

Ischemic heart disease in the older patient

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Advanced age is not only a powerful predictor for the development of ischemic heart disease (IHD), it also becomes, in established IHD, the most important risk factor for morbidity and mortality. The reasons lie in the increased comorbidity and frequently atypical presentation of IHD in the elderly, making diagnosis more challenging and often delaying the initiation of therapy. Age-related changes in the cardiovascular system compound the risk by making compensation more difficult once ischemic damage occurs. Even though many randomized controlled trials have enrolled relatively few older patients, the management of acute coronary syndromes in this population should still be informed by the resulting guidelines. Therapy in older patients with acute coronary syndrome has to be balanced against their known propensity to bleeding risk. Dose adjustments based on creatinine clearance can optimize benefit and decrease this risk. Given the increase in morbidity and mortality with acute coronary syndromes in the elderly, aggressive risk factor modification is vital for decreasing recurrent events. Appreciation of the benefits of such therapies in the older patient with IHD will hopefully decrease the high morbidity and mortality risk.

Advanced age is hugely relevant both to the development and consequences of ischemic heart disease (IHD), and to the treatment response. Over 85% of cardiovascular deaths occur in the elderly, along with most cases of congestive heart failure, atrial fibrillation, and hypertension. The consequences of IHD are also more severe, including fatal and nonfatal outcome, stable and unstable angina, and acute myocardial infarction (MI). Age is also commonly the most important determinant of the efficacy of aggressive therapeutic intervention, including angioplasty and bypass. The impact of advanced age on the development and consequences of IHD can be attributed in part to increased comorbidity, the severity and complexity of cardiac disease, and frequency of treatment complications. However, even after adjusting for such factors, there remains a significant and independent effect of age. The purpose of this article is to describe the known mechanisms of the age effect, estimate its magnitude in different ischemic settings, and review the management of IHD in the rapidly growing elderly population.

Studies of cardiovascular physiology in animal models and humans demonstrate several important changes in vascular and cardiac properties with age that increase the likelihood of atherosclerosis and decrease cardiovascular reserve.¹⁻⁴ Increases in central vascular stiffness (due to altered elastin and collagen) and in advanced glycation end-products elevate systolic and pulse pressures, and lower diastolic pressure.^{5,6} Elevated systolic pressure increases workload during left ventricular ejection, and decreases the efficiency of ventricular/vascular coupling at rest and during exercise.⁷ It is also responsible for isolated systolic hypertension, which is the most widespread reversible risk factor for IHD in the elderly.⁸⁻¹⁰ Lower diastolic pressure decreases coronary perfusion, particularly in the fixed IHD setting. Another age-related change is increased intimal proliferation, which is an important and independent cardiovascular risk factor.¹¹ Although it is sometimes considered as subclinical atheroscle-

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rosis, it also occurs in animal models in the absence of atherosclerosis. Endothelial dysfunction is one of the most important age-related changes in vascular properties and is believed to be involved in nearly every step in the development and manifestations of IHD.^{12,13} In men, the inflection point of change occurs at the beginning of the fifth decade, and for women in the seventh decade. Endothelial dysfunction is evidenced by a decreased response of the nonatherosclerotic brachial artery to endothelial-mediated induction of vasodilators. Increases in adhesion molecule expression and permeability to low-density lipoprotein (LDL) and macrophages are associated with smooth muscle cell migration and inappropriate vasoconstriction, resulting in rupture of the fibrous atherosclerotic cap. Endothelial function is believed to be largely dependent on the bioavailability of nitric oxide (NO), a coproduct of the conversion of L-arginine to citrulline catalyzed by endothelial NO synthase (eNOS).¹⁴ It is unlikely that a decrease in L-arginine availability is a contributing factor to decreased NO, since intracellular L-arginine levels are high and long-term supplementa-

tion is not associated with improved indices of vascular function or clinical events.^{15,16} However, eNOS activity decreases with age,¹⁷ and arginase I- and II-mediated conversion of L-arginine to urea and citrulline may decrease NO production in aged vessels. An increase in NO metabolism to peroxynitrite may also be associated with aging. There is an increase in arginase activity and peroxynitrite levels in animal models of vascular aging, and both are associated with mediators related to inflammation and oxidative stress.^{18,19}

Primary and secondary IHD prevention has been mainly directed at decreasing factors that cause vascular injury (eg, hypertension, hyperlipidemia, smoking). However, it is becoming evident that it is equally important to address existing mechanisms that repair, regenerate and/or restore injured or damaged vascular cells. Mature endothelial cells from regions neighboring injured vascular tissue are known to participate in vasculogenesis. These replicative mechanisms are likely to be more limited in older vascular cells due to telomere shortening, decreased telomerase activity,

SELECTED ABBREVIATIONS AND ACRONYMS

ACE	angiotensin-converting enzyme	MI	myocardial infarction
ACS	acute coronary syndrome	NO	nitric oxide
ACUITY	Acute Catheterization and Urgent Intervention Trial strategy	NSTE-ACS	non-ST-segment-elevation acute coronary syndrome
ARB	angiotensin receptor blocker	OASIS-5	Fifth Organization to Assess Strategies in Acute Ischemic Syndromes
CABG	coronary artery bypass graft	OAT	Occluded Artery Trial
CARE	Cholesterol And Recurrent Events	PCI	percutaneous coronary intervention
CCP	Cooperative Cardiovascular Project	PROVE-IT	PRavastatin Or atorVastatin Evaluation and Infection Therapy
CD34	cluster of differentiation 34	PURSUIT	Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin (eptifibatide) Therapy
COMMIT	Clopidogrel and Metoprolol in Myocardial Infarction Trial	SHEP	Systolic Hypertension in the Elderly Program
eNOS	endothelial nitric oxide synthase	STEMI	ST-segment-elevation myocardial infarction
EPESE	Established Populations for the Epidemiologic Studies of the Elderly	SYNERGY	Superior Yield of the New strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa inhibitor
GUSTO-I	Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded arteries	Syst-Eur	Systolic Hypertension in Europe
HDL	high-density lipoprotein	UFH	unfractionated heparin
HIT	heparin-induced thrombocytopenia	VEGFR-2	vascular endothelial growth factor receptor-2
HMG-CoA	3-hydroxy-3-methylglutaryl-CoA		
HPS	Heart Protection Study		
IHD	ischemic heart disease		
LDL	low-density lipoprotein		
LMWH	low-molecular-weight heparin		

