Management of acute myocardial infarction in the elderly

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SUMMARY Thrombolysis and other new therapies have proved beneficial in elderly patients with myocardial infarction, but are underused in this age group. Because elderly patients are at greater cardiac risk than younger patients, they have more to gain from treatment. However, these treatments may pose more risk for elderly patients. Physicians must constantly assess the elderly patient's risk status and make treatment decisions based on risk-benefit analysis.

KEY POINTS Streptokinase may be as beneficial as tissue-plasminogen activator in older patients. Aspirin is recommended for all patients. Long-term anticoagulation therapy is reserved for patients at risk of thromboembolic events. Beta blockers are beneficial but underused in older patients, even in patients who have no contraindications to them. Coronary artery bypass grafting and percutaneous transluminal coronary angioplasty produce excellent results in selected elderly patients. Angiotensin-converting enzyme inhibitors are recommended for all patients who have a left ventricular ejection fraction of 40% or less. Empirical use of antiarrhythmic drugs lacks benefit, but elderly patients with life-threatening ventricular tachyarrhythmias do benefit from aggressive management guided by electrophysiologic studies.

INDEX TERMS: MYOCARDIAL INFARCTION; AGED
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FEW WOULD DOUBT the value of aggressively treating an acute myocardial infarction (MI) in a middle-aged person. But what of the elderly, who account for most MI deaths?

Changes associated with aging place elderly patients at greater risk of complications of MI and of the therapies used to treat it. Extensive evidence has confirmed that elderly patients derive just as much benefit from treatment for MI as younger patients, if not more. However, treatment decisions should be made only after carefully considering the risks and possible benefits for the individual patient.

This article presents an overview of the risks and benefits of current therapeutic options in elderly MI patients.

THROMBOLYTIC THERAPY

Thrombolytic therapy significantly reduces the mortality rate in acute MI,[1–6] and pooled data from major studies show it is as beneficial in elderly patients as it is in younger patients (*Table*).[7] In fact, in two of five major studies, elderly patients derived *more* benefit: the risk of death was reduced by 60% and 34% in the older patients who underwent

thrombolytic therapy, compared with 39% and 14% in the younger patients.[5,6] Further, two studies indicate that thrombolytic therapy in patients over age 75 is as beneficial and as cost-effective as many other accepted medical therapies, such as treating younger patients for moderate hypertension.[8]

The comparative benefits of streptokinase and tissue-plasminogen activator (t-PA) are controversial. Two large trials found both drugs increased the survival rate equally.[9,10] The Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) trial[11] reported a significant advantage with t-PA for the overall population, but patients over age 75 had a significantly higher risk of hemorrhagic stroke if they were treated with t-PA than with streptokinase, and the incidence of death or nonfatal disabling stroke was not significantly different between the two therapies in this age group. Therefore, streptokinase may be appropriate in patients over age 75.

TABLE
ACUTE MYOCARDIAL INFARCTION:
EFFICACY OF THERAPY IN YOUNGER VS OLDER PATIENTS*

Therapy	No. of patients	Mortality rate, % Therapy	Control	Reduction in mortality, %	P value
Thrombolysis[31–36]					
Early mortality					
Younger patients	26 941	6.2	8.4	25.7	< .0001
Older patients	9 841	17.2	20.7	16.9	< .0001
Late mortality					
Younger patients	11 706	9.1	11.2	18.1	.0003
Older patients	6 278	26.6	28.6	10.3	.009
Beta blockers[75–79]					
Early intervention					
Younger patients	14 687	2.5	2.6	5.0	NS†
Older patients	8 513	6.9	8.9	23.2	.0005
Late intervention					
Younger patients	4 654	5.5	7.6	28.3	.004
Older patients	2 462	8.9	14.9	40.0	.0001

*Pooled data from major trials. Younger age limit varied from ≤ 65 to < 60 years old; older age range varied from ≥ 60 to 70 years old, 66 to 75 years old, and > 75 years old. Adapted from Forman et al, reference 37
†NS = not significant

Why thrombolytic therapy is underused in the elderly

Despite overwhelming proof that thrombolytic therapy is beneficial in elderly MI patients, it is underused in this group,[12–14] for several reasons.

