Management of Older Persons After Myocardial Infarction
[Special Series]

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Abstract

OBJECTIVE: To review the management of the older person after myocardial infarction (MI).

DATA SOURCES: A computer-assisted search of the English language literature (MEDLINE database) followed by a manual search of the bibliographies of pertinent articles.

STUDY SELECTION: Studies on the management of persons after MI were screened for review. Studies in persons older than 60 years and recent studies were emphasized.

DATA EXTRACTION: Pertinent data were extracted from the reviewed articles. Emphasis was on studies involving older persons. Relevant articles were reviewed in depth.

DATA SYNTHESIS: Available data about therapy of persons after MI, including control of risk factors, use of aspirin and beta-blockers, and indications for use of angiotensin-converting enzyme inhibitors, long-term anticoagulant therapy, nitrates, calcium channel blockers, hormone replacement therapy, antiarrhythmic drugs, the automatic implantable cardioverter-defibrillator, and revascularization, with emphasis on studies involving older persons, were summarized.

CONCLUSIONS: Risk factors for coronary artery disease should be controlled after MI in older persons. A serum low-density lipoprotein (LDL) cholesterol > 125 mg/dL after MI should be treated with lipid-lowering drug therapy to decrease the serum LDL cholesterol to < 100 mg/dL. Aspirin in a dose of 160 mg to 325 mg daily should be given indefinitely. Indications for long-term anticoagulant therapy with warfarin after MI to maintain an international normalized ratio between 2.0 and 3.0 include secondary prevention of MI in persons unable to tolerate daily aspirin, persistent atrial fibrillation, and left ventricular thrombus. Beta-blockers should be given indefinitely. Angiotensin-converting enzyme inhibitors should be given to persons who have congestive heart failure, an anterior MI, or a left ventricular ejection fraction <= 40%. Calcium channel blockers should not be used unless there is persistent angina pectoris despite beta-blockers and nitrates. Antiarrhythmic drugs other than beta-blockers should not be used. An automatic implantable cardioverter-defibrillator should be used in persons who have a history of ventricular fibrillation or serious sustained ventricular tachycardia or who are at very high risk for developing sudden cardiac death. Until data from the Heart Estrogen/Progestin Replacement Study are available, use of an estrogen/progestin regimen is recommended in the treatment of postmenopausal women after MI unless they are at increased risk for developing breast cancer. The two indications for revascularization in older persons after MI are prolongation of life and relief of unacceptable symptoms despite optimal medical management.
Coronary artery disease (CAD) is the leading cause of death in older persons. Although persons older than 65 years of age comprise 12% of the population, 1 approximately 60% of hospital admissions for acute myocardial infarction (MI) are for persons older than 65 years of age, and persons older than 75 years of age account for nearly half of these admissions. The inhospital mortality and the post-discharge mortality rates are higher in older persons than in younger persons with MI. The 1-year cardiac mortality rate is 12% for persons aged 65 to 75 years and 17.6% for persons older than 75 years of age. Approximately two-thirds of these 1-year deaths are sudden or related to a new MI. This review article discusses the appropriate management of the older person after MI.

CONTROL OF CORONARY RISK FACTORS

Cigarette smoking

Cigarette smoking is a risk factor for new coronary events in older persons. The Coronary Artery Surgery Study registry found at the 6-year follow-up of older men and women that the relative risk of MI or death was 1.5 (95% CI, 1.0 to 2.3) for persons aged 65 to 69 years and 2.9 (95% CI, 1.4 to 5.9) for persons 70 years of age or older who continued smoking compared with those who quit during the year before study enrollment. At 48-month follow-up of 1488 older women, mean age 82 years, and at 40-month follow-up of 664 older men, mean age 80 years, current cigarette smoking increased the relative risk of new coronary events (nonfatal or fatal MI or sudden cardiac death) 2.0 times (95% CI, 1.7 to 2.9) in older women and 2.2 times (95% CI, 1.7 to 2.9) in older men. The author has also found that cigarette smoking aggravates angina pectoris and precipitates silent myocardial ischemia in older persons after MI. On the basis of the available data, older women and men who smoke cigarettes should be encouraged strongly to stop smoking to decrease cardiovascular mortality and all-cause mortality after MI.