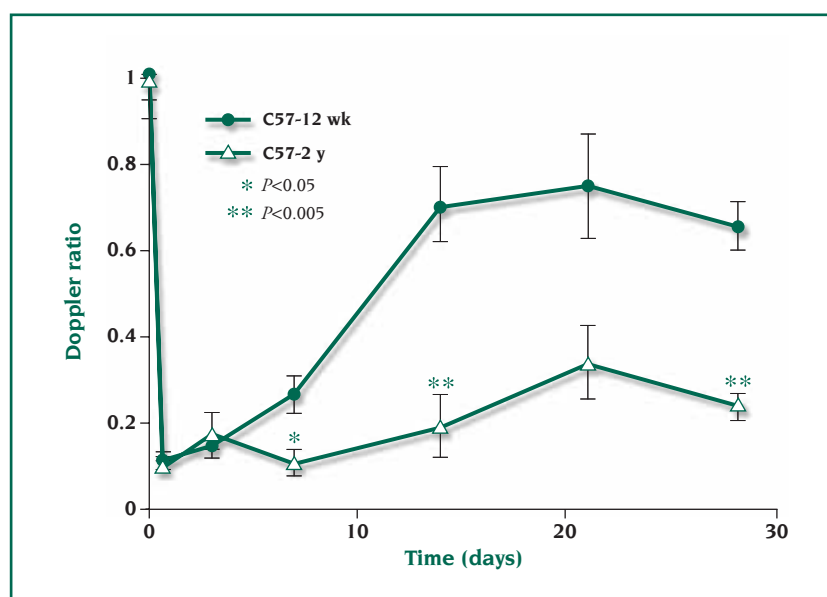


Figure 1. Relationship of age and collateral blood flow after femoral artery resection in young versus old mice, showing significantly greater femoral artery Doppler flow in young mice.

Abbreviations: C57, mouse strain; w, weeks; y, years.

Modified from reference 22: Rivard A, Fabre JE, Silver M, et al. Age-dependent impairment of angiogenesis. *Circulation*. 1999;99:111-120. Copyright © 1999, American Heart Association, Inc.

and oxidative damage.^{20,21} It is now recognized that new blood vessels are also formed by cells from distant sites, primarily bone marrow. There appears to be a significant age-related impairment in this ability, as demonstrated in studies in which angiogenesis following induced hindlimb ischemia was significantly diminished in an older animal model (*Figure 1*).²² In addition, in murine models of accelerated atherosclerosis, transplantation of bone-marrow-derived cells from young, but not old, animals was associated with significantly decreased aortic atherosclerosis.²³ Cells most closely associated with vascular repair are termed endothelial progenitor cells and are usually identified by the presence of both cluster of differentiation 34 (CD34) and vascular endothelial growth factor receptor-2 (VEGFR-2) markers.²⁴ The number of these cells and their ability to give rise to colony-forming units are independent predictors of adverse outcome in patients with established IHD.^{25,26} In humans, age-related decreases in endothelial progenitor cell number and function have been described in patients undergoing coronary artery bypass graft (CABG) surgery.^{27,28} In one animal study, in which circulatory systems were shared between two animals, the pairing of an older with a younger animal restored the older animal's progenitor cell count almost to the level of that in the younger animal.²⁹ Thus, soluble factors from the young environment can reverse age-related progenitor cell changes present in the old environment.

In summary, important age-related vascular changes increase the likelihood of atherosclerotic disease and decrease the repair potential. Endothelial dysfunction

is probably the most important factor contributing to the development of atherosclerosis. Although mechanisms are still being explored, increased inflammation and/or oxidative stress appear to be important underlying phenomena. In terms of repair, important age-related differences have been identified, but these do not appear related to intrinsic decreased progenitor cell number and/or function, and may be susceptible to modulation.

Age-related changes also limit cardiac muscle reserve following ischemic insult.¹ Altered diastolic properties that increase early left ventricular end-diastolic pressure probably raise left atrial pressure. This is particularly evident during tachycardia but may also occur at normal heart rates, thereby increasing the risk of pulmonary edema, atrial arrhythmias, and congestive heart failure. The age-related changes include alterations in active state properties. Changes in myosin isoforms and sarcoplasmic reticulum function delay calcium removal from troponin and increase heterogeneity in the timing of relaxation. There are also changes in passive properties, including increased fibrosis. This delays early diastolic filling. Thus early left ventricular filling pressure has to be higher in the older individual to achieve the same stroke volume from the same end-diastolic volume.

One of the most important changes limiting cardiac muscle reserve is decreased β -adrenergic sympathetic responsiveness. This has been demonstrated in isolated trabeculae and whole heart animal models as well as in healthy subjects. It can be partly attributed

to decreases in β_1 -receptors (in both absolute number and the proportion in the high affinity state), as well as to signaling changes distal to the receptor. These factors probably decrease the ability of noninfarcted myocardium to achieve the workload necessary to compensate for ischemic tissue damage. There are also age-related changes in the healing process that decrease the ability to form scar tissue resistant to infarct expansion and rupture. Important phenomena known to decrease ischemic injury are pre- and post-conditioning. In this paradigm, brief periods of ischemia before or after ischemic insult severely limit resultant damage. The mechanisms responsible are unclear, but the preconditioning effect is markedly attenuated or absent in older patients with IHD, while the postconditioning effect is lost in aging animal models.³⁰⁻³²

It is now recognized that heart muscle is not terminally differentiated. Very small numbers of endogenous cardiac progenitor cells can replace cardiomyocytes during an individual's normal lifespan.³³ These progenitor cells can self-renew or differentiate into smooth muscle, endothelial, or cardiac cells. They can improve cardiac performance when transplanted into syngeneic animals with infarction.^{33,34} Bone marrow cells also traffic to the heart and this phenomenon is significantly augmented in the presence of ischemic injury. It is probably a response to the release of proliferating and homing signals from injured tissue.³⁵ Trafficking may be at least partly responsible for the gradual improvement in left ventricular function and shrinkage of infarct size that occur in the first postinfarction weeks. Nevertheless, this repair system is unable to restore normal structure and function after significant infarction, and is even less effective in most older individuals.^{36,37}

The age-related decrease in repair potential may also be explained by the increased comorbidity associated with advanced age. For example, progenitor cells from patients with diabetes³⁸ and congestive heart failure are less able to regenerate. Limits on progenitor cell number and function are also believed to be intrinsic to the aging process.³⁷ The colony-forming activity of bone marrow-derived mesenchymal stem cells is decreased in animal models of aging and the replicative capacity of these cells is limited by similar mechanisms to those described above for endothelial cells.³⁹ In aged mice, cardiac stem cell apoptosis is also increased.⁴⁰ Administration of progenitor cells enhances myocardial function following infarction in animal models. The mechanisms responsible for this benefit are currently not clear. In addition to differentiation and cell fusion, secretion of paracrine factors from these cells en-

hances intrinsic progenitor cell migration, proliferation, and differentiation. Growth factors released from other sites also enhance these processes. Age-related decreases in several such growth factors, including platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and estrogen, may also limit the production, homing, and function of progenitor cells.^{41,42} Additionally, older animals fail to respond to the exogenous cytokines (granulocyte colony-stimulating factor and stem cell factor) that improve endogenous repair processes in young animals.⁴³

RISK FACTORS FOR ISCHEMIC HEART DISEASE IN OLDER PATIENTS

In general, the known cardiovascular risk factors originally identified in the Framingham and other observational studies apply equally in the elderly, except that their impact is more marked, while the effect on survival, although significant for most interventions, diminishes with age. In an elderly population, it is unrealistic to expect a long-term survival effect, meaning that it is especially important to focus on quality of life. This is not only significant for patients themselves, but also for their families and caregivers.