Fear of hemorrhage. The incidence of bleeding increased significantly with age in the Thrombolysis in Myocardial Infarction trials (TIMI-1 and TIMI-2).[15] However, these patients all underwent invasive procedures within 36 hours of thrombolysis, and most bleeding occurred at the puncture site. There were few cases of cerebral hemorrhage in these studies, and there was no difference in the incidence of cerebral hemorrhage between the older and younger patients. In 20 891 patients in the GISSI-2 and International Study trials, the risk of stroke increased with age, although the association between hemorrhagic stroke and age was not statistically significant.[16]

Atypical presentation of acute MI in the elderly. Approximately 25% of acute MIs are not clinically recognized, and of these, 48% are truly silent.[17] The incidence of unrecognized or silent MI increased with age in some studies,[18,19] and 60% of MIs in the very elderly were not recognized. Instead of having typical chest pain, elderly MI patients may demonstrate unexplained behavioral changes, acute cerebral insufficiency, abdominal distress, or dyspnea as their presenting symptom. Some studies have shown acute pulmonary edema without chest pain to be a common presentation.[20] The electrocardiographic profile may also be different: elderly MI patients more commonly present with nonspecific ST-T wave changes, whereas younger patients more commonly demonstrate typical ST elevation and Q waves.

Delay in seeking assistance. Weaver and associates[14] reported that patients age 75 or older waited an average of 6.1 hours after chest pain began before seeking medical assistance, compared with 5.2 hours in patients under age 55.

ASPIRIN

Aspirin reduces the increased platelet aggregation associated with MI, reduces the risk of MI in patients with unstable angina, and reduces the mortality rate in MI survivors.[21–23] In the ISIS-2 trial,[24] aspirin given alone (160 mg daily) significantly re-

duced the mortality rate by 23%, the stroke rate by 36%, and the reinfarction rate by 44%. The combination of aspirin and streptokinase further reduced the mortality rate by 42%. By 5 weeks, among patients age 70 and older, 21% fewer aspirin-treated patients had died. Aspirin's side effects always need to be considered; however, in the ISIS-2 trial, no increase in cerebral bleeding was demonstrated with the use of aspirin.[24]

Therefore, aspirin is recommended immediately at the onset of an acute MI, with or without thrombolytic therapy. It should be continued indefinitely, regardless of the patient's age. The dose remains controversial: as little as 20 mg produces antiplatelet effects, but in general a daily dose of 160 mg is recommended in MI patients. Other antiplatelet drugs such as dipyridamole, sulfinpyrazone, and ticlopidine have not been found clinically to be more effective than aspirin.

ANTICOAGULATION THERAPY

Anticoagulants reduce thromboembolic events, a considerable problem in elderly MI patients. However, they can cause bleeding, their long-term benefits are controversial, and their advantage over aspirin is questionable. Therefore, anticoagulants cannot be routinely recommended for elderly MI patients. However, heparin given intravenously is recommended for certain patients at high risk of thromboembolic events, particularly elderly patients with large anterior-wall Q-wave MIs and heart failure and patients with echocardiographically documented ventricular thrombi.[25] After the acute phase, warfarin should be substituted for heparin and continued for approximately 3 months after hospital discharge. In elderly patients at high risk of bleeding, it may be desirable to give heparin subcutaneously instead of intravenously.

BETA BLOCKERS

Beta blockers have been studied in both the early stages of MI (within hours) and in the later stages (months to years).[26–33] In most studies, younger patients did not benefit from the early administration of beta blockers, whereas older patients did (*Table*). In the later stages of acute MI, beta blockers reduced the incidence of reinfarction, death, and sudden death in patients with Q-wave MI or non-Q-wave MI,[34] young and old.[26–31,35] Elderly patients may derive greater benefit from beta blockers as secondary prevention than younger patients do (*Table*). Such benefit has been reported to last at least 6 years after an acute MI.[36]

Despite their benefits, beta blockers are also underused in older patients. Forman and Wei[37] found only 31% of patients age 70 and older were taking beta blockers after an MI, compared with 49% of younger patients. As expected, contraindications to beta blockers were common in the elderly patients; however, only 39% of the patients over age 80 who did not have contraindications to beta blockers were taking them, compared with 70% of patients age 50 to 59.

The side effects of beta blockers are worrisome, especially with lipophilic agents, which can pass into the central nervous system more easily. Beta blockers that do not enter the central nervous system as easily are preferable in elderly patients, and it is prudent to start with low doses and gradually increase the dosage.

