Myocardial infarction in the elderly

RSK Lo, J Woo

Older people are more at risk of acute myocardial infarction, and suffer a higher morbidity and mortality. With a rapidly ageing population, there will be an increasing number of elderly patients presenting with acute myocardial infarction. In the past, the elderly have been undertreated, partly due to an erroneous impression that they cannot tolerate active treatment. However, evidence is accumulating that the older age group can derive significant benefit from thrombolysis, cardiological interventions, secondary prevention, and rehabilitation. This article reviews the latest literature on the various treatments available for acute myocardial infarction, concentrating on the proven benefits for the older age group.

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The elderly population is expected to increase dramatically over the next 40 years.[1] In Hong Kong, there is expected to be a 50% increase in the sector of the population older than 75 years by the middle of the twenty-first century.[2] As the risk of ischaemic heart disease increases with age, there will be an increasing proportion of older patients presenting with myocardial infarction. More importantly, morbidity and mortality are much higher for the older age group. The Worcester Heart Attack Study showed that 80% of deaths from myocardial infarction occurred in those older than 65.[3] Similarly, the Second International Study in Infarct Survival (ISIS 2) demonstrated that the 35-day mortality for acute myocardial infarction (AMI) was 24% for those older than 75 years, compared with only 6.2% for those younger than 60.[4] The Royal College of Physicians of London published a report in 1991 which recommended a more active approach in the investigation and treatment of cardiac diseases in the older age group.[5]

Department of Medicine and Geriatrics, Shatin Hospital, Shatin, Hong Kong
RSK Lo, MRCP, Dip Ger Med RCP (Glasgow)
Department of Medicine, Prince of Wales Hospital, Shatin, Hong Kong
J Woo, MD, FRCP
Correspondence to: Dr RSK Lo

However "rationing of care by age" still exists internationally,[6-8] and the improvement in AMI mortality seen in recent years has not been realised in the older age group.[9] This may be due to a general shortage of cardiac resources, with the result that older patients often lose out to the young. A second reason is the erroneous impression that older patients have little to gain from active treatment.[10] However, there is increasing evidence that as the elderly are at a higher risk, they have more to benefit from current treatment of AMI. This has important implications locally in Hong Kong, as we have a high prevalence of ischaemic heart disease in the older age group.[11] This article will review the latest literature regarding the management and secondary prevention of myocardial infarction, illustrating the numerous important benefits which older patients can obtain.

Difficulties in diagnosing acute myocardial infarction in the elderly

Diagnosing AMI in the elderly is often a challenge. As with other diseases in the older age group, classical symptoms and signs may be absent on presentation. Data from the Myocardial Infarction Treatment Intervention (MITI) group showed that 42% of those older than 75 with AMI did not experience any chest pain, compared with 25% of those younger than 75; a difference statistically significant at $P<0.0001$.[7] As this group can present in other ways, a high level of awareness is mandatory. Furthermore, the typical ST changes

on electrocardiogram (ECG) are often initially lacking.[12] This might be due to a higher incidence of old myocardial infarction, left ventricular hypertrophy and strain, or conduction abnormalities such as bundle branch block. Frequent repeat of ECG, together with a 24-hour cardiac enzyme service, would help establish diagnoses earlier in difficult cases. Prompt diagnosis is obviously essential, if the opportunity for thrombolysis is not to be missed. This is especially true for the older patients, who may have already suffered a longer pre-hospital delay.[13]

Thrombolysis in the elderly

Early thrombolysis trials excluded elderly patients.[14] Some authors even suggested that patients over 75 years of age should not receive thrombolytic therapy.[15] It is becoming increasingly apparent that age does not prevent the favourable effects of early thrombolysis. A combined analysis of five large thrombolysis trials demonstrated that elderly patients treated with thrombolysis had a lower mortality of 18%, compared with a higher incidence of 22% in control patients, a statistically significant difference ($P<0.0001$).[16] Krumholz also demonstrated that age alone should not contraindicate the use of streptokinase, and thrombolytic therapy is cost-effective with a survival benefit in the elderly, using a decision analytic model that incorporated estimates of risks and benefits in various clinical circumstances.[17]