Hypertension

Hypertension is the most important reversible risk factor in the older population due to its prevalence and impact on mortality, IHD, and quality of life indices such as stroke and dementia. Prevalence exceeds 60% in the over-65s. The predominant presentation is isolated systolic hypertension caused by increased vascular stiffness. Analysis in over 1 million individuals reported a logarithmic increase in vascular events with increasing systolic blood pressure; it was steepest in the elderly.⁴⁴ Two major trials have shown significant decreases in cardiovascular events with pharmacologic therapy in older individuals with isolated systolic hypertension. As first-line therapies the Systolic Hypertension in the Elderly Program (SHEP) used diuretics, and the Systolic Hypertension in Europe (Syst-Eur) trial a long-acting dihydropyridine calcium antagonist.^{45,46} They reported reductions in treated groups versus placebo of 27% in MI and coronary deaths, and 26% in cardiac events, respectively. Treatment was also associated with significant reductions in stroke and a 50% decrease in Alzheimer's and non-Alzheimer's dementia.⁴⁷ A more recent larger study found no difference in primary cardiovascular end point when patients were randomized to a diuretic, angiotensin-converting enzyme (ACE) inhibitor, or long-acting calcium antago-



nist.⁴⁸ The selection of an agent is often dependent on comorbidity. A β -blocker is often recommended in the presence of active or recent ischemia, and an ACE inhibitor in ischemic left ventricular dysfunction (or angiotensin receptor blocker [ARB] if the ACE inhibitor is not tolerated). However, achieving the blood pressure goal using a cost-effective agent acceptable to the patient is more important than the particular agent used.

Hyperlipidemia

Hyperlipidemia is also common in the elderly. Although earlier studies did not adequately characterize its impact on coronary events, recent large studies have shown the benefit of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors for both the primary and secondary prevention of IHD. This topic is fully reviewed in Lynne Braun's article on lipid management and the elderly, in the present issue.

Smoking

Although smoking is less prevalent in the older population, it is associated with an increased risk for coronary events. Thus, the Established Populations for the Epidemiologic Studies of the Elderly (EPSE) project estimated the relative risk of cardiovascular death for current smokers versus never-smokers as 2.0.⁴⁹ Smoking is also associated with other ischemic outcomes, including stroke and peripheral vascular disease. Smoking cessation is associated with significant clinical benefit, and those either side of 70 years enjoy a similar relative reduction in infarction risk.⁵⁰ Thus it is important to emphasize to older individuals that by stopping smoking they can significantly reduce their stroke, MI, and other risks regardless of how long they smoked. Unfortunately, this is a difficult goal for most individuals. Success is best achieved with combined behavioral and pharmacologic approaches. Multiple attempts may be necessary. For the patient with known IHD, nicotine replacement products are not usually advised; the non-nicotine options of bupropion and varenicline are preferred. In randomized controlled short- and long-term trials, varenicline was associated with higher abstinence rates (40%-45% and 20%-25%, respectively).⁵¹

Diabetes

The prevalence of diabetes and insulin resistance increases with age. Surveys conducted nearly 20 years ago estimated that over 13% of subjects aged ≥ 75 years had diabetes and another 14% had impaired glucose tolerance.⁵² These prevalences have probably risen

higher since due to increases in sedentary lifestyles and obesity. The cardiovascular complications of diabetes, primarily IHD, are responsible for most deaths in this population. Although the cardiovascular benefits of tight glycemic control in patients with insulin resistance diabetes are not well defined, a hemoglobin A_{1c} level below 7% is generally recommended. Most importantly, healthy lifestyle factors should be emphasized and blood pressure and lipid goals more vigorously pursued in this population.

DIAGNOSIS AND TREATMENT OF ISCHEMIC HEART DISEASE

Stable ischemic heart disease

Diagnosis

Despite the greater likelihood of IHD in the older population, symptoms may be less classic and evident. An older person is more likely to present with dyspnea than typical exertional chest pain. Indeed, symptoms of exertion may be less relevant due to activity limitations imposed by comorbidity. If IHD is suspected, stress testing may be confounded by preexisting ST-T-segment abnormalities, in which case imaging is useful, in particular stress echocardiography if the patient is echogenic. Testing may also be hindered by an inability to exercise to 90% of predicted maximum heart rate, in which case pharmacologic rather than exercise stress is employed, usually with dobutamine or dipyridamole (especially in patients on β -blockers). The sensitivity of such tests increases with age, up to 80% to 90%, but specificity declines, to about 70%.⁵³ In addition, the likelihood of a false negative test increases in the elderly, while pharmacologic tests do not provide a functional estimate of IHD. Patients with a recent change in anginal pattern should also be investigated for potentially reversible factors, such as apathetic hyperthyroidism, new arrhythmias (particularly atrial fibrillation), anemia, and infection.

Pharmacologic therapy

A recent large randomized trial in stable angina patients with at least 70% coronary stenosis, documented ischemia, and anatomy suitable for angioplasty compared attempted optimal medical therapy alone versus optimal medical therapy plus percutaneous angioplasty. It found no differences in the primary end point of all-cause mortality and non-fatal MI over a median follow-up of 4.6 years.⁵⁴ In the 904 patients older than 65 years, the primary end point event rates were 22% on medical therapy alone and 24% on medical therapy plus angioplasty.

The therapy used in this study defined current pharmacologic goals in stable angina and included aspirin, a long-acting β -blocker, dihydropyridine calcium channel blocker, and long-acting nitroglycerin alone or in combination, an HMG-CoA reductase inhibitor with an LDL goal of 60-85 mg/dL, a fibrate and/or niacin preparation with a high-density lipoprotein (HDL) goal of 40 mg/dL or higher, and a triglyceride goal of <150 mg/dL. The bleeding risk with aspirin increases with dose and age; increasing the dose from 75 to 325 mg/day provides no significant additional benefit, although it is not unreasonable to use up to 162 mg/day. Clopidogrel can be used in patients intolerant of aspirin.

