J.Sadowski, P.Rudziński, J.Piątek, T.Myrdko, K.Wrobel, B.Kapelak, K.Wierzbicki

TRANSMYOCARDIAL LASER REVASCULARIZATION FOR TREATMENT PATIENTS WITH END STAGE CORONARY ARTERY DISEASE

Department of Cardiovascular Surgery & Transplantology Jagiellonian University
Krakow, Poland

Abstract : The purpose of the present study was to analyze the effects of transmyocardial laser revascularization (TMLR) on myocardial perfusion. The value of 99 m Tc –MIBI scintig-raphy in the detection of changes in perfusion of the lased and nonlased segments was assessed as well. In 120 patients before TMLR and then 3 and 6 months after-wards, MIBI scintigraphy and a stress test were carried out. At the beginning of the study, all patients were clas-sified as having angina pectoris class III or IV (according to the criteria of the Canadian Cardiac Society); their ejection fraction was >30%. The parameters of the stress test increased significantly in 70% of the patients. Car-diac scintigraphy revealed improved perfusion of 33.7% of the transient defects within 3 months after TMLR which persisted at 6 months with a clear trend towards further improvernent in the Iased segments. TMLR has been found to be particularly beneficial in patients in whom other invasive methods of treatment cannot be applied.
Key words: Transmyocardial laser revascularization , coronary artery diseases, stress testing.

Introduction

Advances in medical science such as percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG) have contributed to the general relief of angina symptoms as well as have been effective in considerably extending the life span of many patients with coronary artery disease. There remains, however, a group of patients suffering from intractable angina that has been resistant to all forms of therapy except heart transplantation.

Transmyocardial laser revascularization (TMLR) is an emerging surgical technique, making use of laser to create channels from the epicardial to endocardial surface of the heart, so as to allow oxygenated left ventricular blood to directly perfuse the ischemic myocardium. TMLR has recently been approved as a therapeutic modality in the treatment of patients with intractable angina and severe coronary artery disease not amenable to CABG or PTCA. This technique is based on the theory of the reptilian model of circulation. It is common knowledge that rep-tiles do not have coronary arteries and obtain their blood supply for the myocardium through channels originating directly from the lumen of the left ventricle.Mirhoseini commenced animal experiments in 1970 r with the aim of having this circulation reduplicated . Eventually Mirhoseini et al. [1,2] proposed the use of laser to create transmyocardial channels. Transmyocar-dial revascularization utilizing later technology has been shown to improve the functional class of.angina pectoris[3]. It still remains an open question, however, to what extent an improvement of a patient's clinical status is impacted by the advantageous changes in myocardial per-fusion and which specific noninvasive cardiac imaging procedures may prove of tangible benefit in the actual assesment of the structural changes occurring after TMLR.

Stress myocardial perfusion scintigraphy has gained wide acceptance as an accurate technique for the detec-tion localization of coronary artery disease. In addi-tion to utilizing exercise scintigraphy to identify patients who are suitable for cardiac surgery, stress myocardial perfusion imaging can be carried out after revasculariza-tion in order to determine the changes in myocardial per-fusion during the long-term follow-up period.

The present study set out to test the hypothesis that TMLR can reduce ischemia and improve perfusion in patients with refractory angina pectoris and diffuse coro-nary artery disease. Another objective consisted in assess-ing the effectiveness of myocardial scintigraphy in establishing- the likelihood of perfusion improvement following the application of the TMLR procedure.

Materials and Methods

This present study included 120 patients (90 men and 30 women; mean age 57 ± 9 years) who underwent TMLR between November 1996 and December 2003.

The patients selected to receive TMLR had been previously previously excluded from both CABG and PTCA due to the specific location and diffuseness of the disease and/or because of poor results from the previous revascularization procedures. Preoperative assess-ment included a review of all cardiac medications being used by the patients and the determination by echocardiography of a left ventric-ular fraction in excess of 30%; all patients were classified as it class III or IV angina pectoris according to the CCS criteria.

