Secondary prevention after myocardial infarction

An extensive database has firmly established the efficacy of several therapeutic interventions following myocardial infarction including their effectiveness in elderly people. Several guidelines are available to guide clinicians and recommending best clinical practice. This article is an update on the management approaches following acute myocardial infarction focusing on secondary cardiovascular protection.

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The incidence and mortality after acute myocardial infarction (MI) increases with old age and ischaemic heart disease remains the most important cause of death in the elderly population worldwide. When compared internationally, the UK death rate from coronary heart disease (CHD) is relatively high with more than 103,000 deaths per year.[1] Most of the established risk factors for heart disease are highly prevalent in the elderly population such as hypertension, hypercholesterolaemia, obesity, diabetes and physical inactivity and control of risk factors is important for controlling the burden of ischaemic heart disease.

The care of MI patients has improved substantially in the past few decades due to a major design of services, clinical enthusiasm, UK national audits and implementation of the NSF for Coronary Heart Disease.[2] Major advances have occurred resulting in 59% reduction in CHD death rates between 1950 and 1999.[3] More than 90% of the reduction in mortality is attributable to reduction in major risk factors (smoking, high blood pressure, cholesterol) and more widespread utilisation of evidence based medical therapies for secondary prevention[4] and only 5% decline in mortality is attributed to revascularisation procedures. Thus there are clear benefits from evidence based secondary prevention after MI and several guidelines[5,6] are available to provide clinicians with recommendations and best practice.

Acute management

The majority of patients with acute MI including the elderly would require admission to a coronary care unit after diagnosis for cardiac monitoring and specific therapy such as thrombolysis and early percutaneous coronary intervention as appropriate. This article focuses on secondary prevention which should be initiated soon after the diagnosis of acute MI.

Pharmacotherapy

Several drugs have shown benefits in management of MI in an attempt to limit infarct size, improve left ventricular function and reduce mortality. The elderly are a high risk group and should receive all evidence based secondary preventions following an acute MI. Therapeutic recommendations should not be based on age and attention to comorbidities and appropriate dosing is important for older patients.[7]

Antiplatelets

Aspirin is the most convenient and widely used antiplatelet drug. It acts by inhibition of cyclo-oxygenase dependant platelet aggregation. Early aspirin should be considered in all patients without contraindications and continued daily long term. It is effective, cheap and has reasonable safety profile. Every patient with confirmed or suspected MI should receive aspirin within the first hour.

Pooled data from more than 18,000 patients included in randomised trials has shown that aspirin significantly reduces long term vascular mortality.[8] Moreover aspirin does not pose a major hazard to elderly patients.[9] American[5] and NICE[6] guidelines strongly

recommend use of aspirin for all survivors of acute MI to prevent recurrence of MI and death.

In a randomised trial clopidogrel (Plavix) plus aspirin was more effective than aspirin alone in non-ST elevation coronary syndromes for composite outcomes of cardiovascular deaths (RR 0.80 CI 0.72-0.90).[10] Clopidogrel in combination with low dose aspirin is recommended in the management of non-ST segment elevation acute coronary syndrome in patients with moderate to high risk of MI or death and continued for one year. Thereafter aspirin alone is continued unless other indications for dual antiplatelet therapy. Following an ST elevation MI patients are given this combination for at least four weeks then followed by aspirin long term. This combination can however, increase risk of bleeding. In patients with true aspirin allergy, clopidogrel monotherapy is an alternative treatment. Patients with dyspepsia should receive a proton pump inhibitor plus aspirin.[6]

Vitamin K antagonists

In patients with coronary artery disease in a meta-analysis of four randomised trials, moderate intensity anticoagulation (INR 2–3) compared with control reduced reinfarction, but was associated with increased risk of major bleeding.[11] A meta-analysis of seven randomised trials showed that warfarin compared with aspirin did not reduce all cause mortality, reinfarction or stroke but increased risk of major bleeding.[11] For patients with MI who are unable to tolerate aspirin or clopidogrel, treatment with moderate intensity warfarin keeping INR 2–3 should be considered for upto four years and possibly longer.[6] Warfarin is definitely indicated for patients with mechanical valve, recurrent deep vein thrombosis, atrial fibrillation and left ventricular thrombus.