Hypertension

Systolic hypertension in older persons is diagnosed if the systolic blood pressure is 160 mm Hg or higher on three occasions. Diastolic hypertension in older persons is diagnosed if the diastolic blood pressure is 90 mm Hg or higher on three occasions. Isolated systolic hypertension in older persons is diagnosed if the systolic blood pressure is 160 mm Hg or higher on three occasions, and the diastolic blood pressure is <90 mm Hg.

Isolated systolic hypertension and diastolic hypertension are both associated with a higher incidence of cardiovascular morbidity and mortality in older persons. Increased systolic blood pressure is a greater risk factor for cardiovascular morbidity and mortality than is increased diastolic blood pressure. The higher the systolic or diastolic blood pressure, the greater the morbidity and mortality from CAD in older women and men. At 48-month follow-up of older women and 40-month follow-up of older men, systolic or diastolic hypertension increased the relative risk of new coronary events 1.6 times (95% CI, 1.5 to 2.5) in women and 2.0 times (95% CI, 1.5 to 2.5) in men.

Older persons with hypertension should be treated initially with salt restriction, cessation of drugs that increase blood pressure, avoidance of alcohol and tobacco, weight reduction if necessary, increase in physical activity, decrease of dietary saturated fat and cholesterol, and maintenance of adequate dietary potassium, calcium, and magnesium intake.

Antihypertensive drugs have been shown to reduce new coronary events in older men and women with hypertension (Table 1). The Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure recommends diuretics or beta-blockers as initial drug therapy because these drugs have been shown to decrease cardiovascular morbidity and mortality in controlled clinical trials. The goal of therapy in older persons should be the same as in
younger persons, to decrease the blood pressure to less than 140/90 mm Hg if possible. Older persons with hypertension who have had a MI should be treated initially with a beta-blocker.

Table 1. Reduction in New Coronary Events in Older Persons with Hypertension Treated with Antihypertensive Drugs Versus Placebo

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**Serum Lipids**

Serum total cholesterol is a risk factor for new coronary events in older men and women. In the Framingham Study, serum total cholesterol was most strongly related to death from CAD and to all-cause mortality among persons aged 65 years or older with a previous MI.20 At 48-month follow-up of older women and 40-month follow-up of older men, an increment of 10 mg/dL of serum total cholesterol increased the relative risk of new coronary events 1.12 times (95% CI, 1.10 to 1.15) in women and 1.12 times (95% CI, 1.09 to 1.17) in men.10

A low serum high-density lipoprotein (HDL) cholesterol is a risk factor for new coronary events in older men and women. At a 48-month follow-up of 1488 older women and at a 40-month follow-up of 664 older men, there was a 1.95 times (95% CI, 1.79 to 2.33) higher probability of developing new coronary events in women and a 1.70 times (95% CI, 1.54 to 2.10) higher probability of developing new coronary events in men for a decrement of 10 mg/dL of serum HDL cholesterol. Hypertriglyceridemia has been reported to be a risk factor for new coronary events in older women but not in older men.10,19

**Drug Therapy of Hypercholesterolemia**

At a 5.4-year median follow-up of 4444 men and women with CAD and hypercholesterolemia in the Scandinavian Simvastatin Survival Study, compared with placebo, simvastatin reduced major coronary events 34%, coronary death 42%, and total mortality 30% (Table 2).28 The decreases in coronary events and in total mortality in persons treated with simvastatin were similar in men and in women between 60 and 70 years of age at study entry (65 to 75 years of age at follow-up) and in those younger in age.28

Table 2. Effects of Reducing Increased Serum Total Cholesterol and Low-Density Lipoprotein Cholesterol Levels by Simvastatin and Pravastatin Versus Placebo in Older Persons With Coronary Artery Disease (CAD)

