Heart disease in older patients: myocardial infarction

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Abstract

Almost a half of all myocardial infarctions occur in those over 70 years of age and this is projected to rise further as the number of older patients in the total population increases. Following myocardial infarction, complications are more common in the older patient and the mortality outlook is much worse in those aged over 75 years. Guidelines generally favour the administration of thrombolysis post-myocardial infarction to older patients, although there is a lack of randomised clinical trials with thrombolysis in this group. Observational data, however, suggest that there is a significantly increased risk of mortality in patients aged over 75 years and this means the elderly are less likely to receive thrombolytic therapy, even when no contraindications are present. Randomised trials have shown that percutaneous coronary intervention is associated with a better outcome in the older patient. With the advances in antiplatelet therapy and the advent of intracoronary stents, this outcome is expected to improve further. The article also discusses therapeutic options in secondary prevention.

Key words: older patient, coronary heart disease, myocardial infarction, thrombolysis, percutaneous coronary intervention.

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Introduction

Myocardial infarction (MI) is a disease of the elderly. While the incidence of MI in the general population is in decline, the number of older patients presenting with their first MI is increasing. Nearly one half of all MIs occur in those aged over 70 years,[1] and the mean age of patients with MI continues to rise. The proportion of older patients in the total population is projected to rise greatly resulting in further increases in these numbers. The proposed redefinition of MI[2] – which depends on much more sensitive cardiac markers than the enzymes of traditional definitions – will also result in a significant increase in the incidence of MI in both the general and elderly populations.

Equally importantly, older patients have a much poorer outlook following MI, with increasing age recognised as an independent predictor of outcome.[3] The mortality rate for those aged over 75 years is almost 10 times higher than that for patients aged under 65 years.[4] Indeed 80% of all deaths due to MI occur in those aged over 75 years.[5] In addition, complications of MI including left ventricular failure, reinfarction, arrhythmia and stroke, are all more common in older patients.[6] There are other important differences between older and younger patients with MI. Smoking and hypercholesterolaemia are less prevalent, co-morbidity including contraindications to thrombolysis is much greater, and women account for a greater proportion of patients.[7] In addition, non-ST elevation MIs are more common,[8] as are silent,[9] atypical[9] and late[10] presentations.

Treatment of ST elevation myocardial infarction

Patients presenting with chest pain and ST segment elevation or new left bundle branch block require reperfusion therapy either by intravenous thrombolytic therapy or percutaneous coronary intervention (PCI). When thrombolytic treatment does not result in reperfusion, rescue PCI should be performed. Access to primary and rescue PCI is, however, limited in the UK.

Table 1 shows contraindications to fibrinolytic therapy; patients aged 65 years or over are more likely to have contraindications to this therapy.[11] Those who do undergo thrombolysis benefit less than younger patients, with a relative risk reduction in mortality of 13% compared to 21% for younger patients.[12] However, because more elderly patients die following MI, the absolute benefit of thrombolysis in MI is suggested to be similar to younger patients. In addition, there is a significantly higher complication rate associated with thrombolytic therapy in the elderly, especially intracerebral haemorrhage.[13] A greater risk of ventricular rupture in older patients receiving thrombolysis has also been reported.[14] As a result of these facts, the elderly are less likely to receive thrombolytic therapy even when no contraindications are present.[15]

Eligible patients with MI aged between 65 and 74 years have been shown in clinical trials to clearly benefit from thrombolysis, with 35-day mortality reduced from 16.1% in the control group to 13.5% in the group receiving a fibrinolytic agent. This translates into 27 lives saved per 1,000 patients treated, which is greater than the benefits in patients < 65 years.[12] The picture, however, is much less clear in those aged 75 years or more. No randomised controlled studies focussing specifically on these patients have been performed. One randomised study from several years ago was

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Table 1. Contraindications to fibrinolytic therapy (European Society of Cardiology)

Absolute contraindications
Haemorrhagic stroke or stroke of unknown origin at any time
Ischaemic stroke in preceding six months
Central nervous system damage or neoplasms
Recent major trauma/surgery/head injury (within preceding three weeks)
Gastro-intestinal bleeding within the last month
Known bleeding disorder
Aortic dissection

Relative contraindications
Transient ischaemic attack in preceding six months
Oral anticoagulant therapy
Pregnancy or within one week post-partum
Non-compressible punctures
Traumatic resuscitation
Refractory hypertension (systolic blood pressure > 180 mmHg)
Advanced liver disease
Infective endocarditis
Active peptic ulcer

Table 2. Absolute differences in 35-day mortality[12]

Age (years)	Fibrinolytic patients	Control patients	Fibrinolytic deaths (%)	Control deaths (%)	Benefit per 1,000 (SD)
<55	8,082	8,158	278 (3.4)	373 (4.6)	11 (3)
55–64	9,911	9,678	709 (7.2)	864 (8.9)	18 (4)
65–74	8,487	8,496	1,144 (13.5)	1,372 (16.1)	27 (5)
75+	2,835	2,953	689 (24.3)	748 (25.3)	10 (13)