Thrombolysis achieves a greater reduction in absolute mortality in the older age group than in the young, as can be seen from the results of major thrombolytic trials.[4,18-20] The ISIS 2 results suggested that for every 100 patients aged 70 years or older treated with aspirin and thrombolysis, eight lives can be saved compared with 2½ lives in a similar number of patients younger than 60 years of age.[4] It is very important to realise that for the same relative risk reduction, the absolute impact and benefit will be greater in the elderly due to their higher mortality if left untreated (Table 1).

Contrary to common belief, contraindications played only a small role in influencing the use of thrombolysis in the elderly.[21] Indeed, a patient 110 years of age received streptokinase, heparin, and aspirin, and was alive after one year of follow up.[22] Despite the clear evidence of benefit from thrombolysis, aged patients are still undertreated. One study in Britain found that 40% of coronary care units surveyed refused to give thrombolysis to older people because of age alone.[6] In the MITI study, Weaver found that only 5% of those older than 75 received thrombolysis compared with 39% of those younger than 55.[7]

Coronary angiogram and angioplasty in the elderly

Initially, in the 1980s, early studies quoted a lower clinical success rate for angioplasty in the older age group.[23]

Table 1. Comparison of relative and absolute risk reduction for short term mortality in thrombolytic trials according to age

Trial	Age (y)	Total no.	Mortality treated (%)	Mortality placebo (%)	Relative risk reduction (%)	Absolute risk reduction (%)
GISSI[18]	<=65	7608	5.7	7.7	26.0	2.0
	66-75	2886	16.6	18.1	8.3	2.0
	>75	1215	28.9	33.1	12.7	4.2
AIMS[19]	<65	816	5.2	8.5	38.8	3.3
	65-70	176	12.2	30.2	59.6	18
ASSET[20]	<=55	1493	3.9	4.4	11.4	0.5
	55-65	1859	6.5	7.9	17.7	1.4
	66-75	1679	10.8	16.4	34.1	5.6
ISIS[4]	<60	7720	4.2	5.8	27.6	1.6
	60-69	6056	10.6	14.4	26.4	3.8
	>70	3411	18.2	21.6	15.7	3.4

However, with better operating experience and improvements in angioplasty equipment, the success rate has increased.[24] This has led to an expanded use in older patients. In a series of 1640 elderly patients (65 years or older), who underwent multivessel coronary angioplasty, angiographic success was obtained in 96% of lesions, achieving revascularisation in 52% of patients. There were major complications in only 3.2%. For those elderly patients with successful angioplasty, the long term outcome is favourable. Actuarial survival has been reported at 92% at one year, 86% at three years, and 78% at five years. Event-free survival (freedom from death, AMI, or coronary artery bypass grafting) was 81% at one year, 69% at three years, and 56% at five years.[24]

While angioplasty is certainly feasible and practical in the elderly, more trials are needed to demonstrate convincingly their benefit in various acute situations in myocardial infarction. For instance, there is no conclusive data yet on direct angioplasty (immediate angioplasty as soon as possible after presentation) versus thrombolysis in elderly patients with acute myocardial infarction. One reason for supporting direct angioplasty is that a large proportion of patients fail to achieve complete reperfusion with the current intravenous thrombolytic regimen.[25] Several recently completed randomised trials have shown that direct angioplasty is as effective as thrombolysis.[26,27] The Primary Angioplasty and Myocardial Infarction (PAMI) trial was a multicentre study of 395 patients aged from 18 through 75 years, who were randomly assigned to receive direct angioplasty or intravenous tissue plasminogen activator for AMI. The combined death rate and nonfatal reinfarction rate was 5.1% in the angioplasty group compared with 12% in the thrombolytic group.[27] However, the data on direct angioplasty in elderly patients were from small nonrandomised studies. Lee reported direct angioplasty in 105 patients older than 70 years, with a primary success rate of 91% and an inpatient mortality rate of 18%.[28] Another study reported less favourable results, showing a 34% mortality rate with direct angioplasty in 35 patients older than 70 years of age, with a technical success rate of 66%.[29] Even if direct angioplasty is proven to be superior, it may not be a practical option yet in Hong Kong. When facilities are available—and if there are contraindications to thrombolysis—elderly patients should be strongly considered for direct angioplasty.[30] Those elderly not reperfused after AMI face significant morbidity and mortality. Results from trials using more aggressive or combination thrombolysis are eagerly awaited.