CABG AND PTCA

Older patients undergoing coronary artery bypass grafting (CABG) have slightly (but acceptably) higher rates of perioperative morbidity and mortality than younger patients do, but most enjoy symptomatic relief and an excellent long-term prognosis. Even in octogenarians, the surgical mortality rate during CABG is less than 3%, and more than 85% of patients survive at least 5 years.[38]

The results of percutaneous transluminal coronary angioplasty (PTCA) in elderly patients are also favorable. Since PTCA does not require general anesthesia or major surgery, PTCA patients usually enjoy a low morbidity rate and a short hospital stay. The in-hospital mortality rate was higher in octogenarians undergoing PTCA than in younger patients in some studies,[39,40] which may reflect their higher prevalence of multiple-vessel coronary disease and their more unstable clinical state. Restenosis remains a considerable problem after successful PTCA, and studies comparing CABG with PTCA report more hospitalizations for repeat procedures in PTCA patients.[41,42]

The studies that reported favorable results of interventional therapy in elderly patients mainly excluded unstable patients who underwent emergency interventions. Freeman and associates,[43] examining the Mayo Clinic experience with CABG in octoge-

narians, found the mortality rate to be 5.6% in elective operations, but 23% in emergency operations. Significant left ventricular dysfunction (an ejection fraction < 50%) also boded ill for survival, as did mitral valve surgery. Similar results have been noted with PTCA.[44,45]

Therefore, the physician should determine early in the hospital stay whether an elderly MI patient can safely undergo interventional therapy and would benefit from it. Once the complications of acute MI arise, the risk associated with these interventions increases considerably.

ACE INHIBITORS

The Survival and Ventricular Enlargement (SAVE) trial evaluated the prophylactic use of the angiotensin-converting enzyme (ACE) inhibitor captopril in MI patients who had a left ventricular ejection fraction of 40% or less.[46] After a mean of 42 months, the captopril group had significantly lower rates of mortality (19% lower), heart failure (37% lower), and recurrent MIs (25% lower) than did the control group. Fifteen percent of the patients in the study were over age 70. As expected, older patients had more MI complications; however, captopril significantly lowered the mortality rate in all age groups. Therefore, unless ACE inhibitors are contraindicated, they are recommended for all MI patients who have a left ventricular ejection fraction of 40% or less, regardless of age.

The ideal dosage of ACE inhibitors is controversial, although inadequate dosage is thought to be common. In the SAVE trial, the target dosage of captopril was 50 mg three times daily; in trials of enalapril, the usual daily dose was 20 mg. Such doses may be difficult for elderly MI patients to tolerate because of problems with orthostatic hypotension and renal disease. However, the only limiting symptom reported in most studies of ACE inhibitors has been cough. ACE inhibitors should be started at a low dosage (captopril 6.25 mg three times a day or enalapril 2.5 mg daily) in elderly patients and gradually increased to the recommended dosage. Mild azotemia or a small decrease in blood pressure is not sufficient reason to reduce the dosage.

CALCIUM ANTAGONISTS

Calcium antagonists have not been as beneficial after MI as beta blockers[47,48]: in most studies they did not reduce mortality, and in some studies the mortality rate increased.[49] However, in a Danish trial of 1775 MI patients, the rates of mortality and reinfarction were lower in patients treated with verapamil than in a placebo group.[50] The maximum age of the study patients was 76, and the mean follow-up was 16 months.

Diltiazem has been reported to significantly reduce the risk of reinfarction and refractory angina after non-Q-wave MI.[51] Non-Q-wave MI is common in elderly patients, but only 6% of the patients in this study were age 75 or older. In contrast, diltiazem is detrimental in certain patients with Q-wave MI. Patients with Q-wave MI and pulmonary congestion who were treated with diltiazem in the Multicenter Diltiazem Postinfarction Trial had a higher cumulative rate of cardiac events (including cardiac death) than did patients treated with placebo. The mean age was 58, and the mean follow-up was 25 months. The detrimental effect of diltiazem was thought to be related to its cardiodepressant effect.[49]

Therefore, calcium antagonists are contraindicated in patients with significant left ventricular dysfunction. In elderly patients with non-Q-wave MI, diltiazem is recommended; in elderly patients with Q-wave MI who cannot tolerate beta blockers and have good left ventricular function, verapamil may be considered.