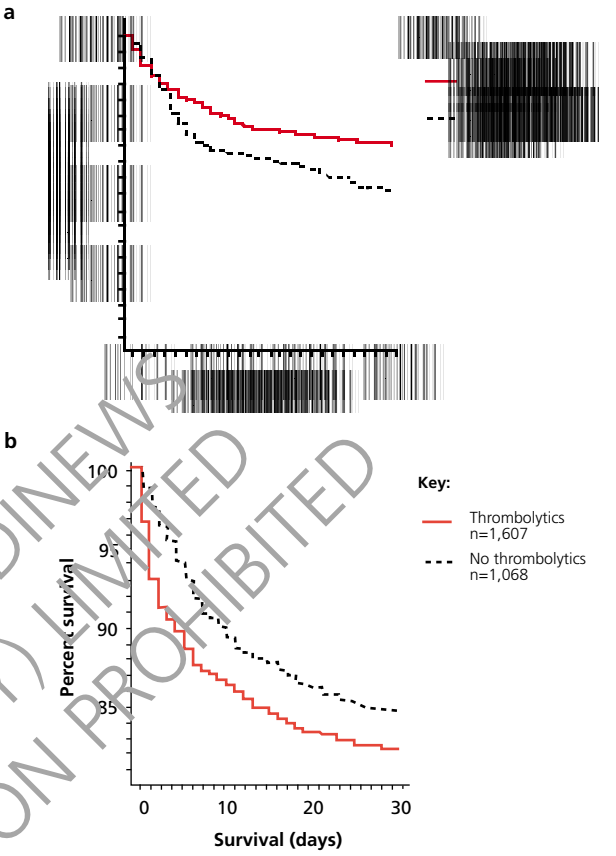


Figure 1. Crude 30-day Kaplan–Meier survival curves by age cohort and thrombolytic use.[17] **a)** shows the survival curves in the 65–75 years cohort. **b)** shows the survival curves in the 76–86 years cohort

aborted because physicians were unwilling to randomise patients to non-thrombolytic therapy. Subgroup analysis of the Global Utilisation of Streptokinase and t-PA for Occluded coronary arteries-I (GUSTO-I) study did suggest a benefit from thrombolysis in those aged over 75 years although this was not statistically significant.[16] A meta-analysis of the large randomised trials of thrombolytic therapy reported a small absolute risk reduction of 1%, although this also was not statistically significant.[12] Some of the trials making up this analysis specifically excluded patients in this age group, and, in the other trials, those aged 75 years or over with MI were under-represented. As a result, older patients accounted for only 10% of the study population compared to 30% of all MI patients. In addition, 40% of patients in these trials did not receive aspirin, now established best practice, making it difficult to reliably extrapolate the results to current practice. The absolute reductions in 35-day mortality from thrombolysis in various age groups reported in this analysis are shown in table 2.

This paucity of evidence from randomised trials is compounded by the results of observational studies suggesting a significantly increased risk of mortality in those aged over 75 years.[17] The results of this study, including the contrasting benefits of thrombolysis in those aged between 65 and 75 years, are shown in figure 1. In another study patients > 75 years receiving thrombolysis had a mortality rate more than one and a half times higher than the non-thrombolysed group.[18] This was partly as a result of approximately one in seven of the thrombolysed patients having a contraindication. When the analysis was repeated after excluding these patients, there was no significant difference between the risks of mortality in the thrombolysed and non-thrombolysed groups. These studies have also estimated an annual increase in risk of between 5.6%[17] and 8%[18] from thrombolysis with increasing age, with a neutral mortality benefit at the age of 74.3 years.

There is thus a little evidence indicating a small benefit from thrombolysis in patients aged over 75 years, while observational studies suggest the opposite. Randomised, controlled studies are rightly regarded as providing a higher quality of evidence than observational studies, although the latter do have the advantage of reflecting everyday clinical practice. This is borne out by the incidence of patients in the observational studies receiving thrombolysis despite contraindications. The under representation of older patients in the randomised studies is likely to be a reflection of selection bias resulting in a tendency to enrol only healthier older

Table 3. Fibrinolytic therapy guidelines for patients aged over 75 years

British Cardiac Society	'Age is not in itself a contraindication to thrombolysis'[19]
European Society of Cardiology	Recommended for all eligible patients[20]
American College of Cardiology/American Heart Association	Class IIa recommendation (weight of evidence and expert opinion in favour but conflicting evidence and divergence of opinion exists)[21]