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At 5-year follow-up, 4159 men and women with MI and serum total cholesterol levels less than 240 mg/dL, but serum LDL cholesterol levels 115 mg/dL or greater, in the Cholesterol and Recurrent Events (CARE) trial, compared with placebo, pravastatin decreased major coronary events 27% in persons 60 to 75 years of age at study entry (65 to 80 years of age at follow-up) and 20% in persons younger than 60 years of age at study entry (Table 2).29 The reduction in coronary events was greater in women (46%) than in men (20%) treated with pravastatin. The American College of Cardiology/American Heart Association guidelines recommend that after

MI, persons with serum LDL cholesterol more than 125 mg/dL despite the American Heart Association Step II diet should be treated with lipid-lowering drug therapy to reduce the serum LDL cholesterol to less than 100 mg/dL.\textsuperscript{30}

On the basis of the above data, older persons with a previous MI who have elevated serum LDL cholesterol levels despite dietary therapy should be treated with a statin drug such as simvastatin, pravastatin, lovastatin, fluvastatin, or atorvastatin. The serum LDL cholesterol level should be reduced to 100 mg/dL or lower.\textsuperscript{30,31}

**Diabetes Mellitus**

Diabetes mellitus is a risk factor for new coronary events in older men and women.\textsuperscript{10,32} At 48-month follow-up of older women and 40-month follow-up of older men, diabetes mellitus was found to increase the relative risk of new coronary events 1.8 times (95% CI, 1.4 to 2.5) in women and 1.9 times (95% CI, 1.4 to 2.5) in men.\textsuperscript{10}

Older persons with diabetes mellitus who have experienced MI should be treated with dietary therapy, weight reduction, if necessary, and appropriate drugs, if needed, to control hyperglycemia. Other coronary risk factors should be controlled.

**Obesity**

Obesity\textsuperscript{32} and disproportionate distribution of fat to the abdomen assessed by the waist-to-hip circumference ratio\textsuperscript{33,34} have been shown to be risk factors for new coronary events in older men and women. At 48-month follow-up of older women and 40-month follow-up of older men, obesity was a risk factor for new coronary events in women and men by univariate analysis but not by multivariate analysis.\textsuperscript{10}

Obese persons who have had a MI must undergo weight reduction. Weight reduction is also a first approach to controlling hyperglycemia, mild hypertension, and dyslipidemia before placing persons on long-term drug therapy. Regular aerobic exercise should be added to diet in treating obesity.

**Physical Inactivity**

Exercise training programs have been found to improve endurance and functional capacity in older persons after MI.\textsuperscript{35} Moderate exercise programs suitable for older persons include walking, climbing stairs, swimming, and bicycling.

**ASPIRIN**

Randomized trials comprising 19,791 persons demonstrated that aspirin and other antiplatelet drugs administered to persons after MI reduced the incidence of recurrent MI, stroke, or vascular death by 25% at 27-month follow-up.\textsuperscript{36} The benefit of aspirin in decreasing MI, stroke, or vascular death in persons after MI was irrespective of age, sex, blood pressure, and diabetes mellitus.\textsuperscript{36}

Data from the Multicenter Study of Myocardial Ischemia in 936 persons enrolled 1 to 6 months after an acute MI (70% of persons) or unstable angina pectoris (30% of persons) showed at 23-month follow-up that the cardiac mortality rate was 1.6% for aspirin users and 5.4% for nonusers of aspirin.\textsuperscript{37} Cardiac mortality was decreased 90% in aspirin users who underwent thrombolytic therapy compared with nonusers of aspirin who underwent thrombolytic therapy.\textsuperscript{37}
The Coumadin Aspirin Reinfarction Study (CARS) randomized 8803 low-risk persons with previous MI to 160 mg aspirin daily, 80 mg aspirin plus 1 mg warfarin daily, or to 80 mg aspirin plus 3 mg warfarin daily. At 14-month follow-up, the combined incidence of cardiovascular death, recurrent MI, and stroke was similar in the three treatment groups. The incidence of mortality was similar in the three treatment groups. However, the incidence of nonfatal stroke was reduced by taking 160 mg aspirin daily.

