombolytic therapy (box 2). First, patency rates over 90% are obtained^{10,11} and TIMI grade III flow can be established in 95% of patients within two hours of hospital admission.¹² Our experiences have supported these findings. This is significantly greater than the optimal patency rate of 55% with intravenous streptokinase, the commonest thrombolytic agent in use in the UK.¹³ Restoration of antegrade coronary blood flow and normalisation of the electrocardiogram is not only more rapid but is also more predictable. The more rapid and greater success is due to dislodgement and mechanical disruption of thrombus as well as the reduction of the residual atheromatous stenosis, hence reducing the risks of recurrent ischaemia, reocclusion and reinfarction.¹⁴

More important than patency rate alone is coronary artery blood flow. In their prospective, randomised, multicentre study involving 395 patients, Grines *et al* not only achieved a patency rate of 99% with primary PTCA, but also achieved a TIMI grade III flow in 95%.⁸ In contrast, the GUSTO study patency

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Figure 1 (Left) Angiographic appearance of a totally occluded right coronary artery in a 64-year-old woman with a 2-hour history of acute inferior myocardial infarction and (right) the same artery following primary PTCA recanalisation. Note that the residual plaque-related stenosis has been alleviated, resulted in a widely patent artery and brisk antegrade flow

Figure 2 (Left) Left coronary arteriogram in a 49-year-old woman with a 90-minute history of acute anterior myocardial infarction and hypotension. The proximal left anterior descending artery is totally occluded. (Right) Following re-opening of the left anterior descending artery by primary PTCA there was a dramatic haemodynamic improvement in left ventricular function

Advantages of primary PTCA
<ul style="list-style-type: none">● patency rates > 90%● more rapid restoration of TIMI III coronary blood flow● more rapid normalisation of the ECG● less post-infarction angina, re-infarction and exercise-induced ischaemia● no systemic fibrinolysis – avoids bleeding complications● reduces infarct size and improves residual left ventricular function● angiography may improve risk stratification● comparable cost to thrombolytic therapy

Box 2

rate was 81% in the front-loaded tPA arm, although TIMI grade III flow was achieved in only 54%.¹⁵ Furthermore, the GUSTO angiographic substudy demonstrated that in-hospital survival was directly related to the ability to achieve a patent infarct-related vessel with TIMI grade III flow.¹⁶ Figures 1 – 3 are examples of the excellent angiographic result that is frequently achieved by primary PTCA within minutes of entering the catheter suite.

Since systemic fibrinolysis is avoided, the likelihood of bleeding complications as well as intra-plaque and intra-myocardial haemorrhage is reduced.^{17,18} If necessary, residual intracoronary thrombus can be simultaneously and effectively treated with small doses of clot-specific thrombolytic drugs administered directly down the relevant vessel. Primary PTCA can also be performed successfully when thrombolytic therapy is contraindicated due to a high risk of bleeding or an adverse haemodynamic state such as cardiogenic shock.^{19,20} It is probably the treatment of choice for achieving rapid reperfusion in such high-risk subsets.²¹

Primary PTCA leads to a reduction in infarct size and improved left ventricular function when compared to streptokinase therapy, with the most pronounced benefits in those with anterior myocardial infarction presenting within two hours after the onset of symptoms.²² These impressive results are presumably due to a rapid and effective restoration of blood flow to jeopardised myocardium. In addition to less frequent recurrent myocardial ischaemia and

Figure 3 (Left) Angiographic appearance of a totally occluded left circumflex artery in a 69-year-old man with a 3-hour history of acute inferolateral myocardial infarction and (right) following successful primary PTCA recanalisation showing a large and dominant distal vessel

reinfarction, the need for early additional revascularisation and in-hospital mortality is less than in patients treated with intravenous thrombolytic therapy. Brodie *et al* have shown that after primary PTCA, patency of the infarct-related artery is the most important determinant of hospital survival and that left ventricular function measured after recovery is the most important determinant of late cardiac survival.²³ The beneficial effects of primary PTCA have also been shown to be sustained up to 36 months after discharge^{22,24} although as many as 28% may require a repeat PTCA for restenosis.

Concern about the potential increased cost of primary PTCA has been examined by two studies^{9,25} which have found that although the expense involved in the interventional equipment was considerably greater than thrombolytic therapy, this was offset by a significantly shorter in-hospital period, fewer re-admissions and reduced follow-up costs. Both these studies were carried out in the US and used tPA which is much more expensive than streptokinase. It was argued that, in the UK, where streptokinase is the commonest thrombolytic agent in use, this would negate the reduction in overall cost attributed to PTCA. However, in a recent study from The Netherlands using intravenous streptokinase, a comparable cost difference was observed.²² They concluded that additional cost savings in primary PTCA patients could be expected during longer term follow-up.

Over and above these benefits the necessary immediate coronary angiography provides crucial information for treatment stratification. Those patients with significant left main coronary artery stenosis, severe three-vessel coronary artery disease or occluded vessels unsuitable for PTCA can be referred for by-pass surgery. Conversely, those with a patent or insignificant infarct-related vessel may be selected for medical treatment rather than unnecessary thrombolytic therapy.