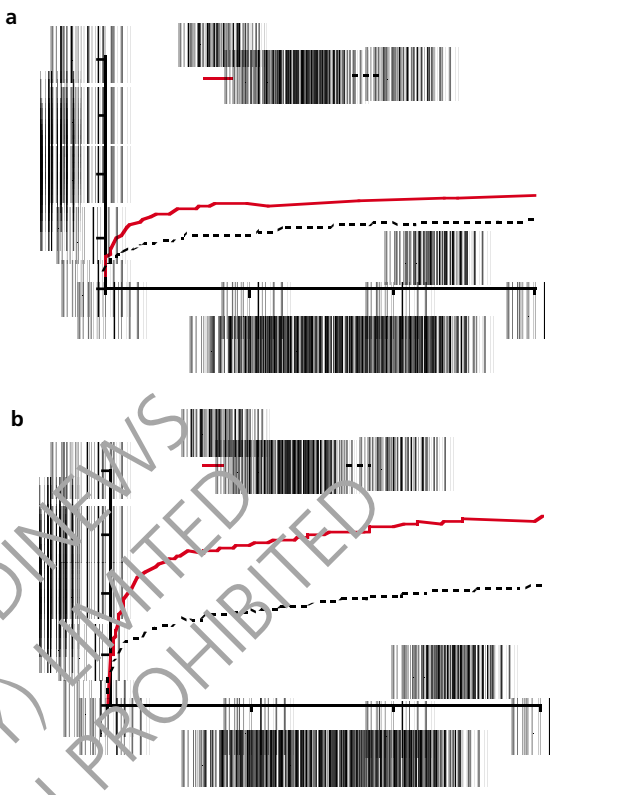
patients. It seems very likely that predictors of outcome other than recognised contraindications exist explaining the discrepancy between the randomised trials and the observational studies.

The uncertainty of benefit of thrombolysis for elderly patients is only partly reflected in national and international guidelines, which generally favour the use of fibrinolytic therapy in this group, perhaps recognising that lack of evidence of benefit is not the same as evidence of lack of benefit (table 3). British Cardiac Society guidelines state that 'age is not in itself a contraindication to thrombolysis'.[19] Recently published European Society of Cardiology guidelines go further, recommending the administration of thrombolysis to all eligible patients aged over 75 years.[20] Current American College of Cardiology/American Heart Association practice guidelines, by contrast, assign a class IIa designation to the recommendation for use of thrombolytic therapy in persons older than 75 years.[21] This indicates their belief that while the weight of evidence and expert opinion is in favour of the usefulness of treatment, there remains conflicting evidence or a divergence of opinion about whether the treatment is beneficial, useful and effective. Randomised trials focussing specifically on those > 75 years would provide considerable clarification but are not likely to be performed. Perhaps the best strategy to adopt is to treat each case individually by endeavouring to rigidly exclude any contraindications, and then consider thrombolysis in those with potentially the greatest benefit such as patients presenting with anterior infarction within 4–6 hours of the onset of pain.

Thrombolysis versus percutaneous coronary intervention

An alternative reperfusion strategy to fibrinolytic therapy is primary PCI. PCI is better at restoring patency in the infarct-related artery than thrombolysis[22] and has been shown to significantly reduce mortality, reinfarction and recurrent ischaemia compared to treatment with the fibrinolytic tissue-type plasminogen activator.[23] The greatest reductions were demonstrated in those aged 65 years or more. Similar results were recently reported in a re-analysis of the six-month outcomes in 11 randomised trials of early primary angioplasty versus thrombolysis, which demonstrated a 27% proportional risk reduction in mortality, and a 54% reduction in the relative risk of MI.[24] These results are illustrated in figure 2. A proportion of these trials had upper age limits of either 75 or 79 years. The absolute benefits were greater in high-risk groups including the elderly. In this analysis, for every eight patients over 70 years treated with primary PCI instead of thrombolysis, one death or MI was prevented, demonstrating a clear benefit of primary PCI in the elderly.

Figure 2. Time-to-event analysis for patients undergoing percutaneous transluminal coronary angioplasty (PTCA) or thrombolysis for **a)** mortality and **b)** death plus myocardial infarction (MI)[24]



None of the patients in the randomised trials comparing PCI with thrombolysis were treated with intracoronary stents which are associated with better outcomes than balloon angioplasty.[25] In addition there have been significant advances in antiplatelet therapies, including the use of glycoprotein IIb/IIIa inhibitors. By contrast, there have been few changes to thrombolytic treatment over this time; the relative advantages of PCI discussed above are likely to underestimate the current picture in clinical practice. The increasing availability of drug-eluting stents will result in even better results from PCI. Operator experience, however, is more important in PCI than thrombolysis, and availability of PCI varies greatly. PCI at present has only limited availability in the UK while in the Mayo Clinic, US, for example, PCI is always preferred to thrombolysis for the treatment of MI in older and younger patients alike.

