Optimal treatment for complex coronary artery disease and refractory angina

The many advances made in treating myocardial infarction and coronary artery disease has brought a new challenge – that of refractory angina. This is defined as chronic stable angina that persists despite optimal medical treatment in patients where revascularisation is unfeasible or where the risks are unjustified.

Refractory angina is becoming increasingly prevalent as patients with coronary artery disease live longer and reach a stage where intervention or medication does not adequately control symptoms. These patients very often have good left ventricular function and therefore a good prognosis. But we need to ensure that the outcome of increased life expectancy results in a life that is worth living.

Epidemiology

The absolute prevalence of refractory angina is unknown but it is estimated to be in the region of 5–10% of those with a diagnosis of angina. In Europe, there are an estimated 30–50,000 patients who present each year with refractory angina,[1] while in the US there are an estimated 25,000–75,000 patients each year.[2]

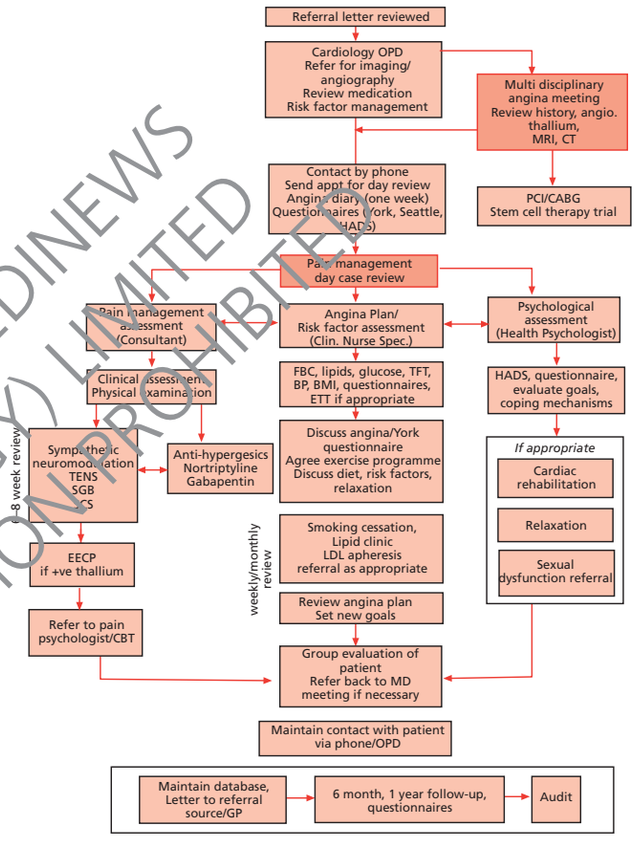
The many treatment options that are available to relieve angina need to be explored to help the patient feel they are not at the 'end of the road', particularly since they often have a good prognosis. At the Royal Brompton Hospital in London, cardiological, pain medicine and surgical teams, along with other colleagues, have set up a Specialist Angina Service to treat such patients.

Treatment options

Sharing the decision-making within a multidisciplinary format is the way forward. The Royal Brompton's aim is to provide a patient-centred model of management. These are complex patients who may have had a variety of interventions and treatments. The treatment pathway outlined in figure 1 demonstrates the wide range of options that are available.

Further intervention, especially with the use of imaging to ascertain the target areas of ischaemia as well as assessing left ventricular function, should always be considered. Advances in surgical and percutaneous interventions have also enabled more patients to be considered eligible for such techniques. Medication should be revised and new agents considered, bearing in mind that there is often little benefit to loading the patient with triple or quadruple therapy. The importance of secondary prevention cannot be underestimated and careful attention should be given to blood pressure control, monitoring of lipid profile and management of diabetes.

Figure 1. Specialist angina service treatment pathways



Key: OPD = out-patients department; MRI = magnetic resonance imaging; CT = computed tomography; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting; HADS = Hospital Anxiety and Depression Score; FBC = full blood count; TFT = thyroid function test; BP = blood pressure; BMI = body mass index; ETT = exercise tolerance test; TENS = transcutaneous electrical nerve stimulation; SGB = stellate ganglion block; SCS = spinal cord stimulator; EECP = enhanced external counterpulsation; LDL = low-density lipoprotein; CBT = cognitive behaviour therapy; MD = multidisciplinary

Anxiety and depression

It is important that all health professionals caring for patients with angina are aware of the high level of anxiety and depression associated with this condition. It is often described as discomfort rather than pain, yet it causes amongst the highest degree of anxiety and depression compared to sufferers of other chronic painful conditions.[3] Moore *et al.* studied 69 patients with refractory angina and found anxiety in 50% and depression in 33%. This played a major role in reduced quality of life.[4] The Hospital Anxiety and Depression Score (HADS)[5] is a well validated, short questionnaire for assessing such conditions. The Royal Brompton unit also uses the UK Seattle Angina Questionnaire (Seattle Questionnaire)[6] and York[7] Questionnaire to assess functional capacity and comprehension of coronary disease, respectively.