Beta-blockers

Data from several clinical trials involving >50,000 patients have firmly established the ability of beta-blockers to reduce the risk of mortality and nonfatal reinfarction in patients after an MI. These include the Metoprolol in Acute MI trial (MIAMI trial),[12] the first International Study of Infract Survival (ISIS)[13] and US Beta Blocker Heart Attack trial.[14] An overview of beta -blocker trials by Yusuf et al[15] showed approximately 15% reduction in mortality within the first 24 hours and that they are safe and well tolerated in the majority of patients. Treatment during the acute phase is most effective when initiated within the first few hours but chronic long term therapy also reduces mortality post MI. Beta-blockers can reduce one year mortality from 27% to 11% overall and the incremental benefit is regardless of age (below or above 72 years) presence of diabetes, history of heart failure or prior MI.[16] Hence unless contraindicated, beta-blockers should be used in all post MI patients and continued long term. They are particularly useful in patients with LV dysfunction and ventricular arrhythmias. Only those beta-blockers licenced for heart failure should be used such as metoprolol, carvedilol or bisoprolol.[16]

Table 1. ACE inhibitor and target dose (adapted from British National Formulary)

Drug	Starting dose	Target dose
Captopril	6.25mg tds	50mg tds
Lisinopril	2.5 to 5mg od	10mg od
Ramipril	1.25 to 2.5mg bd	5 mg bd
Trandolapril	0.5mg od	4 mg od
Enalapril	2.5mg od	10mg bd or 20mg od
Perindopril	2mg od	8 mg od

ACE inhibitors

MI is associated with neurohormonal activation of substances such as rennin, angiotensin, catecholamines and increase in cardiac ACE activity has been linearly linked to the size of infarct. These findings have resulted in several trials using ACE inhibitor drugs. (Table 1).

A meta-analysis of six randomised trials in patients with stable coronary artery disease and preserved LV function showed that treatment with ACE inhibitor compared with placebo was associated with reduction in cardiovascular mortality (RR 0.83), nonfatal MI (RR0.84), all cause mortality (RR 0.87) and coronary revascularisation rates (RR 0.93) with mean duration of follow up of 4.4 years.[17] A systematic review of long term trials of patients after MI with systolic dysfunction showed reduction in mortality (OR 0.74), readmission for heart failure (OR 0.73), and recurrent MI (OR 0.80) compared with placebo over median follow up of 31 months.[18]

ACE inhibitor trials had different selection criteria, but results in general show that five lives could be saved for every 1000 patients treated with

ACE inhibitor regardless of LV function or presence of heart failure. The results are more striking when ACE inhibitors are used for patients with low ejection fraction or clinical heart failure. Hence all patients following MI would benefit from ACE inhibitor unless contraindicated.

ACE inhibitor therapy dose should be initiated at low dose and titrated upwards every one to two weeks post MI until the maximum tolerated or target dose is reached. Some patients cannot tolerate ACE inhibitors due to cough or allergy and an angiotensin receptor blocker (ARB) drug should be substituted.[6] Renal functions and blood pressure should be monitored after ACE inhibitor or ARB treatment regularly. The elderly are particularly susceptible to side effect of these drugs.

Calcium channel blockers

Calcium channel blockers are not routinely used to reduce cardiovascular risk after MI. If beta-blockers are contraindicated then diltiazem or verapamil may be considered for secondary prevention in patients without LV dysfunction.[6] Calcium channel blockers may be useful to treat hypertension and/or angina. Verapamil and diltiazem are avoided in heart failure.

Other drugs and interventions

Nicorandil (Ikorel) has no role in reducing cardiovascular risk following MI. In patients with MI and heart failure, treatment with an aldosterone antagonist can be initiated a few days after an acute event. However, renal function especially serum potassium needs to be monitored during treatment. In the RALES trial, spironolactone, an aldosterone antagonist, increased life expectancy and reduced hospitalisation in patients with chronic heart failure.[19]

Eplerenone (Inspra), another aldosterone antagonist, initiated three to 14 days after acute MI amongst patients with reduced ejection fraction plus clinical heart failure (in addition to ACE inhibitor and beta-blocker) reduced all cause mortality, death from cardiovascular causes, sudden cardiac death and episodes of heart failure[20] but with increased risk of serious hyperkalaemia.

In suitable patients following a MI, a cardiological assessment can decide the need for coronary revascularisation or the need for implantable cardioverter defibrillator for arrhythmias.