ANTIARRHYTHMIC THERAPY

The risk of ventricular arrhythmias and sudden death increases with age. Empirical drug therapy for ventricular arrhythmias after MI, however, has not proved beneficial in patients of any age,[52–55] and in some studies, antiarrhythmic drugs have even been detrimental. The much-publicized Cardiac Arrhythmia Suppression Trial (CAST) demonstrated a threefold higher mortality rate in post-MI patients with asymptomatic ventricular arrhythmias who received flecainide and encainide than in patients who received placebo.[56] Two recent studies, however, suggest that amiodarone may be beneficial in certain patients with complex ventricular arrhythmias after MI.[57,58]

Nevertheless, we recommend assessing the risk of sudden death in elderly MI patients. Complex ventricular ectopy, usually defined as nonsustained ventricular tachycardia, is an independent risk factor for sudden death in post-MI patients, as is left ventricular dysfunction. Post-MI patients with a

left ventricular ejection fraction of less than 40% plus significant ventricular ectopy (10 or more ventricular premature beats per hour) have an incidence of sudden death approximately 11 times that of patients with neither of these findings.[59] In addition, abnormal signal-averaged electrocardiographic findings portend sudden death in post-MI patients.[60–62]

Aggressive interventional management guided by electrophysiologic studies is considered the best strategy for post-MI patients at high risk of sudden cardiac death. Many physicians, however, are reluctant to subject elderly patients to such aggressive management because of the increased risks associated with intervention in this age group. Recent studies have shown that elderly patients with life-threatening ventricular tachyarrhythmias do benefit from such therapy.[63–65] Tresch and associates[63,64] demonstrated that elderly patients with life-threatening ventricular tachyarrhythmias managed with drug therapy (directed by electrophysiologic studies), CABG, ventricular resection, and automatic implantable cardioverter defibrillators had a long-term survival rate similar to that of younger patients. Complications related to the interventional therapies were not significantly different between the age groups. At a mean follow-up of 2 years, fewer than 6% of the patients over age 65 with life-threatening ventricular arrhythmias treated with implantable defibrillators had died suddenly, a rate comparable to that in similarly treated younger patients.[64]

PREDISCHARGE ASSESSMENT

Elderly MI patients with symptomatic myocardial ischemia should undergo coronary angiography before leaving the hospital, unless the procedure is contraindicated. Asymptomatic elderly MI patients require some form of stress testing before discharge to rule out silent ischemia and to assess for myocardium at risk.[66,67] Exercise electrocardiographic testing, the accepted method in younger patients,[66,67] may not be appropriate for elderly patients. Patients with intraventricular conduction defects and ST-T wave changes at rest (common in the elderly) need radionuclide exercise perfusion testing.[68] More important, many elderly patients cannot adequately exercise owing to concomitant diseases, and in some, exercise testing is contraindicated. For these patients, pharmacologic stress testing with dipyridamole-thallium has proved effective in detecting myocardial ischemia after an acute MI.[69] Echocardiography with dobutamine or dipyridamole is also effective.[70,71]

The problem of reocclusion after thrombolysis has not been specifically addressed in elderly MI patients. Elderly MI patients who receive thrombolytic therapy are similar to those who sustain a non-Q-wave MI. Transient occlusion of the coronary artery leads to myocardial damage, the artery may still be significantly narrowed, and reocclusion is possible, which could cause further myocardial damage, significant complications, and death. Elderly patients with non-Q-wave MI are at high risk of death following hospital discharge,[72,73] especially those with previous MI, pulmonary congestion, recurrent angina, and persistent ST-T wave changes.

At present, there is no good way to predict reocclusion after thrombolysis. Routinely performing angiography after thrombolytic therapy does not appear to improve the outcome, compared with a more selective approach.[33,74] The American College of Cardiology-American Heart Association Joint Task Force recommends performing angiography before discharge only in high-risk patients who demonstrate symptomatic or asymptomatic ischemia.[75] This approach again stresses the importance of assessing mortality risk in elderly MI patients before they are discharged, regardless of whether they receive thrombolytic therapy.

CONCLUSIONS

Extensive coronary artery disease, significant underlying left ventricular dysfunction, cardiovascular aging changes, and concomitant diseases place elderly MI patients at high risk of complications and death. New drugs and therapies, including thrombolysis and interventional procedures, enable physicians to favorably influence the disease process and prevent many deaths. Studies have demonstrated that elderly patients benefit as much as younger patients do from these new treatments, if not more. Elderly patients, however, are at greater risk of complications from some of the new therapies. Clinicians must therefore continually assess their patients' risk throughout the hospital course and make decisions about therapy after weighing the risks against the possible benefits.

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