COMMENTARY

Approach to symptomatic coronary disease in the elderly: TIME to change?

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Patients 75 years or older account for about 37% of the admissions to hospital with acute myocardial infarction (MI),[1] yet for 60% of the deaths from this event.[2] Elderly patients also have an increased risk of several of the complications of acute MI, such as congestive heart failure (CHF), cardiogenic shock, myocardial rupture, hypotension, conduction disturbances, and supraventricular tachyarrhythmias. Despite these higher risks, only 6·7% of 719 922 patients enrolled in 593 published trials of acute coronary syndromes from 1966 to 2000 were 75 years or older (panel);[3] since 1996 this proportion has increased to only 10·3% of 201 357 patients.[3] Because safety and efficacy of cardiovascular therapies may differ between elderly and younger patients, it is important to enrol enough elderly patients in randomised controlled trials to provide evidence-based medical care to this high-risk population.

Older patients with coronary artery disease (CAD) treated with simvastatin or pravastatin in the Scandinavian Simvastatin Survival trial,[4] Cholesterol and Recurrent Events trial,[5] and Long-Term Intervention with Pravastatin in Ischaemic Disease study[6] had a greater absolute reduction in subsequent cardiovascular events than younger patients. However, the oldest patient enrolled in these studies was 70 years,[4] 75 years,[5] and 75 years,[6] respectively. Doctors may not treat without such evidence. For example, many physicians state that they will not treat patients with previous MI and hypercholesterolaemia older than 75 years with HMG co-A reductase inhibitors (statins) because of the lack of convincing evidence that such treatment would benefit this population.

Proportion of elderly patients in 593 published randomised trials of acute coronary syndromes

Therapy	Total number of patients	% aged ≥75 years
Magnesium	64 411	13·8
Vasodilator	91 986	13·1
Angiotensin-converting-enzyme inhibitor	135 412	9·2
Antithrombotic	167 878	8·6
Thrombolytic	259 179	8·0
Antiarrhythmic	45 430	7·6
Antiplatelet agent	91 712	6·9
β-blocker	56 517	3·7
Primary angioplasty	22 511	2·8
Calcium-channel blocker	20 692	1·1
Lipid-lowering agent	25 294	0

Adapted from reference 3.

Some evidence that treatment of very elderly people with statins may be beneficial comes from an observational study of 1410 older men and women with a previous MI and a serum LDL-cholesterol concentration greater than 3·2 mmol/L. In this study 679 patients (48%) were treated with statins and 731 patients (52%) did not receive any lipid-lowering drug.[7] The attitude of the physician towards treating hypercholesterolaemia in older patients with a previous MI determined whether or not a statin was prescribed. At the 36-month follow-up, a significant reduction in new coronary events was seen among patients treated with statins aged 60–70 years, 71–80 years, 81–90 years, and 91–100 years.[7] However, these data need to be confirmed by randomised controlled trials.

The importance of observational data had supported the use of hormonal therapy in postmenopausal women with CAD. However, the Heart Estrogen/progestin Replacement Study,[8] which randomised 2763 post-menopausal women with documented CAD to hormonal therapy or placebo found that hormonal therapy caused a 52% increase in non-fatal MI or CAD death during the first year of treatment. Among patients with an acute MI complicated by cardiogenic shock who had a coronary revascularistion procedure, there was a significant 30% decrease in mortality at 6 months in those younger than 75 years of age and an increase of 41% (p=0·003) among those older than 75.[9]

Data from randomised controlled trials among very elderly people are still required to confirm efficacy of therapy for various coronary disorders. One is thrombolytic therapy for acute MI, especially since angioplasty is not available in many hospitals. Observational data have shown that thrombolytic therapy reduces mortality at 30 days by 12% in people 65–75 years old but significantly increases it by 38% in patients 76–86 years old.[10]

Another area is treatment for CHF, the commonest cause of hospital admission and readmission in elderly patients. However, in five randomised controlled trials of long-term use of angiotensin-converting-enzyme inhibitors in patients with CHF or left-ventricular dysfunction, only 1066 of 12 740 patients (8%) were older than 75.[11] In the Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure, only 10% of 3991 patients were 70 years or older.[12] In the Veterans Affairs Cooperative Studies Vasodilator Heart Failure Trials I and II, recruitment was limited to men aged 18–75 years.[13,14]

The prevalence of CHF with a normal left-ventricular ejection fraction increases with age, is higher in older women than in older men, and is approximately 50% in patients with CHF over 60 years of age.[15] Despite these data, few studies have investigated the effects of drug therapy in elderly or younger patients with CHF and normal ejection fraction.[16-21] Three of these six studies[16–18] enrolled fewer than 100 patients.

Yet another area for which data are required is angina pectoris. In today's *Lancet*, M Pfisterer and colleagues report on a randomised prospective multicentre trial in patients aged 75 years or older with angina pectoris of Canadian Cardiac Society class II despite at least two antianginal drugs. They compared an invasive strategy with optimum medical treatment. The invasive strategy consisted of coronary angiography followed, if thought necessary, by percutaneous coronary intervention or coronary artery bypass graft surgery. 74% of patients in the invasive group had a revascularisation procedure (54% percutaneous intervention, 20% bypass grafting). After 6 months, severity of angina decreased and measures of quality of life increased in both treatment groups. However, these improvements were significantly greater for those in the revascularisation group. Death, non-fatal MI, or hospital admission for acute coronary syndrome with or without the need for revascularisation occurred in 49% of the medical group and in 19% of the invasive group ($p<0{\cdot}0001$). Mortality at 6 months did not differ between the two groups (8·4% in the invasive group, 4·1% in the medical group), but the study was not powered to detect such a difference. A third of the patients in the medical group needed a revascularisation procedure during follow-up for uncontrollable symptoms.

Revascularisation was associated with better improvements in quality of life and a lower frequency of events in the composite endpoint than medical therapy. Thus, despite their high-risk profile, patients over 75 should be offered invasive evaluation and coronary revascularisation procedures as clinically indicated.

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Role of inflammatory biomarkers in prediction of coronary heart disease

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Early atherosclerosis has an inflammatory component characterised by leucocytic infiltration of the vascular endothelial wall. The adhesion and transendothelial migration of circulating leucocytes is thought to be important in the initiation and progression of atherosclerotic disease.[1] These processes are mediated largely by cellular-adhesion molecules (CAMs)—a diverse group of integrin, immunoglobulin, and selectin proteins involved in the binding of cell to cell as well as cell to extracellular matrix.

The evidence that CAMs have a role in the progression of atherosclerosis comes from several sources. On histological analysis, human atherosclerotic plaque contains many CAMs. Mice deficient in CAMs develop fewer atherosclerotic lesions than wild-type mice, and the administration to mice of antibodies directed against CAMs decreases intimal hyperplasia and the vascular inflammatory response seen after