Angina in elderly people

Morbidity from ischaemic heart disease increases as patients age, and the burden of angina in elderly individuals can severely reduce their quality of life. The most common interventions are angioplasty, stenting, and coronary artery bypass grafting. However, the COURAGE trial showed that medical management had similar outcomes to percutaneous intervention. Several drug options are available for medical management of angina.

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Ischaemic heart disease is an important cause of morbidity, admission to hospital, and death, despite progress in both prevention and treatment. It is the most common cause of death in the UK, and accounts for more than 20% of premature deaths in men and about one in eight premature deaths in women.[1-3]

More than 1·4 million people suffer from angina and 275,000 people have a heart attack every year.[4] Ischaemic heart disease is more common with age: death rates from this condition are more than 10 times higher in those aged 65–74 compared with those younger than 65,[2] and around 20% of men and women aged over 75 have been diagnosed with angina.[5] Morbidity from ischaemic heart disease is also concentrated in the later years. The 2003 Health Survey for England noted that less than 1% of men in their 30s and 40s complained of symptoms of angina, compared with 17-19% of people in their 60s and 70s, with similar relative differences in women.[6]

The burden of angina is substantial, and the debilitating symptoms can severely reduce a patient's quality of life. Its widespread and often devastating personal impact can also make it costly. According to a study by the Health Economics Research Centre at the Department of Public Health at the University of Oxford, the cost of care of ischaemic heart disease to the NHS, particularly in-patient care, runs into hundreds of millions of pounds a year.[7] With approximately 1·4 million patients in the UK being treated for angina and with prevalence increasing with age, effective management of the older population is fundamental for reducing both the social and financial effects of this condition.

Interventions

Angioplasty, stenting, and coronary-artery bypass grafting are the most commonly deployed interventions for patients with ischaemic heart disease, but these procedures are generally restricted to a relatively small subset of patients, especially those with severe or diffuse coronary artery disease, and those with unstable or troublesome symptoms that do not settle with intensive medical therapy. Although these procedures are used selectively and effectively, many patients only obtain temporary respite from angina symptoms because, over time, grafts tend to fail and restenosis is not uncommon after angioplasty or stenting. The UK has fairly conservative use of revascularisation procedures, and older patients, often with comorbidities, are frequently deemed unsuitable for coronary-artery bypass grafting, or indeed their angina has recurred 10 or more years after coronary surgery.

The COURAGE trial

A recent comparative trial supported the conservative approach of the UK, and suggested that optimum medical therapy is an appropriate management choice for many patients with stable ischaemic heart disease.[8] The COURAGE trial, which was first presented at the American College of Cardiology meeting in March 2007, and later published in the *New England Journal of Medicine*, found that for many patients, optimum medical therapy had a similar outcome to percutaneous coronary intervention.

In this trial, 2,287 patients who had objective evidence of myocardial ischaemia and substantial coronary artery disease were investigated. Participants were randomly assigned to optimum medical therapy with or without percutaneous intervention. Optimum medical therapy consisted of long-acting metoprolol, amlodopine, and isosorbide mononitrate alone or in combination with lisinopril or losartan for secondary prevention. Patients received aggressive lipid lowering therapy with a target of between 1·55 mmol/l and 2·20 mmol/l for low-density lipoprotein.

Percutaneous intervention was balloon angioplasty or stenting, or both, although a few patients (n=31) received drug-eluting stents. The patients, who had a mean age of 61 years, were mostly male (85%) and largely white, were

followed-up for between 2·5 and 7 years. In all, 89% had angina (grades I to III) that had lasted for a median of 5 years. About a third had diabetes or a previous myocardial infarction, and two-thirds had hypertension.

No significant difference was seen in the primary endpoint of death from any cause and non-fatal myocardial infarction between those who had percutaneous intervention and medical therapy and those who had only medical therapy. Key outcomes, including rates of myocardial infarction, for the composite endpoint of death or myocardial infarction, or stroke, and for hospital admission rates for acute coronary syndrome also showed no significant differences between the two groups. Angina symptoms improved in both groups, although the improvement was greater in the group that underwent percutaneous intervention.