Choice of β -blocker depends on comedication, concomitant renal or hepatic impairment (favoring hydrophilic and lipophilic agents, respectively), the requirement for relative β_1 specificity in those with obstructive pulmonary disease, and half-life. Ophthalmic β -blockers are commonly used in the older population and may add to the effect of oral agents. For patients already on β -blocker therapy, a dihydropyridine calcium antagonist is preferred, while a nondihydropyridine is preferred in those not receiving a β -blocker. It is important to assess the blood pressure response, including orthostatic changes, whenever starting a patient on β -blocker or calcium antagonist, and when changing the dose. Long-acting nitrates can be tried, although intolerance is common. Trimetazidine, a metabolic agent with anti-ischemic properties due to inhibition of long-chain fatty acid oxidation, can improve angina when added to standard therapies. Creatine clearance in the elderly patient with angina should be calculated prior to initiation.⁵⁴ Patients should be instructed in the proper use of sublingual nitroglycerin, particularly as a prophylactic before undertaking an activity likely to cause angina. It is important to warn of the dangers of combining nitroglycerin with a phosphodiesterase-5 inhibitor for the erectile dysfunction that is more common in the elderly. In patients with stable coronary disease, the addition of the ACE inhibitor perindopril to standard medical therapy reduces the 4-year risk of cardiovascular death, myocardial infarction, or cardiac arrest by 20% compared with matching placebo. This benefit was also notable in the 3831 subjects above the age of 65 years who were part of the study.⁵⁵ Other important measures include lifestyle modifications, eg, weight loss if indicated, and exercise programs, which should initially be supervised.

Revascularization

An initial strategy of revascularization can be pursued in patients with suitable anatomy and without in-

creased risk due to comorbidity. It should also be considered in patients who continue to experience ischemia despite medical therapy. In general, advanced age is associated with increased CABG mortality and morbidity, including stroke, dementia, and long-term disability. Thus although CABG may be associated with more complete and longer-lasting revascularization, percutaneous angioplasty or a hybrid approach, combining angioplasty with minimally invasive bypass surgery, should be considered if the anatomy is suitable.⁵⁷

Preexisting limited mobility may also influence the choice of therapies, since revascularization may not improve a physical activity status already compromised by other conditions, eg, arthritis or stroke.

Procedural success with percutaneous coronary intervention (PCI) is generally high ($\geq 90\%$) in older patients with appropriate anatomy, and associated with a low complication rate.⁵⁸ In stable angina, adverse outcome is most likely in patients with renal insufficiency, low ejection fraction, age over 85 years, inability to achieve complete revascularization, and coexisting diabetes.⁵⁹ Recommendations regarding the short and longer-term use of dual antiplatelet therapy for patients with drug-eluting stents apply in equal measure to the elderly.

The increasing success of medical and catheter-based therapy for IHD has increased the number of older patients presenting for bypass and other surgical procedures. Although outcomes are generally worse without surgery in the elderly, predictors of early adverse outcome in stable patients include combined procedures (eg, valve and bypass surgery), advanced age, impaired left ventricular function, and comorbidity, particularly renal failure and pulmonary disease.⁶⁰ Stroke risk is also increased in those with proximal aortic calcification and pre-existing cerebrovascular disease. Thus preoperative assessment should focus on pulmonary and renal function, cerebrovascular status, as well as the routine history, physical examination, chest x-ray, and laboratory tests. Postoperative care should include measures to decrease the likelihood of delirium, pneumonia, embolism, and bedsores.

Acute coronary syndromes

Clinical decision-making in elderly with an acute coronary syndrome (ACS) is complicated by the exclusion or under-representation of patients aged ≥ 75



years in many trials of relevant therapies or strategies. Mean population age in such trials has typically been several years below that of registry patients.⁶¹ Comorbidity such as chronic renal disease is also more common in ACS registries than in clinical trials.

This makes certain cardiovascular therapies and diagnostic tests more challenging in the elderly. A high clinical index of suspicion plus careful attention to the appropriate diagnostic tests and therapies are therefore especially important in assessing, diagnosing, and treating ACS in this population.

Non-ST-segment–elevation acute coronary syndrome (NSTEMI-ACS)

Diagnosis

The incidence of MI in the elderly has increased over the last 15 years, particularly in older women.⁶² Non-ST-segment–elevation acute coronary syndrome (NSTEMI-ACS) is more often diagnosed in older than younger patients. Such older patients are more likely to be female and to have comorbidity such as angina, heart failure, hypertension, and diabetes.^{63,64} As in stable IHD, older ACS patients are more likely to present with atypical symptoms of acute myocardial ischemia and infarction, such as shortness of breath, confusion, and failure to thrive. Almost one-half of MI in the elderly goes clinically unrecognized.⁶⁵ Such atypical presentations delay diagnosis and treatment initiation, thus helping to account for the elevated in-hospital mortality. A high index of suspicion for NSTEMI-ACS is mandatory in this age group.

Prognosis

Age is a powerful independent predictor of short- and long-term morbidity and mortality in NSTEMI-ACS.⁶⁶⁻⁶⁸ The Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin (eptifibatid) Therapy (PURSUIT) trial in 9461 patients with NSTEMI-ACS showed an increase in 6-month mortality from 2% in patients <50 years of age to 11% in those aged 70-79 years, and to 19% in those aged ≥80 years.⁶⁸ Elderly patients with NSTEMI-ACS also have significantly higher incidences of cardiogenic shock and heart failure than their younger counterparts.^{69,70}

The high morbidity and mortality associated with ACS in the elderly dictate an aggressive approach to management. However, the evidence on which to base the care of elderly with NSTEMI-ACS is limited by the few patients above 75 years of age enrolled into clinical trials.⁷¹ Even ACS trials with no age restrictions usually

exclude elderly patients with comorbidity, such as renal insufficiency or cerebrovascular disease.⁷² Thus, guidelines for treating elderly ACS patients are often based on limited information.

Pharmacologic therapy

Large registry cohorts show that most patients admitted with NSTEMI-ACS are aged ≥65 years; 38% are aged ≥75 years, and 11% ≥85 years.^{61,73} As age advances, recommendations about contraindicated treatments become more frequent, especially for glycoprotein IIb/IIIa antagonists. Nevertheless, even in patients without stated contraindications, in-hospital use of aspirin, β-blockers, and anticoagulation agents decreases with increasing age.⁷³ Early invasive approaches to NSTEMI-ACS management are also reduced with advancing age, with only 40% of patients above 75 years of age proceeding to early catheterization. Decreased utilization of medications and procedures in elderly with ACS is mirrored by escalating in-hospital mortality, which is 2.5- and 3-fold higher in the 75-84 and ≥85 year age groups, respectively, than in under-65's.^{61,71} As guideline recommended therapies are used more commonly in-hospital and at discharge, the risk of in-hospital and short-term death is lowered in patients aged ≥75 years.⁷⁴

Antiplatelet and antithrombotic therapy in non-ST-segment–elevation acute coronary syndrome

In elderly patients with NSTEMI-ACS, antiplatelet therapy initiated on hospital admission decreases the number of events, while aspirin in daily doses from 75 mg to 1300 mg decreases short-term death and MI.⁷⁵⁻⁷⁸ In the Cooperative Cardiovascular Project (CCP) that reviewed over 10 000 MI patients aged ≥65 years, aspirin use reduced 30-day mortality by 22%.⁷⁹ Aspirin therapy for NSTEMI-ACS appears as effective in preventing MI and death in elderly as in younger patients. Therefore, unless contraindicated, NSTEMI-ACS patients should receive nonenteric (rapidly absorbed) aspirin at doses from 162 to 325 mg as soon as possible after admission.⁸⁰ After discharge, the daily dose should be reduced to between 75 mg and 162 mg to lower bleeding risk.⁸¹ In elderly patients treated with PCI and a bare metal stent, the aspirin dose should be lowered 1 month after stenting, and not for 3 to 6 months in those given a drug-eluting stent.⁸⁰