Further trials are also needed to confirm the perceived benefit of emergency angiograms for elderly people with AMI. Emergency angiogram may be indicated when the diagnosis of AMI is not certain due to atypical symptoms or ECG.[31] This can establish diagnosis early in doubtful cases, avoiding unnecessary empirical thrombolysis. An additional perceived advantage is that the identity and status of the infarct-related artery and extent of disease can be identified and suitability for angioplasty determined. Acute episodes post-AMI may also warrant urgent angiography. One study described 12 elderly patients with post-infarction ventricular septal defect, treated by aortic balloon counterpulsation and early surgical repair. Seven patients survived and remained well on follow up.[32] Urgent angiogram should be considered in patients with unsuccessful reperfusion (suspected by significant refractory chest pain or ECG changes despite thrombolysis) or suspected reocclusion, as these patients have high morbidity and mortality.[33] Rescue angioplasty may be useful,[34] and results from further trials are awaited.

There is no definitive data regarding the use of a selective or routine approach to angiogram following uncomplicated AMI in any age group. With the selective approach, cardiologists would only perform an angiogram for definite recurrent ischaemia, whereas an angiogram would be a standard component in risk stratification in the routine approach. Analysis of the Thrombolysis In Myocardial Infarction II (TIMI II) data revealed that a routine angiogram did not result in reduction in either acute or one-year adverse clinical outcomes.[35] More importantly, there is a small but definite risk of complications in the elderly, e.g. nonfatal reinfarction or embolisation.[36] Together with cost considerations, the selective use of angiograms following uncomplicated AMI is to be strongly recommended. Similarly, routine empiric angioplasty did not improve global left ventricular function, morbidity or mortality, compared with the selective use of angioplasty.[37] In the Should We Intervene Following Thrombolysis (SWIFT) trial, prophylactic angioplasty in stable patients actually led to a higher rate of reinfarction than occurred with the conservative approach.[38]

When studying an invasive procedure in elderly patients, it is important to compare the benefits and risks with untreated age-matched controls, rather than younger patients. Although there is often a lower success rate and more complications from angiograms or angioplasty in the older age group, this should not pre-

clude their use. For older patients who are most at risk, an individualised approach rather than an age-related one should be used.

Secondary prevention of acute myocardial infarction in the elderly

Because elderly survivors of AMI have a much higher morbidity and mortality than do the young, secondary prevention has an especially important role. Paradoxically, large secondary prevention trials have excluded the older age group. The available data has mostly been extracted from subgroup analysis of large randomised trials. The various modalities of secondary prevention are discussed below.

Beta blockers

The use of beta blockers after AMI has been shown to be beneficial, and the effect is actually more pronounced in the elderly. The largest trials to date include the Beta Blocker Heart Attack Trial[39] and the Norwegian Timolol Trial.[40] The former trial comprised a total of 1249 patients aged between 60 and 69 years of age. A significant reduction in mortality was demonstrated for those treated with beta blockers. The relative reduction in mortality was greater in this cohort than in the young, with a 33.7% reduction in those aged 60 through 69 years ($P = 0.01$) compared with an 18.7% reduction in those aged 30 through 59 years. In the Norwegian trial, there was a total of 732 patients aged from 65 through 75 years. Significant reductions in cardiac and overall mortality were also demonstrated in the treatment group in this cohort. Despite evidence suggesting a greater mortality risk reduction, beta blockers have been prescribed less often in the elderly.[41]