Medical management

Medical management can achieve long-term control of symptoms of stable angina using several drugs. The choice of a particular drug or combination of drugs can vary depending on comorbidity and patient's tolerance.

β-blockers are first-line therapy for relief of symptoms of stable angina, unless contraindicated. They effectively reduce heart rate and myocardial contractility. The use of β-blockers can be associated with adverse effects for some patients including lethargy, tiredness, and sometimes bradycardia, exacerbations of asthma, and increased hypoglycaemia in patients with diabetes. These adverse effects can limit the use of β-blockers in older patients with existing comorbidities such as peripheral artery disease, asthma and diabetes.

Vasodilating nitrates can provide short-term relief of angina symptoms by reducing myocardial oxygen requirements and improving myocardial perfusion, thus helping symptoms such as breathlessness to subside. Evidence from the GISSI 3 and ISIS-trials,[9,10] however, suggests that although oral nitrates are effective at relieving symptoms, these drugs do not have an effect on mortality or rates of myocardial infarction and there is an added problem of pharmacodynamic tolerance to long-acting nitrates.

Calcium channel blockers have various cardiovascular effects that can be helpful in stable angina. Longer-acting calcium channel blockers, such as verapamil, reduce myocardial contractility and limit heart rate, in turn reducing symptoms. They should only be used with extreme caution in patients taking β-blockers and are not suitable for patients with significant left ventricular impairment. Verapamil and diltiazem can worsen heart failure, especially in elderly patients. About one in 35 people aged 65–74 years have heart failure. This increases to about one in 15 of people aged 75–84 years, and to more than one in seven people aged 85 years and older.

Potassium channel activators offer a further option for control of symptoms by reducing the preload and afterload on the heart and increasing total coronary perfusion. Aspirin, statins, and angiotensin-converting -enzyme inhibitors are also well established secondary-prevention treatments in many patients with ischaemic heart disease, and have each been shown to reduce mortality in higher risk patients.

The I_f inhibitor ivabradine is a new treatment for patients with stable angina. By selectively inhibiting the I_f receptor of the sinus node, ivabridine reduces heart rate and myocardial oxygen consumption, decreases angina frequency, and improves exercise tolerance. It is indicated for patients who have a contraindication to, or cannot tolerate, β-blockers. Like β-blockers, ivabradine reduces heart rate, but it does not affect myocardial contractility.

Ivabradine is well tolerated and a recent subanalysis of 232 patients aged 65 and older in the INITIATIVE study[11] showed that ivabradine was at least as effective as atenolol in older people with angina, without the common side-effects of β-blockers. In patients older than 65, total exercise duration was increased by 88·7±119 seconds (from 567·2±157·9 seconds) with ivabradine 7·5mg and by 65·6±136·6 seconds (from 555·5±154·8 seconds) with atenolol 100 mg once daily. Time to 1 mm ST-segment depression on exercise testing increased by 101·9±145·9 seconds (from 485·2±175.3 seconds) with ivabradine and by 81·7±150·5 seconds (from 473·3±156·3 seconds) with atenolol.[11] This substudy showed that the good clinical efficacy and tolerability of ivabradine, previously demonstrated versus atenolol in 939 patients with stable angina, is maintained in elderly patients.

Conclusion

Elderly people are at increased risk of angina as with all forms of ischaemic heart disease. Effective symptom relief is available, but comorbidities and polypharmacy can often limit therapeutic options in this particularly vulnerable patient population. Optimum medical treatment appears to be as effective as the more invasive strategy of percutaneous coronary intervention in stable angina, and ivabradine is a new treatment option that effectively controls angina symptoms in patients with intolerance or contraindications to standard β-blocker treatment.

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