On the basis of the available data, all persons should receive aspirin in a dose of 160 mg to 325 mg daily on Day 1 of an acute MI and continue this dose of aspirin for an indefinite period unless there is a specific contraindication to its use.

ANTICOAGULANTS

The routine use of warfarin after MI is controversial. However, three well controlled studies have demonstrated a decrease in mortality and/or morbidity in persons receiving long-term oral anticoagulation therapy after MI. The Sixty Plus Reinfarction Study Group reported at 2-year follow-up after MI of persons with a mean age 68 years that compared with placebo, acenocoumarin or phenprocoumon caused a 26% nonsignificant reduction in mortality, a 55% significant decrease in recurrent MI, and a 40% nonsignificant reduction in stroke. The Warfarin Reinfarction Study Group showed at 37-month follow-up after MI of persons aged 75 years or younger that compared with placebo, warfarin caused significant decreases in mortality (24%), recurrent MI (34%), and stroke (55%).

The CARS trial showed that after MI, the combined incidence of cardiovascular death, recurrent MI, and stroke and the incidence of mortality in 8803 low-risk persons were similar in persons treated with 160 mg aspirin daily, 80 mg aspirin plus 1 mg warfarin daily, or 80 mg aspirin plus 3 mg warfarin daily. The incidence of nonfatal stroke was lower in persons treated with 160 mg aspirin daily than in persons treated with 80 mg aspirin plus 1 mg warfarin daily or 80 mg aspirin plus 3 mg warfarin daily. On the basis of the available data, older persons treated with oral warfarin after MI should achieve an international normalized ratio of 2.0 to 3.0.

The American College of Cardiology/American Heart Association guidelines recommend as Class I indications for long-term oral anticoagulant therapy after MI:

1. Secondary prevention of MI in post-MI persons unable to tolerate daily aspirin
2. Post-MI persons with persistent atrial fibrillation
3. Post-MI persons with left ventricular thrombus

BETA-BLOCKERS

Beta-blockers are very effective antianginal and antiischemic agents and should be administered to all persons with angina pectoris or silent myocardial ischemia caused by CAD unless there are specific contraindications to their use. Teo et al. analyzed 55 randomized controlled trials comprising 53,268 patients that investigated the use of beta-blockers after MI. Beta-blockers significantly reduced mortality by 19% in these studies. A randomized, double-blind, placebo-controlled study of propranolol in high-risk survivors of acute MI at 12 Norwegian hospitals showed a 52% decrease in sudden cardiac death in persons treated with propranolol for 1 year.

Table 3 shows that metoprolol, timolol, and propranolol caused a greater reduction in
mortality after MI in older persons than in younger persons. The decrease in mortality after MI in persons treated with beta-blockers was due to both a reduction in sudden cardiac death and recurrent MI.46-48 A retrospective cohort study also showed that MI patients aged 60 to 89 years treated with metoprolol had an age-adjusted mortality reduction of 76%.49

| Table 3. Effect of Beta-Blockers on Mortality After Myocardial Infarction |

In the Beta-blocker Heart Attack Trial, propranolol use resulted in a 27% decrease in mortality in persons with a history of CHF and a 25% reduction in mortality in persons without CHF.50 In this study, propranolol caused a 47% decrease in sudden cardiac death in persons with a history of CHF and a 13% reduction in sudden cardiac death in persons without CHF.50

In the Beta-Blocker Pooling Project, results from nine studies comprising 3519 patients with CHF at the time of acute MI demonstrated that beta-blockers caused a 25% reduction in mortality.51 In the Multicenter Diltiazem Post-Infarction Trial, the 2.5-year risk of total mortality in persons with a left ventricular ejection fraction (LVEF) less than 30% was 24% for persons receiving beta-blockers (relative risk = .53, 95% CI, 0.44 to 0.95) versus 45% for persons not receiving beta-blockers.52 Beta-blockers have also been shown to decrease mortality in persons with CAD and CHF associated with a LVEF of 35% or less 53 or 40% or greater.54