Aspirin

Large meta-analysis has shown that long term aspirin use significantly reduces morbidity and mortality in patients who survive AMI.[42] Unfortunately, data on the very elderly is lacking. A review of nine randomised controlled trials involving 17 039 patients showed only one—the Medical Research Council trial—which included patients older than 70 years of age. Even then, only 27 patients were recruited.[43]

Angiotensin converting enzyme (ACE) inhibitors

Angiotensin converting enzyme (ACE) inhibitors have been shown to improve survival in patients with symptomatic heart failure after AMI.[44,45] The Survival and Ventricular Enlargement Trial demonstrated that with the early use of captopril in patients with ejection fractions of less than 40%, there was a significant reduction in the rate of recurrent AMI, development of congestive heart failure, fatal and non-fatal cardiac events, and late mortality. Thirty-five per cent of the treated group were older than 65 years of age, and the relative risk reduction in the elderly cohort was greater than in the young.[44] The Survival of Myocardial Infarction Long-Term Evaluation (SMILE) study also showed that ACE inhibitors significantly improved both short term and long term outcomes when administered within 24 hours of the onset of anterior AMI, and were continued for six weeks.[46]

Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico III (GISSI 3) further showed that the early use of ACE inhibitors benefited all AMI patients, regardless of left ventricular function. In this trial, oral ACE inhibitors were begun within 24 hours of AMI, and produced significant reductions in overall mortality, and the combined outcome measure of mortality and severe ventricular dysfunction after six weeks. This study was also designed to formally assess high-risk groups such as women and the elderly. Nearly 27% of the lisinopril group were older than 70 years of age, and a significant reduction in their combined endpoint rate was also found. It was estimated that 16 lives were saved per 1000 patients over the age of 70, compared with only eight per 1000 for all patients.[47] Results from the Fourth International Study in Infarct Survival (ISIS 4) showed an absolute difference of 4.9 fewer deaths per 1000 patients treated with captopril for one month, and also provided indirect evidence of benefit in older patients, in accord with the GISSI 3 results.[48]

Cholesterol reduction

The Framingham Heart Study showed that for patients aged 65 years or older, those with a high serum cholesterol had a higher risk of reinfarction.[49] A meta-analysis of eight randomised trials of lipid-lowering drugs for secondary prevention after AMI, showed that a 10% reduction in cholesterol level reduced the rate of non-fatal and fatal reinfarction.[50] Other authors estimated that a long term reduction in serum cholesterol concentration of 0.6 mmol/L can lower the risk of ischaemic heart disease by 20% at age 70.[51] The recently published Scandinavian Simvastatin Survival Study recruited 4444 patients and showed conclusively that over the 5.4-year median follow up period, there were significantly fewer total mortality and coronary events in the treatment group.[52] Although patients older than 70 years were not included in the trial, almost half of the total patients recruited were older than 60 years. The reduction in mortality or coronary events in those older than 60 was also significant. For those

older than 75, no direct prospective study has been conducted. Whether regression of coronary atheroma is still probable in this age group is not known.

Calcium channel blockers and antiarrthymic therapy

Secondary prevention trials using calcium channel blockers have not significantly altered mortality after AMI.[53] In fact, trials studying nifedipine and diltiazem have shown increased mortality.[54,55] The results of the CAST trial also showed that prophylactic use of antiarrhythmic agents led to a higher mortality, regardless of age.[56] Routine use is not recommended.