Dyslipidaemia

There is strong scientific evidence supporting lipid lowering for primary and secondary prevention of CHD. A meta-analysis of 14 trials of secondary prevention in CHD[6] showed that statin therapy compared from placebo was associated with reduction in all cause mortality (RR 0.79), cardiovascular mortality (RR 0.75), coronary disease mortality (RR 0.72), fatal MI (RR 0.57), unstable angina (RR 0.82), nonfatal stroke (RR 0.75), intermittent claudication (RR 0.64), and coronary revascularisation (RR 0.77). In posthoc analysis of a US study the absolute risk reduction for all cause and CHD related mortality in treated patients was twice as great in elderly patients.[21] The PROSPER trial showed that pravastatin in high risk older patients (>70 years) had a significant reduction in CHD related mortality and non fatal MI.[22] The Heart Protection Study further supported benefits of statin in elderly patients with CHD, other vascular disease, diabetes with reduction in all cause mortality, fatal and non fatal MI including patients with LDL cholesterol <3mmol/L.[23] The CARE trial[24] amongst patients with "average" cholesterol levels, showed that compared with placebo the active treated group with pravastatin had lower MI and fatal CHD. Hence lipid lowering with a statin should be considered in all post MI patients and as soon as possible after MI. Patients intolerant of statins can be considered for other lipid lowering agents.

Omega 3 acids

A randomised trial of 11,324 patients with prior MI showed that omega 3 ethylester treatment was associated with lower risk of death, nonfatal MI, nonfatal stroke.[25] The clinical benefit of omega 3 acids may be restricted to commencing therapy within three months of an MI.[6]

Hypertension

High blood pressure is a common risk factor and present in more than two third patients older than 65 years. Antihypertensive therapy in patients 60–80 years of age can reduce all cause mortality, stroke and heart failure.[26] Agents such as ACE inhibitors and calcium channel blockers are as effective as more conventional therapies (diuretics, beta-blockers) in improving

clinical outcomes.[27] Hypertension is treated to currently recommended target of 140/90mmHg or lower as per NICE hypertension guidelines.[28] Patients with renal disease or diabetes are treated to a lower target.[28] The HYVET trial showed that antihypertensive treatment is beneficial even in patients older than 80 years in reducing fatal or nonfatal stroke, cardiovascular deaths and heart failure.[29]

Diabetes

The prevalence of diabetes is increasing in the western population. Exercise training can improve insulin resistance and glucose control. Attention to diet and pharmacological treatment is needed to control glucose levels.

Cardiac rehabilitation

In a meta-analysis of a total of 27 trials amongst 11,723 patients, comprehensive cardiac rehabilitation programmes reduced recurrent MI compared to usual care (RR 0.86) while an exercise only cardiac rehabilitation programme did not reach statistical significance.[30] Structured cardiac rehabilitation services offer the optimal setting where trained personnel can educate the patient and address risk factors. The exercise programme needs to be individualised with an intensity targeting 75% of patients maximum heart rate but taking into account comorbidities such as arthritis and peripheral vascular disease. Even in elderly patients, exercise training is part of multidisciplinary approach to secondary prevention. A standard exercise programme can improve functional capacity. Moreover, it positively impacts CHD risk factors such as obesity, hypertension, insulin resistance even in patients older than 75 years.[31,32]

Lifestyle

Patients should be advised to be physically active for at least 20 to 30 minutes a day. They should start at a level that is comfortable and increase duration and intensity of activity. All patients should be advised smoking cessation and to eat a Mediterranean diet with more bread, fruit, vegetable and fish. Patients should keep weekly consumption of alcohol to safe limits and avoid binge drinking. Obese patients should try to achieve and maintain a healthy weight. Most patients following uncomplicated MI can return to work. Patients should be offered social and psychological support as needed.

Summary

CHD remains a substantial financial burden to health services due to significant morbidity and mortality especially in the elderly population. Large randomised clinical studies have provided strong evidence based therapies over the past few decades. The elderly have been poorly represented in many trials. The first priority should be to ensure all MI patients are treated with aspirin, thrombolytic therapy (if eligible) and beta blockers (if not contraindicated). ACE inhibitor is then started if not contraindicated when the patient is stable after six to eight hours. Lipid lowering with statins should be considered in all patients. Secondary prevention can decrease mortality, morbidity and recurrent vascular events in elderly survivors of MI.

Conflict of interest: none declared

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