A retrospective analysis of the use of beta-blockers after MI in a New Jersey Medicare population from 1987 to 1992 demonstrated that only 21% of older persons without contraindications to beta-blockers were treated with beta-blockers after MI.55 Older persons who were treated with beta-blockers after MI had a 43% reduction in 2-year mortality and a 22% decrease in 2-year cardiac hospital readmissions compared with older persons who were not treated with beta-blockers.55 Use of a calcium channel blocker instead of a beta-blocker after MI doubled the risk of mortality.55

Beta-blockers have also been shown to decrease mortality in older persons with complex ventricular arrhythmias after MI and a LVEF >=40%56 or <=40%.57 The reduction in mortality in older persons with heart disease and complex ventricular arrhythmias caused by propranolol is attributable more to an antiischemic effect than to an antiarrhythmic effect.58 In these older persons, propranolol also markedly reduced the circadian variation of ventricular arrhythmias,59 abolished the circadian variation of myocardial ischemia,60 and abolished the circadian variation of sudden cardiac death or fatal MI.61

A meta-analysis of trials also demonstrated that the use of beta-blockers after non-Q-wave MI is likely to decrease mortality and recurrent MI by 25%.62 Therefore, older persons with Q-wave MI or non-Q-wave MI without contraindications to beta-blockers should be treated with beta-blockers for at least 6 years after MI. Beta-blockers with intrinsic sympathomimetic activity should not be used. The American College of Cardiology/American Heart Association guidelines recommend that persons without a clear contraindication to beta-blocker therapy should receive beta-blockers within a few days of MI (if not initiated acutely) and continue them indefinitely.30

NITRATES

Long-acting nitrates are effective antiangiinal and antiischemic drugs.63 These drugs should be
prescribed after MI, along with beta-blockers, to persons who have angina pectoris. The dose of oral isosorbide dinitrate administered should be increased gradually to a dose of 30 to 40 mg given three times daily if tolerated. A 60-mg dose of isosorbide-5-mononitrate may also be administered once daily. To avoid nitrate tolerance, there should be a nitrate-free interval of 12 hours each day.64 Beta-blockers should be used to prevent angina pectoris and rebound myocardial ischemia during the nitrate-free interval. The medical therapy of angina pectoris in older persons is discussed in detail elsewhere.65

ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

Angiotensin-converting enzyme (ACE) inhibitors improve symptoms, quality of life, and exercise tolerance in persons with CHF and either an abnormal LVEF 66 or a normal LVEF.67 An overview of 32 randomized trials comprising 7105 patients with CHF demonstrated that ACE inhibitors decreased mortality by 23% and mortality or hospitalization for CHF by 35%.68 Three hundred fifty persons, mean age 75 years, with CHF and a LVEF 40% or greater were followed for 6 months.69 Of the 350 persons, 190 (54%) were treated with ACE inhibitors. Persons treated with ACE inhibitors had a nonsignificant 37% decrease in all-cause mortality and a 22% nonsignificant reduction in CHF rehospitalization.69 Persons who develop CHF after MI should be treated with ACE inhibitors unless there are specific contraindications to their use.

Table 4 shows that ACE inhibitors decrease mortality in persons after MI.70-73 In the Survival and Ventricular Enlargement Trial, asymptomatic persons with a LVEF of 40% or less treated with captopril 3 to 16 days after MI had at 42-month follow-up, compared with placebo, a 19% decrease in mortality, a 21% reduction in death from cardiovascular causes, a 37% decrease in development of severe CHF, a 22% reduction in development of CHF requiring hospitalization, and a 25% decrease in recurrent MI.70 Captopril reduced mortality independent of age, sex, blood pressure, LVEF, and use of thrombolytic therapy, aspirin, or beta-blockers.70