The thienopyridine derivative, clopidogrel, was evaluated in 12 562 patients with NSTEMI-ACS, all treated with aspirin.⁸² Treatment for a mean 9 months reduced the composite primary end point of cardiovascular mortality, nonfatal MI, or stroke by 20% versus placebo. This

benefit was also evident in the >65-year subgroup (n=6208). Thus in elderly patients with NSTEMI-ACS with low bleeding risk, clopidogrel added to aspirin for up to 1 year reduces future cardiovascular events. Chronic clopidogrel therapy is also indicated in elderly who are hypersensitive or intolerant to aspirin. Older patients in whom initially conservative management is indicated should receive a loading dose of clopidogrel 300 mg on admission followed by 75 mg daily. If the initial strategy is invasive, antiplatelet therapy in addition to aspirin is recommended prior to angiography. Current choices include clopidogrel, a glycoprotein IIb/IIIa inhibitor, or both.⁸⁰ PCI outcomes are likely to be improved by a clopidogrel loading dose given at least 6 hours, and preferably at least 15 hours, before the procedure.^{83,84} Improved outcomes in elderly NSTEMI-ACS patients treated with clopidogrel prior to angiography must be weighed against the increased bleeding risk in the 10% to 11% of patients requiring CABG. A 5-day interval between a clopidogrel dose and surgery is recommended in order to reduce the bleeding risk.^{85,86}

Studies show that the addition of a parenteral glycoprotein IIb/IIIa inhibitor to standard anti-ischemic therapy including aspirin and heparin reduces short-term risks of death, MI, and refractory angina.⁸⁷⁻⁸⁹ The effect of a glycoprotein IIb/IIIa antagonist is consistent across age groups and is most beneficial in higher-risk patients, including those with positive troponin, ST-segment depression, and indications for coronary revascularization. In (positive troponin) patients undergoing PCI, the addition of a glycoprotein IIb/IIIa antagonist to aspirin, a loading dose of clopidogrel, and heparin reduces the 30-day rates of death, MI, and urgent infarct-related artery revascularization.⁹⁰ Bleeding is more common with glycoprotein IIb/IIIa inhibitor therapy than with placebo, although there is no increase in the risk of cerebrovascular accident. Although it is important to monitor creatinine clearance prior to dosing in the elderly, due to the frequent need for dose adjustments, age should not exclude the addition of a glycoprotein IIb/IIIa inhibitor to standard anti-ischemic therapy for NSTEMI-ACS. This is particularly the case in higher-risk elderly proceeding to coronary revascularization.

Four anticoagulants recently studied in NSTEMI-ACS patients include unfractionated heparin (UFH), low-molecular-weight heparin (LMWH), the direct thrombin inhibitor bivalirudin, and the factor Xa inhibitor, fondaparinux. The Superior Yield of the New strategy of Enoxaparin, Revascularization and Glycoprotein IIb/IIIa

inhibitor (SYNERGY) study randomized 10 000 high-risk patients (NSTEMI-ACS plus age >60 years) due for coronary revascularization to UFH or the LMWH enoxaparin, in addition to standard aspirin and antiplatelet therapy.⁹¹ The primary end point of 30-day death or MI was similar in both groups. Bleeding risk was slightly higher in the enoxaparin group. The Fifth Organization to Assess Strategies for Ischemic Syndromes (OASIS 5) trial randomized over 20 000 NSTEMI-ACS patients, most managed medically, to enoxaparin or fondaparinux for 6 days.⁹² The primary end points of death, MI, or refractory ischemia at 9 days were similar in both groups. Results were also similar in a subgroup of approximately 12 000 subjects aged ≥ 65 years. Major bleeding was significantly lower in fondaparinux patients, significantly reducing the secondary end point of 30-day mortality. The Acute Catheterization and Urgent Intervention Trial Strategy (ACUITY) randomized nearly 14 000 NSTEMI-ACS patients, median age 63 years, to heparin plus glycoprotein IIb/IIIa inhibitor, the direct thrombin inhibitor bivalirudin plus glycoprotein IIb/IIIa inhibitor, or bivalirudin alone.⁹³ In all patients the treatment goal was an invasive strategy. Patients treated with heparin plus glycoprotein IIb/IIIa inhibitor or bivalirudin alone had similar ischemic events at 30 days. The latter group had a significantly lower risk of major bleeding, suggesting that net clinical outcome was best with bivalirudin. Subgroup analyses indicated that patients treated with bivalirudin should also be treated with a thienopyridine to minimize ischemic risk.

The choice of anticoagulant for elderly patients with NSTEMI-ACS depends on bleeding risk and management strategy (*Table I*). In candidates for invasive therapy, enoxaparin, UFH, or bivalirudin appear appropriate. Patients treated with bivalirudin are unlikely to require routine glycoprotein IIb/IIIa inhibitor therapy, but should be given a thienopyridine. In those managed conservatively, enoxaparin or fondaparinux appear reasonable options, given their ease of use, especially the lower risk of bleeding with fondaparinux.⁸⁰ Although antithrombotic and antiplatelet drugs reduce cardiovascular events in elderly patients with ACS, they must be used judiciously, due to the increased bleeding risk in this age group.⁹⁴ Elderly with NSTEMI-ACS are often overdosed with anticoagulants and glycoprotein IIb/IIIa inhibitors, resulting in increased major bleeding risk, hospital stay, and in-hospital mortality.⁹⁵ The most common cause of overdosing is failure to appreciate the dose adjustments required for antithrombotic agents, and several glycoprotein IIb/IIIa inhibitors, by the reduced creatinine clearance that is so common in elderly.⁹⁵



Agent	Pros	Cons
UFH	Long history of use Readily measurable effect Reference therapy (standard against which new therapies are compared)	Variable anticoagulant response Intravenous use HIT
LMWH	Easy to use, subcutaneous Less platelet activation than with UFH Excellent bioavailability Good for conservative management	Effect not readily measurable No antidote Unusable with HIT Dose needs adjustment in renal failure
Bivalirudin (direct thrombin inhibitor)	Readily measurable effect No HIT Less platelet activation, may avoid use of glycoprotein IIb/IIIa inhibitors	Clopidogrel pretreatment may be needed to minimize ischemic events Only studied in ACS patients proceeding to PCI Dose needs adjustment in renal failure Intravenous administration
Fondaparinux (factor Xa inhibitor)	Easy to use, subcutaneous Less bleeding than with LMWH Excellent bioavailability Good for conservative management No HIT	Long half-life, no antidote Effect not readily measurable May need intravenous heparin if proceeding to PCI

Table 1. Anticoagulant use in NSTEMI-ACS.