The perception of angina being linked to imminent death has a seriously deleterious effect on the total morbidity associated with angina. Where appropriate, a positive discussion about prognosis is a vital part of treatment. The Angina Plan[8] is a home-based package for helping patients understand their condition and allay fears, as well as facilitating behavioural change with the help of a health professional. The package includes risk factor management, a relaxation tape, and an individual exercise programme. It is particularly helpful for patients not able to make frequent trips to hospital.

Cardiac rehabilitation

The European Guidelines on Refractory Angina consider rehabilitation an important part of treatment for patients with refractory angina. Unfortunately many patients with angina are turned down from cardiac rehabilitation classes. Classes are available to our patients and include a tailored exercise programme, relaxation techniques and lifestyle advice.

Stellate ganglion block (temporary sympathectomy)

In many cases the use of stellate ganglion blockade (SGB) can reduce angina symptoms and increase quality of life. SGB is a simple, quick and safe procedure with reproducible results in the cohort of patients that respond to this therapy.[9] In our unit we initially undertake blockade and, if good analgesia is achieved for more than one month, we can offer this as a potential maintenance therapy.

Neuromodulation

Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation (TENS) has been used for more than 20 years in the treatment of angina.[10] This can also be an extremely effective, yet simple device to reduce angina. The initial regime is to use TENS three times a day for one hour and, additionally, when angina occurs, or for prophylactic use. It is contraindicated with permanent pacemakers and implantable defibrillators. Skin irritation can occur at the electrode site and some patients find the inconvenience of wearing the unit with its accompanying wires and pads can outweigh its benefits.

Spinal cord stimulator

Many trials have demonstrated the benefits of spinal cord stimulation (SCS) and its cost-effectiveness.[11] There is evidence to show that SCS provides excellent symptomatic relief, reduction in anti-anginal medication and frequency of attacks. SCS can also be used as an alternative to coronary artery bypass grafting providing an equivalent quality of life, pain control and much reduced morbidity and mortality. This was shown in Mannheimer's randomised trial of 104 patients comparing redo surgery with SCS implantation.[12] Patients must understand that this procedure is not a 'cure' but an aid to reduce angina and improve quality of life. SCS is a safe procedure and does not mask the warning signs of a myocardial infarction.[13]

Enhanced external counterpulsation

Enhanced external counterpulsation (EECP) works on the same principle as aortic balloon counterpulsation but is applied externally by using sequential pressure compressive cuffs. The reduction of left ventricular overload, increase in venous return and augmentation of diastolic aortic pressure causes increased coronary flow. It is thought that the increase in transmyocardial pressure leads to opening of collaterals. There is one randomised controlled study, the MUST-EECP trial,[14] which looked at the effects of this technique in patients with documented coronary artery disease and positive exercise test. The authors found there was a significant increase in the time to onset of exercise-induced ischaemia but not its duration. This was only seen in the patients that completed the 34 sessions.

The main contraindications for EECP are arrhythmias, bleeding diathesis, active thrombophlebitis, aortic aneurysm and pacemaker.

Stem cell therapy

Studies are beginning to emerge showing that stem cell therapy (SCT) may be beneficial in angina treatment.[15] Fifteen patients with refractory angina were given autologous unfractionated bone marrow administered via the coronary sinus. At one year there were no deaths and significant improvement in quality of life and anginal frequency. Coronary angiography showed more collateral vessels were seen in 10 of the 15 patients. Two patients did show progression of disease. Much more research needs to be done in

this area before we know whether it will be a suitable treatment for refractory angina.

Conclusion

Many patients with refractory angina can get caught in a loop of six-monthly visits to out-patient clinics where their medication is up-titrated, down-titrated, reintroduced and stopped but to no great effect. It results in a poor quality of life with an accompanying feeling of despair. At this stage, referral to a specialist centre should be considered.

- **If you have a patient you consider suitable for referral, please write to Professor Kim Fox, Royal Brompton Hospital, Sydney St, London, SW3 6NP.**

Conflict of interest

None declared.

Editors' note

This editorial is linked to the first of a new series 'Clinics from the Royal Brompton Hospital' (see pages 364–6) in which we will be inviting responses to cases presented at a multidisciplinary meeting.

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