Cardiac rehabilitation

The elderly are most in need of cardiac rehabilitation after AMI as they often have reduced functional mobility, together with more severe coronary disease or coexisting illness. Paradoxically, they are also less likely to receive rehabilitation. One multivariate analysis showed that among 216 patients older than 62 years, the physicians' recommendation was the most powerful predictor of recruitment into a cardiac rehabilitation programme, rather than the severity of the disease.[57] Most studies of post-infarction rehabilitation have excluded elderly patients.

An important element of a rehabilitation programme is exercise training. This is especially true for older individuals, who are vulnerable because of prolonged bedrest and deconditioning after myocardial infarction. In an Italian study, 50 men older than 65 years of age received a four-week supervised, ECG-monitored training programme—lasting 30 minutes each—between 28 to 60 days post-AMI. The intensity of training was individually tailored according to a target heart rate threshold (70% of maximum heart rate, previously determined in a functioning stress test). The result was encouraging, providing substantial improvement in physical activity, which was remarkably maintained after one year. Furthermore, at the end of the programme and 11 months later, the physical capacity of patients did not differ from that of healthy volunteers of a similar age.[58] Another study in the United States, compared 76 men older than 65 years of age who were receiving a supervised exercise training programme within six weeks of AMI or coronary bypass surgery, with 285 similar younger patients.[59] The rehabilitation programme lasted for 12 weeks and consisted of three weekly sessions, 40 minutes each, of circuit station exercise. The results showed that although the elderly had a lower physical work capacity than the younger age group—both before and after training—the improvement in endurance and functional capacity was the same.

Hence, the available evidence shows that older patients post-AMI could improve their functional capacity safely. Reasssuringly, no increased adverse events have occurred during the training programmes. Of course, not all patients have the same functioning ability and can benefit from full exercise training. Nonetheless, a low intensity exercise programmme, training mainly the smaller muscle groups to condition patients for activities of daily living, would still be of considerable benefit.

Rehabilitation after AMI should be comprehensive, including psychosocial support, education, counselling, and risk factor modification. A Danish study compared 119 patients aged 67 years and older, who received home visits by a doctor 1, 3, 6, and 12 weeks after discharge, with a control group of 100 patients, who received only routine follow up in a clinic. During the home visits, solutions were sought to medical, psychological, and social problems. The control group was comparable in age, gender, functional status, and severity of AMI. The one-year mortality rate was significantly lower in the home-visit group, and readmissions were fewer.[60] More strikingly, when compared with matched healthy control patients without AMI, the home visit group had similar functional capacity and state of well-being. Hence, it seems that comprehensive rehabilitation not only improves quality of life, but also reduces mortality and the use of health services.

Ageism

Despite the clear evidence of benefit from various treatment modalities, older patients are still undertreated. Dudley et al found that 20% of coronary care units had an age criteria, refusing to treat patients older than 75 years, and even refusing to treat some as young as 65 years.[6] They also found that 40% refused to give thrombolysis to older patients simply based on age alone. In the MITI study, the authors found that those in the older age group were less likely to receive aspirin, thrombolysis, angioplasty, or coronary bypass.[7] Gurwitz, in his review of recent AMI trials, observed that more than 60% of such trials excluded patients older than 75 years of age.[14]

Conclusion

With a rapidly ageing population, the number of patients with AMI, the average age of patients with AMI,

and the morbidity and mortality associated with AMI, will continue to increase. Older patients are at the most risk, and it is increasingly apparent that they can derive much benefit from treatment, ranging from thrombolysis and acute intervention to secondary prevention and rehabilitation. However, given limited resources, it is very difficult to decide which particular treatment is of the greatest value for the elderly, and suitable for further expansion and provision. Primary prevention is of course one very important area, where future research and resources should be directed. Nonetheless, it is crucial that older patients not be denied the best available medical care. It should also be remembered that elderly patients form a heterogeneous population. Instead of age-related guidelines, an individualised approach should be adopted which takes into consideration such factors as physiological age, comorbidity, higher mental state, functional capacity, and level of independence. This will no doubt remain one of the most difficult and challenging aspects of geriatric medicine.

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