Abbreviations: ACS, acute coronary syndrome; HIT, heparin-induced thrombocytopenia; LMWH, low-molecular-weight heparin; PCI, percutaneous coronary intervention; UFH, unfractionated heparin

Invasive versus conservative strategy in non-ST-segment–elevation acute coronary syndrome

Several randomized trials have assessed the impact of conservative medical strategy versus an invasive approach on short-term outcomes of death, MI, and recurrent ischemic events in patients with NSTEMI-ACS.⁹⁶⁻⁹⁹ Most studies, particularly those performed in the coronary stent and antiplatelet therapy era, show a decrease in death or nonfatal MI for initial invasive strategy compared with conservative strategy.¹⁰⁰ The benefit of an invasive approach was much more evident in higher-risk patients, including those with positive troponin, ST-segment depression on electrocardiography, and importantly, age ≥ 65 years. Analysis of randomized patients with NSTEMI-ACS showed large absolute and relative reductions in death or nonfatal MI at 6 months in subjects aged ≥ 65 years or ≥ 75 years using an invasive as opposed to a conservative approach.¹⁰¹

These data suggest that an early invasive approach should be considered for many older patients with ACS.¹⁰² However, it should be noted that the randomized trials excluded a large percentage of patients due to contraindications, such as chronic renal disease or excess bleeding risk, that are common in the elderly.⁶⁰

ST-segment–elevation myocardial infarction

Prognosis

Age is also a powerful independent predictor of short and long-term morbidity and mortality in patients presenting with ST-segment–elevation MI (STEMI; *Figure 2, page 14*).¹⁰³⁻¹⁰⁵ In one study of patients admitted with a first STEMI and treated with thrombolytic therapy, in-hospital mortality increased exponentially with age from 1.9% in patients aged ≥ 40 years to 31.9% in those aged >80 years.¹⁰³ In the Global Utilization of Streptokinase and Tissue plasminogen activator for Occluded arteries (GUSTO-1) trial, 30-day mortality after STEMI increased from 3% in patients <65 years of age to 19.6% in those aged 75 to 85 years, and to 30.3% in those aged >85 years.¹⁰⁵ Age was the most powerful predictor of hospital stay and 30-day mortality.

Elderly STEMI patients experience a much greater incidence of heart failure, atrial fibrillation, and cardiogenic shock even though indices of infarct size, such as creatinine phosphokinase levels and QRS scores, do not change with age.^{64,103,105} The risks of heart failure and cardiogenic shock increase 3-4-fold in patients

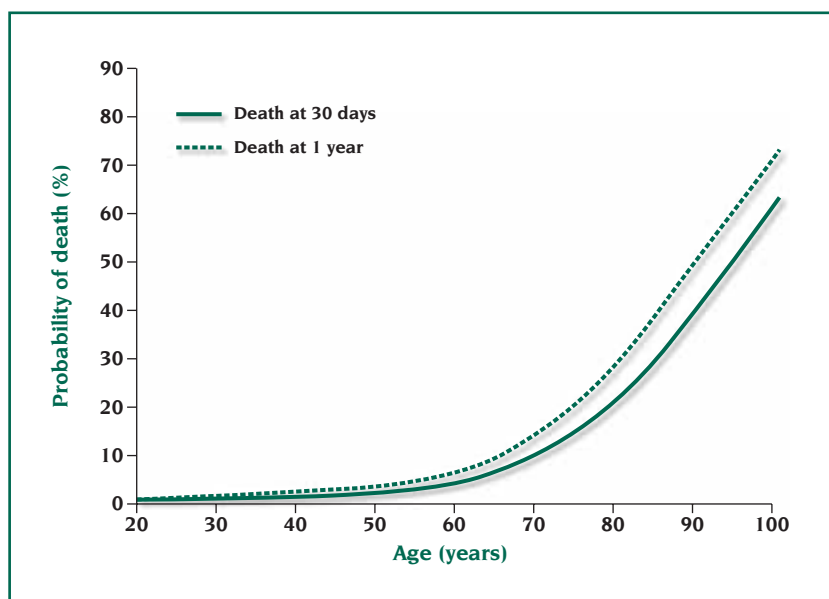


Figure 2. Relationship between age and mortality at 30 days and 1 year in over 40 000 patients with ST-segment-elevation myocardial infarction (STEMI) treated with fibrinolysis, showing age as powerful predictor of short- and long-term outcome.

Adapted from reference 104: Keller NM, Feit F. Atherosclerotic heart disease in the elderly. *Curr Opin Cardiol.* 1995;10:427-433. Copyright © 1995, Lippincott Williams & Wilkins.

aged >85 years compared with those aged <65 years.¹⁰⁵ Mortality in older patients with STEMI is less likely to result from ventricular fibrillation than in younger patients, but the elderly are much more likely to have electromechanical dissociation and cardiac rupture on autopsy. This risk is particularly notable in patients receiving fibrinolytic therapy.¹⁰⁶ In elderly patients with STEMI, the high in-hospital mortality risk continues after discharge, increasing with age by almost 6% per year.¹⁰³ Contributing to the increased risk in this age group is an age-related delay in reaching hospital for therapy. Elderly patients present with heart failure rather than chest pain, and with a much higher frequency of left bundle branch block, thereby complicating the electrocardiographic diagnosis of STEMI.¹⁰⁷

Reperfusion in STEMI

Most practitioners agree that prompt reperfusion of the infarct-related artery is critical in reducing the high mortality in elderly patients with acute STEMI. Unfortunately, the delays in reaching hospital and diagnosing acute STEMI, compounded by increased comorbidity, make elderly patients less eligible for reperfusion therapy. Large registry data in the US show that patients aged >75 years eligible for fibrinolysis are significantly less likely to receive reperfusion therapy than those aged <65 years.^{108,109} Data suggest that fibrinolytic therapy in acute MI reduces mortality in the elderly.

Subset analyses of the nearly 5800 patients aged >74 years in a meta-analysis of large randomized trials of fibrinolytic therapy showed a trend toward treatment benefit with a net saving of 1.0 life per 100 patients

treated at 35 days after infarction.¹¹⁰ The benefit of fibrinolytic therapy was even more apparent over the age of 75 years when this meta-analysis was confined to patients presenting within 12 hours of symptom onset with ST-segment elevation or left bundle branch block on their admission electrocardiogram (34 lives saved per 1000 patients treated).¹¹¹ It is difficult to draw conclusions as to the risk-benefit ratio of fibrinolytic therapy at ≥ 85 years of age, even in the absence of contraindications, as few such patients were enrolled into randomized trials. Currently, observational database studies show no benefit, or even harm, versus no treatment in patients aged ≥ 85 years.^{112,113} Part of the reluctance of physicians to use fibrinolytic agents in the elderly arises from the concerns about intracranial hemorrhage, for which age is a potent risk factor.^{105,114} Recent trials comparing half-dose fibrinolytic therapy plus a glycoprotein IIb/IIIa inhibitor versus full-dose fibrinolytic therapy have revealed the increased hemorrhagic risk of reperfusion strategies in the elderly, as have studies comparing fibrinolytic therapy plus LMWH versus UFH.^{115,116} Careful dose adjustment of the anticoagulant is needed to limit bleeding risk in the elderly.¹¹⁷ In considering fibrinolytic therapy in STEMI patients aged >75 years, mitigating factors include age, body weight, other comorbidity, the number of leads with ST-segment elevation, symptom duration, and the hospital's proximity to a high-volume center with onsite PCI. Recent data show that the benefit of fibrinolytic therapy is less at any time interval if pathologic Q-waves are present compared with those patients with only ST-segment elevation on the admission electrocardiogram.¹¹⁸