Table 4. Effect of Angiotensin-Converting Enzyme Inhibitors on Mortality in Persons After Myocardial Infarction (MI)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Mortality Reduction</th>
<th>CHF Hospitalization Reduction</th>
<th>Severe CHF Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Captopril</td>
<td>19%</td>
<td>21%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Although some cardiologists recommend administering ACE inhibitors to all persons after MI, the American College of Cardiology/American Heart Association guidelines do not support this.30 On the basis of the available data, ACE inhibitors should be administered after MI to older persons who have CHF, an anterior MI, or a LVEF 40% or less unless there are specific contraindications to their use.

CALCIUM CHANNEL BLOCKERS

Teo et al.43 analyzed randomized controlled trials comprising 20,342 persons that investigated the use of calcium channel blockers after MI. Mortality was insignificantly higher (relative risk = 1.04, 95% CI, 0.95 to 1.14) in persons treated with calcium channel blockers.43 A meta-analysis of randomized, clinical trials of the use of calcium channel blockers in persons with MI, unstable angina pectoris, and stable angina pectoris found that the relative risk for mortality in the trials using dihydropyridines such as nifedipine that increase heart rate was 1.16, (95% CI, 1.01 to 1.33).74 The calcium channel blockers diltiazem and verapamil, which decrease heart rate, had no effect on survival.74
Furberg et al. performed a meta-analysis of the effect of nifedipine on mortality in 16 randomized secondary prevention clinical trials in persons with CAD. In this study, the relative risk for mortality was 1.06 (95% CI, 0.89 to 1.27) for persons treated with 30 to 50 mg nifedipine daily, 1.18 (95% CI, 0.95 to 1.50) for persons treated with 60 mg nifedipine daily, and 2.83 (95% CI, 1.35 to 5.93) for persons treated with 80 mg nifedipine daily.

The Multicenter Diltiazem Postinfarction Trial showed at 25-month follow-up in persons after MI that compared with placebo, diltiazem caused no significant effect on mortality or recurrent MI. However, in persons with pulmonary congestion at baseline or a LVEF <40%, diltiazem caused an increase in new cardiac events (hazard ratios = 1.41, 95% CI, 1.01 to 1.96, and 1.31, 95% CI, 0.87 to 1.98, respectively). In this study, diltiazem also increased the incidence of late-onset CHF in persons with a LVEF less than 40%. Use of a calcium channel blocker instead of a beta-blocker after MI in a New Jersey Medicare population also doubled the risk of mortality.

No calcium channel blocker has been shown to improve survival after MI except in the subgroup of patients with normal LVEF treated with verapamil in the Danish Verapamil Infarction Trial II; therefore, calcium channel blockers should not be used in the treatment of persons after MI. However, if persons with previous MI have persistent angina pectoris despite treatment with beta-blockers and nitrates, a nondihydropyridine calcium channel blocker such as verapamil or diltiazem should be added to the therapeutic regimen if the LVEF is normal. If the LVEF is abnormal, amlopidine or felodipine should be added to the therapeutic regimen. The American College of Cardiology/American Heart Association guidelines state that there are no Class I indications for the use of calcium channel blockers after MI.

ANTIARRHYTHMIC THERAPY

Class I Drugs

A meta-analysis of 59 randomized controlled trials comprising 23,229 persons, including older persons, that investigated the use of quinidine, procainamide, disopyramide, imipramine, moricizine, lidocaine, tocainide, phenytoin, mexiletine, aprindine, encaainide, and flecaainide after MI showed that mortality was significantly higher in persons receiving class I antiarrhythmic drugs than in persons receiving no antiarrhythmic drugs (odds ratio = 1.14, 95% CI, 1.01 to 1.28). None of the 59 studies showed a decrease in mortality by class I antiarrhythmic drugs.