Disadvantages of primary PTCA

Although there are overwhelming advantages to primary PTCA, there are also drawbacks (box 3). Some are consequent to the nature of the procedure

Disadvantages of primary PTCA
<ul style="list-style-type: none">• can only be performed when cardiac catheterisation facilities, experienced staff and surgical cover available• high capital and running cost of catheter lab• risks/complications of catheterisation and PTCA present• reperfusion arrhythmias common (may be due to more rapid recanalisation)• primary PTCA more rapid than thrombolysis only if 24 h on-call team available

Box 3

whilst others are major resource and manpower issues. Clearly, the procedure can only be performed when cardiac catheterisation facilities, staff, and experienced operators are available. Cardiac catheter facilities require a high initial capital expenditure as well as generating significant running costs. A 24-hour on-call team and an open, available laboratory are necessary if coronary recanalisation by PTCA is to be more rapid than by thrombolysis. Herein lie the major logistical difficulties in the UK. In our centre, where catheter laboratory staff are on call from home, the average time from admission to re-opening of the infarct-related artery by PTCA may be in the order of 60 minutes.

Complications include those of cardiac catheterisation and PTCA which are slightly more frequent than after elective PTCA for chronic angina. Procedures can be simple and short in duration (<20 min) or complex and prolonged affairs (>2 hours). Ventricular arrhythmias not uncommonly occur shortly after reperfusion, although these can be promptly treated. Right coronary artery procedures are more often troublesome than those in the left and are more often associated with sinus arrest, atrioventricular block, idioventricular rhythm and severe hypotension.^{26,27} Primary PTCA, like elective PTCA, is associated with operator-dependent morbidity and mortality that varies with the skill and experience of the interventional cardiologist.^{22,28} It should only be considered in patients presenting early and when an experienced angioplasty team is available. Cardiac surgical back-up is essential and mechanical support techniques such as intra-aortic balloon counterpulsation should be available for use if risks are to be minimised.

Is patient selection essential?

Unless cases are carefully selected, many patients who are unsuitable for PTCA may undergo angiography. However, this does not preclude them from receiving thrombolytic therapy as an alternative and angiography may help improve their risk stratification and identify appropriate patients who require emergency coronary artery by-pass surgery.

Although not contraindicated, patients with previous myocardial infarction(s), a long history of angina, previous coronary artery by-pass grafting and proven multi-vessel or diffuse coronary disease, are often technically unattractive prospects for primary PTCA. However, even here direct PTCA may be shown to have a greater benefit than thrombolytic therapy if undue time delays to treatment can be avoided. Primary PTCA offers a clear additional benefit over thrombolytic therapy in elderly patients (>65 years), who may be at greater risk from the effects of recurrent ischaemia and re-infarction.²⁹ Moreover, the increased haemorrhagic complications (in particular intracranial bleeding) from thrombolysis are also avoided.

A number of retrospective studies have been carried out to determine the impact of primary PTCA on myocardial function and to identify subsets of patients who are most likely to benefit.^{10,28,30,31} In a study involving 250 patients, Kahn *et al*²⁸ achieved excellent patency rates in excess of 90%, an in-hospital re-occlusion rate of less than 10% and an acceptable hospital mortality of 5%. Infarct patients ineligible for thrombolytic therapy, and those with left anterior descending coronary artery occlusions who were at highest risk of cardiogenic shock and death, were particularly likely to benefit from primary PTCA. The most impressive results are seen in patients with single vessel disease, when a recanalisation rate of 99%, an in-hospital death rate of 1% and urgent coronary artery by-pass grafting rate of <0.5% can be expected.³²

Primary PTCA has also been shown to be of great value in patients with previous coronary artery by-pass grafting³³ and in the elderly,³⁴ and can be performed in patients with hypotension and cardiogenic shock. This latter condition, which has an approximate incidence of 10%,³⁵ is associated with a grave prognosis despite thrombolytic therapy due to the low frequency of recanalisation.³⁶ Primary PTCA has been found to offer a survival advantage in this group of patients.^{21,37,38} In our limited experience, however, it would seem to offer little to those with established cardiogenic shock, late (>6 hours) after extensive infarction.

Conclusions

Evidence is now accumulating that, in experienced hands, primary PTCA is the most effective treatment for acute myocardial infarction.⁷⁻⁹ However, there remain many questions which need to be answered. Perhaps the most important is whether the clinical advantages of primary PTCA over intravenous therapy are sufficient to justify the huge capital outlay and running costs which would be

Learning points

- primary PTCA involves direct recanalisation of an occluded coronary artery by balloon dilatation in a patient presenting with an acute cardiac infarct
- compared to intravenous thrombolytic therapy
 - TIMI grade III flow can be established in 95% of patients (55% for thrombolysis)
 - systemic fibrinolysis and bleeding complications are avoided
 - infarct size, recurrent myocardial ischaemia and reinfarction and the need for early additional revascularisation are less
 - in-hospital mortality is lower and left ventricular function is better
- certain subsets of patients are more likely to benefit from primary PTCA, eg, cardiogenic shock, contraindications to thrombolysis
- a primary PTCA programme is logistically demanding and expensive and requires experienced staff and facilities available on a 24-hour basis plus cardiac surgical support

required to provide a 24-hour nationwide service. No less important is whether it should be offered to all patients; should there be an age or time limit, and when, where and who should perform the procedure? Would other interventional devices, in particular intracoronary stents, prove to be of additional value and can we afford to use them? Despite the evidence favouring primary PTCA, there has been little effort to answer these questions. There is currently a lack of enthusiasm for primary PTCA amongst cardiologists, not only because of the spectre of an overwhelming increase in workload – often at extremely unsociable hours, but also because of the lack of staff and facilities to support such a programme. In the UK, a working party is needed to address the medical, social and financial implications of a nationwide service for primary PTCA, otherwise this effective, but logistically complex form of treatment, will continue to be offered only to a select group of patients, and denied to the majority.

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