Several trials versus fibrinolytic therapy have shown the benefits of primary PCI in terms of mortality, recurrent MI, and recurrent ischemia.¹¹⁹⁻¹²¹ Subgroup analyses indicate a large survival advantage for PCI over fibrinolytic therapy in patients aged ≥ 70 years with STEMI.¹²² Primary PCI confers a lower overall thrombotic or hemorrhagic stroke risk compared to fibrinolysis.¹²¹ Patients with STEMI and a high-risk profile, including advanced age, derive greater benefit than low-risk patients from PCI compared to fibrinolytic therapy.¹²³ One randomized trial of 87 patients aged >75 years with STEMI showed a significant decrease in death, reinfarction, and stroke at 30 days and 20 months after direct angioplasty compared to fibrinolytic therapy.¹²⁴ An important caveat to all these comparative trials is that they involve operators with great expertise from high-volume angioplasty centers. PCI is preferable to fibrinolytic therapy if it can be performed expeditiously, generally with a door-to-balloon time under 90 minutes. However, the door-to-balloon time at which fibrinolysis becomes preferable to PCI in eligible elderly STEMI patients is debatable. In general, the target interval from the ability to open the infarct vessel with PCI compared with initiation of fibrinolytic therapy does not exceed 60 minutes. However, extensive observational data suggest that in STEMI patients aged ≥ 65 years, this interval may be as long as 155

minutes. This longer window for performing PCI in STEMI probably reflects the increased risk of thrombolytic therapy in this age group.¹²⁵

Older patients are at higher risk of cardiogenic shock. Mean 6-year survival was significantly greater with early revascularization than with initial medical stabilization in one randomized study.¹²⁶ Survival curves show that early revascularization confers an absolute long-term survival advantage of 13%. Since there is no interaction between treatment and age (<75 years vs ≥ 75 years) over the long term, these data suggest that elderly acute MI patients with cardiogenic shock should receive urgent revascularization where possible.

Medical therapy for STEMI

β -Blocker therapy is greatly underprescribed in older post-MI patients, despite overwhelming evidence of a significant survival advantage. In the CCP database of over 200 000 Medicare beneficiaries with MI, only 34% of the elderly cohort was discharged home on a β -blocker.¹²⁷ Of post-infarct patients above 65 years of age, with no contraindications to β -blocker therapy, only one half left hospital on this therapy. All age subgroups in this database had a large survival advantage (approximately 40% relative reduction and 10% absolute reduction in 2-year mortality) with β -blocker therapy,

Agent	Pros	Cons
Aspirin	Decreases mortality Decreases reinfarction and stroke	Dose-dependent bleeding risk
Clopidogrel	Decreases mortality Decreases death, reinfarction, stroke	Duration of therapy uncertain Increases bleeding risk if added to aspirin
β -Blocker	Decreases mortality Decreases reinfarction, sudden death	Early aggressive β -blocker therapy increases risk of shock on day 1
ACE inhibitor	Decreases mortality in high-risk elderly with left ventricular dysfunction or heart failure Decreases heart failure and reinfarction	Increases risk in hypotensive elderly Less benefit in preserved left ventricular function
Aldosterone antagonist	Decreases mortality in high-risk elderly with left ventricular dysfunction and heart failure	Close potassium monitoring needed Avoid in elderly with significant renal impairment
HMG-CoA reductase inhibitor (statin)	Decreases cardiovascular events in elderly with average cholesterol Aggressive lipid-lowering decreases cardiovascular events in elderly	Underprescribed in elderly

Table II. Medical treatment in older patients with ST-segment-elevation myocardial infarction.

Abbreviations: ACE, angiotensin-converting enzyme; HMG-CoA, 3-hydroxy-3-methylglutaryl coenzyme A.

confirming data from older randomized trials. The observed benefits extended to subjects with Q-wave and non-Q-wave infarction, age under 70 years to over 80 years, and all categories of left ventricular function. The benefits of chronic β -blocker therapy after MI in the database were similar to those revealed by subgroup analyses of the placebo-controlled trials of chronic β -blocker therapy following post-MI stabilization. Most of the long-term benefits of β -blockers in the large randomized trials were driven by the survival advantage in patients aged >65 years (Table II).^{128,129}

Whereas long-term β -blocker therapy benefits all elderly patients after acute MI, aggressive intravenous then oral β -blocker therapy on hospital admission should be administered judiciously, if at all. In the Clopidogrel and Metoprolol Myocardial Infarction Trial (COMMIT), 45 852 patients with acute MI were randomized to intravenous then oral β -blockers or matching placebo.¹³⁰ Those with cardiogenic shock, heart rate less than 50 beats per minute, or systolic blood pressure persistently below 100 mm Hg, were excluded. The proportion of patients free of reinfarction, cardiac arrest, or death in the first 28 days did not differ significantly in the β -blocker and placebo groups. Although early β -blockade reduced the incidence of reinfarction and ventricular fibrillation, this benefit was countered by a higher risk of cardiogenic shock on the first hospital day. Since age is a powerful predictor for the development of cardiogenic shock, elderly STEMI patients should be hemodynamically stable prior to β -blockade. In most instances, this can be done with oral therapy.

Aspirin decreases mortality and reinfarction in elderly infarct subjects.^{131,132} Nevertheless, among 10 000 Medicare beneficiaries with acute MI and no contraindication to aspirin, only 61% received aspirin in the first 2 hospital days.⁷⁹ Although aspirin therapy in elderly infarct patients was independently associated with lower 30-day mortality and improved 6-month outcome, only 76% were discharged home on aspirin after MI.⁷⁹ In a randomized, placebo-controlled trial of 45 852 medically treated patients with acute STEMI, clopidogrel plus aspirin reduced the short-term composite end point of death, reinfarction, or stroke as well as mortality alone.¹³³ Subgroup analysis showed that all age groups benefited from this therapy. Dual antiplatelet therapy should therefore be considered in elderly infarct patients at low bleeding risk.