In the Cardiac Arrhythmia Suppression Trials I and II (38% of 2731 subjects were 66 to 79 years of age), older age increased the likelihood of adverse effects, including death, in persons receiving encaainide, flecaainide, or moricizine after MI. Compared with no antiarrhythmic drug, quinidine or procainamide did not reduce mortality in older adults (mean age 82 years) with CAD, normal or abnormal LVEF, and presence versus absence of ventricular tachycardia. On the basis of the available data, people should not receive class I antiarrhythmic drugs after MI.

D, L-Sotalol and D-Sotalol

Studies comparing the effect of d, l-sotalol with placebo on mortality in persons with complex ventricular arrhythmias have not been performed. Compared with placebo, d, l-sotalol did not decrease mortality in post-MI patients followed for 1 year. In the Survival with Oral d-Sotalol (SWORD) trial, 3121 survivors of MI, mean age 60 years, with a LVEF of 40% or less, were randomized to d-sotalol or placebo. Mortality was significantly higher at 148-day follow-up in persons treated with d-sotalol (5.0%) than in persons treated with placebo (3.1%). On the basis of the available data, d, l-sotalol and d-sotalol should not be used to treat persons after MI.

Amiodarone

In the European Myocardial Infarction Amiodarone Trial, 1486 survivors of MI with a LVEF 40% or less were randomized to amiodarone (743 patients) or to placebo (743 patients). At 2-year follow-up, 103 patients treated with amiodarone and 102 patients treated with placebo had died. In the Canadian Amiodarone Myocardial Infarction Arrhythmia Trial, 1202 survivors of MI with nonsustained ventricular tachycardia or complex ventricular arrhythmias were randomized to amiodarone or to placebo. Amiodarone was very effective in suppressing ventricular tachycardia and complex ventricular arrhythmias. However, the mortality rate at 1.8-year follow-up was not significantly different in the persons treated with amiodarone or placebo. In addition, early permanent discontinuation of the drug for reasons other than outcome events occurred in 36% of patients taking amiodarone.

In the Cardiac Arrest in Seattle: Conventional Versus Amiodarone Drug Evaluation Study, the incidence of pulmonary toxicity was 10% at 2 years in persons receiving amiodarone in a mean dose of 158 mg daily. The incidence of adverse effects from amiodarone also approaches 90% after 5 years of therapy. On the basis of the available data, amiodarone should not be used in the treatment of persons after MI.

**Beta-Blockers**

However, beta-blockers have been shown to decrease mortality in persons with nonsustained ventricular tachycardia or complex ventricular arrhythmias after MI in persons with normal or abnormal LVEF. On the basis of the available data, beta-blockers should be used in the treatment of older persons after MI, especially if nonsustained ventricular tachycardia or complex ventricular arrhythmias are present, unless there are specific contraindications to their use.

**Automatic Implantable Cardioverter-Defibrillator**

In the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial, 1016 persons, mean age 65 years, with a history of ventricular fibrillation or serious sustained ventricular tachycardia were randomized to an automatic implantable cardioverter-defibrillator (AICD) or to drug therapy with amiodarone or d,l-sotalol. Persons treated with an AICD had a 39% decrease in mortality at 1 year, a 27% reduction in mortality at 2 years, and a 31% decrease in mortality at 3 years. If patients have life-threatening ventricular tachycardia or ventricular fibrillation after MI, an AICD should be inserted. The efficacy of the AICD implanted for ventricular fibrillation or recurrent sustained ventricular tachycardia on survival is similar in older and younger persons.

The Multicenter Automatic Defibrillator Implantation Trial randomized 196 persons with prior MI, a LVEF 35% or less, a documented episode of asymptomatic nonsustained ventricular tachycardia, and inducible ventricular tachycardia or ventricular fibrillation not suppressed by intravenous propranolol or an equivalent drug at electrophysiologic study to conventional medical therapy or implantation of an AICD. At 27-month follow-up, persons treated with an AICD had a 54% decrease in mortality. These data favor considering the prophylactic implantation of an AICD in post-MI persons at very high risk for sudden cardiac death.