Treatment of acute coronary syndromes without ST segment elevation

Acute coronary syndromes without ST segment elevation encompass non-ST elevation MIs and unstable angina. Elevations of sensitive markers of myocardial necrosis, such as cardiac troponins, in these syndromes are well recognised as predicting an adverse outcome.[26] This has resulted in a proposed redefinition of MI.[2] In com-

mon with the trials of fibrinolytic therapy in ST elevation MI, the elderly are excluded or under-represented in randomised trials of treatment of acute coronary syndromes without ST segment elevation. The management of acute coronary syndromes in older patients, including the benefits of early invasive strategies, will be considered in a forthcoming review article in this series.

Secondary prevention

Randomised trials[27] and observational studies[28] have shown that aspirin administered to patients following MI reduces the risk of recurrent MI, irrespective of age. Clopidogrel is an effective alternative antiplatelet agent when patients are intolerant of aspirin.[29] Older patients, however, are less likely to receive these treatments.[30] Similarly beta blockers are underused in the elderly,[31] despite the demonstration of greater mortality reductions following MI.[32] Angiotensin-converting enzyme (ACE) inhibitors have been shown to improve survival following MI in older patients with a low ejection fraction[33] and congestive heart failure (CHF).[34] The Heart Outcomes Prevention Evaluation (HOPE) study extended the benefits of ACE inhibitors by showing a significantly improved outcome in relatively elderly high-risk patients without CHF or a known decreased ejection fraction treated with ramipril.[35] Aspirin (or clopidogrel when aspirin intolerant) and beta blockers should therefore be prescribed to older patients following MI. ACE inhibitors should also be prescribed to patients with CHF or a decreased ejection fraction, and possibly to all patients following MI.

In the Framingham Study, serum total cholesterol was the strongest predictor of death from coronary heart disease and of all-cause mortality among patients aged 65 years or older with a previous MI.[36] It is now well established that lowering cholesterol with HMG-CoA reductase inhibitors ('statins') reduces coronary mortality and morbidity in patients with coronary artery disease.[37,38] Until recently, however, there was only limited evidence about the effects of such treatment in some groups of high-risk patients including the elderly. This is no longer the case following the recently published Heart Protection Study[39] which showed an 18% relative and 2.8% absolute risk reduction with 40 mg of simvastatin compared to placebo, with equal benefits in both those aged under or over 70 years. The results were similar in the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) trial, with a 19% relative risk reduction of death or non-fatal MI in high-risk patients aged 70 years or more treated with 40 mg of pravastatin.[40] Despite these results, very few elderly patients are prescribed statins, with only 16% of patients with coronary heart disease aged > 65 years in the Healthwise study receiving these life saving drugs,[41] and this must be addressed.

Lifestyle changes to control coronary risk factors are also important. Rehabilitation aimed at restoring the patient to as full a life as possible should start as soon as possible after hospital admission, and be continued in the succeeding weeks and months. This has been shown to reduce mortality.[42] Cigarette smoking is recognised as a risk factor for further coronary events in older persons, with those aged 70 years or older who continue to smoke having up to three times the relative risk of death or further infarction than those who quit.[43] On this basis older patients who continue to smoke following MI should be encouraged strongly to stop. Antihypertensive drugs have been shown to reduce new coronary events in older patients with hypertension.[44] The goal of therapy should be to decrease the blood pressure to less than 140/90 mmHg. Weight reduction in the obese, and moderate exercise should also be encouraged in older patients following MI.

Key messages

- The outcome of myocardial infarction is worse in the older patient
- Older patients are less likely to be given beneficial treatments although, with the possible exception of thrombolysis in the very elderly, they are as likely to benefit from these as much as a younger patient. This problem needs to be addressed
- Percutaneous coronary intervention is associated with a better outcome post-myocardial infarction than thrombolysis in the older patient
- Aspirin (or clopidogrel) and beta blockers should be prescribed to older patients; ACE inhibitors are also beneficial in many patients

Conclusions

The majority of MIs occur in older patients. They fare poorly in comparison to their younger counterparts. Furthermore, the number of elderly patients with MI continues to rise. Despite this, older patients are poorly represented in existing clinical trials. In most cases, the available evidence suggests that benefits from treatments recognised as effective in the general population are at least as valuable in older patients. At present the elderly do not receive these benefits and this needs to be addressed urgently. The possible exception is thrombolytic therapy for those older than 75 years. While data about the benefits of PCI in the very elderly is also minimal, early PCI, when available, is likely to be the preferred option. When we ourselves are admitted in later life (or indeed sooner) with an MI, would we choose PCI ahead of thrombolysis? Oh yes!

Editors' note

This is the second article in our series on heart disease in older patients. The first article 'The future of cardiology – heart disease in older patients' was published in the last issue (*Br J Cardiol* 2003;**10**:45–8).

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