ACE-inhibitor therapy after acute MI reduces morbidity and mortality. The randomized placebo-controlled trials in high-risk patients with left ventricular dysfunction

or clinical heart failure showed marked survival benefit in older patients randomized to ACE inhibitor therapy versus placebo.¹³⁴⁻¹³⁶ Meta-analysis of trials in 5966 patients (mean age 63 years) with post-MI left ventricular dysfunction (ejection fraction <40%) or heart failure revealed a 26% reduction in mortality after a mean follow-up of 31 months in patients randomized to an ACE inhibitor¹³⁷; secondary end points were also improved, including a 27% reduction in heart failure hospitalizations, and a 20% reduction in recurrent MI.¹³⁷ Benefit was consistent across age groups (<55 years, 55-75 years, >75 years). ACE inhibitors are distinctly less beneficial in lower-risk elderly without heart failure or left ventricular dysfunction post-MI. Although clinical events do not appear reduced, the addition of an ACE inhibitor does decrease the progressive rise in left ventricular end-diastolic volume over the course of 1 year.¹³⁸ Such patients require individualized treatment based on factors such as the risk of hypotension and renal insufficiency.¹³⁹ Aggressive ACE inhibition on hospital admission should be avoided in the elderly as the resultant hypotension may cause ischemia and poorer outcome.

Older post-MI patients with left ventricular dysfunction, clinical heart failure, or both, failing to tolerate ACE inhibition (eg, cough) may be offered a high-dose ARB as an equivalent alternative.¹⁴⁰ The combination of ACE inhibitor and ARB adds no benefit over either agent alone and often causes greater side effects. In post-MI patients with left ventricular dysfunction, aldosterone production is stimulated, even with ACE-inhibitor therapy, and hepatic clearance is impaired.¹⁴¹ Elevated aldosterone levels may induce left ventricular fibrosis and progressive remodeling post-MI. In animal models of MI, aldosterone blockade prevents this progression.¹⁴² Randomized trials have shown that in post MI patients with both left ventricular dysfunction and heart failure, adding an aldosterone antagonist to standard post-MI therapy decreases cardiovascular morbidity and mortality, as much under as over the age of 65 years.¹⁴³ An important caveat to adding an aldosterone antagonist to an ACE inhibitor or ARB in older post-MI patients is the frequent occurrence of renal insufficiency.¹⁴⁴ Creatinine clearance should be calculated in this age group, and renal function and potassium levels closely monitored when using these agents.

Like β -blockers, aspirin, and ACE inhibitors, HMG-CoA reductase inhibitors (statins) reduce cardiovascular events in older post-MI patients and are similarly underprescribed. The Cholesterol and Recurrent Events (CARE) trial randomized 1283 post-MI patients (60%



Q wave) aged 65-75 years, with total cholesterol <240 mg/dL and LDL cholesterol 115-174 mg/dL, to pravastatin or placebo.¹⁴⁵ Active therapy reduced 5-year cardiovascular event rates by a relative 32% and absolute 9% (19.7% vs 28.1%) versus placebo. Secondary end points (coronary death and stroke) were also significantly reduced. The numbers of older post-MI patients that needed to be treated with statin therapy to prevent one major cardiovascular event and one coronary death were 11 and 22, respectively.

The PRavastatin Or atorVastatin Evaluation and Infection Therapy (PROVE-IT) trial investigated more aggressive lipid-lowering therapy in a large cohort of ACS patients randomized to moderate lipid lowering with pravastatin 40 mg (mean achieved LDL 95 mg/dL) versus atorvastatin 80 mg (mean achieved LDL 62 mg/dL).¹⁴⁶ Over the 2-year follow-up, the incidence of the primary end point of death, MI, stroke, revascularization, or readmission for ACS was significantly lower with aggressive therapy. Analysis showed similar benefit in patients aged ≥ 70 years.

Other large trials of secondary prevention have mirrored these impressive benefits of statin therapy in older post-MI patients. The Heart Protection Study (HPS) showed that the reduction in cardiovascular events after statin therapy for 5 years in its 5806 subjects aged ≥ 70 years, many with a history of MI, was as significant versus placebo as in the overall cohort.¹⁴⁷ An observational study of 7000 patients with angiographic IHD (30% with MI) found significantly lower mortality after discharge on statin therapy, regardless of age, after 3.3 years of follow-up; however, prescription of statin therapy at discharge decreased significantly with age and was prescribed for fewer than one in five patients with IHD over 80 years of age.¹⁴⁸ Although the few side effects of statin therapy are not age-related, only a minority of post-MI elderly leave hospital on statin therapy, and a large proportion stop statin therapy soon after discharge.¹⁴⁹ Education of physicians and older patients in the benefit of risk factor modification after MI, including statin therapy, must continue to improve outcome in this high-risk group.

Left ventricular remodeling

Older STEMI patients are at higher short- and long-term risk of heart failure and left ventricular dilatation than their younger counterparts. Although the mechanisms involved are multifactorial, it is likely that age-related cardiovascular changes contribute. These include an increased arterial load,¹⁵⁰ impaired β -adrenergic re-

sponse,¹ and impaired collateral blood vessel formation to the infarct zone.¹⁵¹ The elderly often present late with STEMI. To determine whether routine opening of an occluded infarct vessel late after MI onset prevents left ventricular remodeling and clinical events, the Occluded Artery Trial (OAT) randomized 2166 patients, with an ejection fraction <50% and/or angiographic proximal epicardial infarct vessel occlusion between 3 and 28 days after acute MI, to routine PCI with stent or medical treatment alone.¹⁵² The enrolment criteria required patients to be clinically stable, and free of heart failure and symptomatic ischemia. After 4 years, the primary end point of death, nonfatal reinfarction, or hospitalization for severe heart failure was 17.2% in the PCI group versus 15.6% in the medical group. In the 632 patients over 65 years of age, there was no reduction in clinical events for routine PCI, suggesting that older clinically stable patients arriving late with STEMI do not benefit from routine PCI of an occluded infarct vessel.

CONCLUSION

Most ACS patients are elderly. Advanced age is a powerful predictor of morbidity (primarily heart failure) and mortality in NSTEMI-ACS and STEMI. Although clinical trials often recruit younger patients with less comorbidity than seen in the community, large registry studies suggest that the application of guideline therapy to ACS patients saves lives. As major bleeding in hospitalized ACS patients is now recognized as a powerful predictor of future mortality, care must be taken to reduce this risk, in particular in the elderly, in whom therapy may trigger bleeding. In elderly STEMI patients, consideration of fibrinolytic therapy versus PCI depends on a variety of factors, most importantly door-to-balloon time and the risk associated with fibrinolytic therapy. Hemodynamically unstable elderly have most to gain from a catheterization-based revascularization strategy. Hypotension is poorly tolerated in the elderly and care must be taken to avoid it. Future studies of ACS need to recruit more elderly and women to determine how to optimize care in these important and growing groups of patients.

Although there are many debatable management issues regarding IHD in older patients, the three most important questions are: how should ACS symptoms be diagnosed in older as distinct from younger patients? Does left ventricular remodeling differ in the elderly and, if so, should treatments differ from those in younger patients? And should cholesterol goals be the same or different in older patients with IHD compared to their younger counterparts?

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