**HORMONE REPLACEMENT THERAPY**

Observational studies suggest that postmenopausal women who use estrogen are at lower risk for developing CAD than those who do not use estrogen. Progestins added to estrogen therapy prevent the excess risk of endometrial carcinoma caused by the unopposed effect of estrogen. Observational studies also suggest that estrogen/progestin regimens have a cardioprotective effect similar to that of estrogen alone.
Studies suggest that the most important mechanism for the cardioprotective effect of estrogen is raising serum HDL cholesterol levels. In the Postmenopausal Estrogen/Progestin Interventions trial, conjugated equine estrogens 0.625 mg daily plus cyclic micronized progesterone 200 mg/day for 12 days per month had the most favorable effect on serum HDL cholesterol with no excess risk of endometrial hyperplasia. In 58 postmenopausal women with serum total cholesterol levels greater than 250 mg/dL treated for 8 weeks with simvastatin and for 8 weeks with estrogen plus progestin, there was 14% reduction in serum total cholesterol with hormone therapy and a 26% decrease in serum total cholesterol with simvastatin, a 24% reduction in serum LDL cholesterol with hormone therapy and a 36% decrease in serum LDL cholesterol with simvastatin, a 7% increase in serum HDL cholesterol with hormone therapy and with simvastatin, and a 29% increase in serum triglycerides with hormone therapy and a 14% reduction in serum triglycerides with simvastatin.

Estrogen-associated changes in coagulation factors may also contribute to a reduction in coronary events. In the Postmenopausal Estrogen/Progestin Interventions trial, placebo was associated with a greater increase in mean fibrinogen than any of the hormone regimens. In addition, enhancement of endothelium-dependent vasodilatation by estrogen may contribute to a decrease in coronary events.

The Heart Estrogen/Progestin Replacement Study (HERS) is a secondary prevention study comparing double-blind placebo or hormonal therapy in postmenopausal women with documented CAD. The five-year duration of this study is scheduled to end in July 1998. This prospective study will provide us with the data showing whether hormonal therapy reduces coronary events in postmenopausal women with CAD. Until data from this study are available, use of an estrogen/progestin regimen is recommended in the treatment of postmenopausal women with MI unless they are at increased risk for developing breast cancer.

REVASCULARIZATION

Medical therapy alone is the preferred treatment in older persons after MI. The two indications for revascularization in older persons after MI are prolongation of life and relief of unacceptable symptoms despite optimal medical management. In persons older than 80 years of age, the goal is less to prolong life than it is to improve the quality of life. If revascularization is performed, aggressive medical therapy must be continued. If revascularization is necessary to achieve the goals of therapy, and if percutaneous transluminal coronary angioplasty (PTCA) can achieve these goals as well as coronary artery bypass graft surgery (CABGS), then PTCA should be performed.

The 5-year survival rate for 522 persons 75 years of age and older undergoing CABGS was 73%. The 5-year survival rate for 154 persons between 80 and 89 years of age who underwent CABGS was 62%. Three-year survivals of persons older than 75 years of age undergoing PTCA have been reported to be 83%, 87%, and 86% respectively. Indications for preferring CABGS or PTCA in older persons who require revascularization after MI are discussed in detail elsewhere.

ADDENDUM

Since this paper was accepted for publication, the results from HERS have been published (Hulsey S, Grady D, Bush T et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. JAMA 1998;280:605-613). At 4.1-year follow-up, there were no significant differences between hormonal therapy and placebo in the primary outcome (nonfatal MI or CAD death) or in any of the secondary cardiovascular outcomes. Women taking hormonal therapy had a higher incidence of venous thromboembolic
events (relative hazard = 2.89, 95% CI, 1.50 to 5.58) and a higher incidence of gallbladder
disease (relative hazard = 1.38, 95% CI, 1.00 to 1.92) than women prescribed placebo. On the
basis of these data, the author cannot recommend the use of hormonal therapy in the treatment of
postmenopausal women with MI.

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Section Description:

THERAPY OF OLDER PEOPLE FOR MYOCARDIAL INFARCTION
