NICE evaluation of transmyocardial laser revascularisation and percutaneous laser revascularisation for refractory angina

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The vast majority of patients with angina due to underlying coronary artery disease can have their symptoms adequately controlled by anti-anginal drugs, percutaneous coronary intervention or coronary artery bypass surgery. There is, however, a cohort of patients with extensive coronary artery disease whose angina persists despite medical treatment and who are not suitable for conventional revascularisation procedures. A variety of treatments have been used in this patient group, including cognitive behavioural therapy, precordial transcutaneous electrical nerve stimulation, spinal cord stimulator implantation, intermittent local anaesthetic, sympathectomy, opioids, external enhanced counter pulsation, percutaneous myocardial laser revascularisation (PMR) and transmyocardial laser revascularisation (TMR). The last two treatments have recently been evaluated by the National Institute for Health and Clinical Excellence (NICE).

TMR is a surgical procedure carried out under general anaesthesia and was first described in 1983. High-energy lasers are used to create channels within the wall of the left ventricular myocardium. The original theory was that these channels carried blood from the ventricular cavity into the myocardium, thereby relieving the symptoms of myocardial ischaemia. This was based on the model of the reptilian heart, in which the left ventricle is directly perfused from endothelium-lined channels which radiate out from the cavity of the left ventricle. This mechanism of action is unlikely, since the channels have been shown to occlude in the weeks following surgery. Other theories on the mechanism of action include the development of new blood vessels (angiogenesis) and also damage to the nerve supply of the heart (denervation). It is possible that there may be a placebo effect which contributes to the improvement in patient’s symptoms. The area to be treated by TMR is usually identified from the coronary angiogram and/or myocardial perfusion scanning and echocardiography. A lateral thoracotomy is performed and the pericardium opened, usually without cardiopulmonary bypass. A variety of laser devices have been used to create channels from the epicardial surface to the endocardial surface of the left ventricle. A transoesophageal echocardiogram is usually used to confirm creation of the channel into the left ventricular cavity. The procedure can be undertaken in conjunction with a standard coronary artery bypass procedure. The review by NICE included 10 randomised controlled clinical trials, involving a total of 1359 patients. Seven of the trials compared TMR with continued medical management and in two trials coronary artery bypass surgery was compared with a combination of TMR and coronary bypass surgery. Six studies involved a Holmium:YAG laser, three a carbon dioxide laser and one an Excimer laser. A meta-analysis found no difference in the 12-month mortality between patients treated by TMR and those in the control groups. When the two trials involving patients undergoing concomitant TMR and coronary artery surgery were excluded, there was still no difference in 12-month mortality.

Six of the randomised controlled trials (RCTs) found no significant difference in myocardial perfusion in the TMR-treated patients as compared with the patients treated medically. One study found a significant difference between the two groups favouring the control arm, while one study showed significant benefit in the TMR limb. When the results of treadmill exercise testing were compared at 5-months of follow-up, the meta-analysis of four RCTs demonstrated a mean improvement from baseline in total exercise time of 120 s in the TMR-treated patients as compared with those treated medically. For the angina score, some trials used the Canadian Cardiac Society Angina (CCSA) and some the New York Heart Association score. The meta-analysis of the angina score, using these four class scales, showed an improvement in angina score in the TMR group as compared with the control group of −1.8 classes at 6 months of follow-up and −1.0 classes at 12 months of follow-up. There were significant improvements in quality of life measurements for the TMR-treated patients as compared with controls, although none of the studies had blinded patients to their treatment. The pooled results of the 10 RCTs showed no difference in postoperative mortality between the TMR group and the control group. When the two trials involving patients with concomitant coronary artery were excluded, postoperative mortality was greater in the TMR group than in controls (OR=0.35; 95% CI 0.13 to 0.93). In seven of the randomised trials there was a higher rate of myocardial infarction at 12 months in the TMR-treated patients (6%) than in the control group (2%). There also appeared to be an increased risk of postoperative heart failure in the TMR-treated patients (34%) as compared with the control group (9%) and an increased risk of thromboembolic events (10% and 3%, respectively). Other complications which have been reported following TMR...
include non-inflammatory pericarditis, acute mitral regurgitation (in up to 5% of patients) and an increased risk of neurological events. The review by NICE has demonstrated that while there is an improvement in the more subjective outcome measures (including exercise tolerance testing, angina score and quality of life) this has to be balanced against the risk of postoperative mortality and morbidity which has been demonstrated. They concluded that the risk:benefit ratio in this patient population was unfavourable.

PMR was developed after initial, encouraging reports of TMR cohorts were published. It was expected that this percutaneous technique would result in symptomatic benefits similar to those of TMR, but at lower risk because a thoracotomy and general anaesthetic were not required. During PMR, energy was applied to the endocardial surface of the left ventricle by a catheter placed in the left ventricle via the femoral artery, and the ‘channels’ created were not intended to be transmural. Like TMR, the channels were created in ‘target’ areas of the myocardium selected by a combination of coronary angiography and myocardial stress perfusion imaging, but generally fewer channels were created during PMR than TMR, and achieving a uniform distribution over this target area could be challenging depending on the size and geometry of the ventricle and papillary muscles.

A wide variety of PMR laser types, energies and techniques have been reported in both observational and analytical studies. This has made the robust review of this field, and its conflicting results, more difficult. The relatively small patient populations in individual PMR studies mean that meta-analysis appears attractive, but the heterogeneity of the interventional techniques, together with variations in comparators and outcomes, makes this an approach with the potential for erroneous conclusion.

The recent NICE evaluation of PMR assessed efficacy with regard to the following outcomes: 12-month mortality, myocardial perfusion by single photon emission CT, left ventricular function by ejection fraction at 3 or 12 months, exercise tolerance by time on Bruce protocol treadmill testing at 6 or 12 months and angina symptoms, measured by an improvement in two classes in the CCSA score at 6 or 12 months. None of these outcomes selected demonstrated differences that were statistically significant in comparison with baseline or with a comparator group.

A meta-analysis of five RCTs of PMR reported that, in contrast to TMR, there was no significant increase in mortality. Postprocedural complications included myocardial infarction, left ventricular perforation and tamponade, cerebrovascular accidents and transient ischaemic attacks, femoral artery pseudoaneurysms and haematomas. The pooled myocardial infarction rate from six RCTs was 7% in PMR patients and 4% in controls. Rates of ventricular perforation were reported to be as high as 4% and as low as 1%, and a small case series of 25 patients reported a tamponade prevalence of 3%. Cerebrovascular accidents or transient ischaemic attacks occurred in 4% of PMR patients and 2% of control patients, in a pooled analysis of four RCTs. The NICE guidance states that PMR ‘shows no efficacy’ and ‘may pose unacceptable safety risks’ and concludes that the procedure should not be used.

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