At the time of enrollment in the present study, all 120 patients underwent exercise ^{99}mTc-MIBI scintigraphy for the assessment of myocardial perfusion. All of them were required to have evidence of an ishemic but viable myocardium demonstrated by scintigraphy that was not limited to the septum. The viability was defined in the with impaired muscle function, as assessed by echocardiog-raphy.

Study Protocol

All patients underwent exercise myocardial perfusion scintigra-phy imaging to evaluate left ventricular perfusion before and 3 and 6 months after TMLR. All patients were evaluated for angina accord-ing to the CCS classification. The angina class was determined at the time of each MIBI imaging. The medical regimen was also reviewed at the time of angina class evaluation.

Transmyocardial Laser Revascularization

In the patients with diffuse coronary artery disease and very nar-row coronary vessels previously enrolled in the study in whumu CABG could not be performed, revascularization was achieved with the aid of TMLR**.** Surgery was carried out following a medial sternotomy approach on the beating heart, without a cardiopulmonary bypass.

The instrument was a 20-watt-pulsed holmium: yttrium-alumi-num-garnet laser. The power output was set at 7 W with a frequency of 5 Hz and a pulse width of 200 ms. Application of energy was not gated to the cardiac cycle and required three to eight pulses to traverse the myocardium. The TMLR procedure consisted of delineating 12—60 channels of 1 mm in diameter from the epicardial surface of the heart to the endocardium, along the course of a diseased During the postoperative period, each patient received anticoagulant therapy in compliance with the protocol used for CABG patients.

Data Analysis

The results are expressed as mean values ± SD, unless othert specified. Comparison of the results of stress test and scintigra before and after TMLR was made with the aid of the Student Differences were considered statistically significant at $p < 0.05$.

Results

All patients, in compliance with CCS classification,

were allo-cated to class III or IV angina pectoris before surgery.

The medications taken by the patients at the time of enrollment included beta blockers (75%), nitrates (100%), angiotensin-converting enzyme inhibitors (84%), and lip-id-lowering agents (63%).

20% died perioperatively due to the left ven-tricular dysfunction and congestive heart failure. Periop-erative myoeardial infarctions (confirmed enzymatically and electrocardiographically) occurred in 30% patients and transient ventricular arrhythmias in 20% .Atrial fibrillation occurred in 10% patient who was treated pharmacologically.7% patient required rethoracotomy due to high postoper-ative drainage.

Before TMLR, 88 patients (73%) were in CCS class IV and 32 (27%) in class III. After TMLR, 79 patients (66%) experienced improvement in their angina class. At the end of the study, no patient had class IV symptoms; 15 (12.5%) were in class III and 90 (75%) in class II and 15 (12.5%) in class I. Despite the significant symptomatic improvement in the patients' symptoms, no major changes of the antianginal medical regimen were per-formed.

Stress test results were evaluated in 80% patients after surgery. During the first 3 months after surgery, all parameters under investigation improved in 67% patients did not change in 16.5% patients , and deteriorated in 16.5 % . Specifficaly, the patients had improved their performance during stress tests, and an increase in the percent-age of the maximal age-predicted value $p<0.06$ was observed.No significant differences were observed between the results obtained 3 and 6 months following surgery.

Three month after the procedure, the perfusion improved globa1ly in 33.7% of the transient defects, did not change in 53%, and deteriorated in 12.4%. A separate analysis of the lased and the nonlased segments revealed that the reduction in ischemia occurred predominantly among the lased segments, with no significant changes in the nonlased ones. The effects of TMLR on the left ven-tricular perfusion evident at 3 months still persisted at 6 months, with a clear trend towards further improvement of regional perfusion.

Discussion

The TMLR method of revascularization is used in the treatment of patients with advanced coronary disease considered ineligible for alternative revascularization procedures. Since 1993, a steadily growing popularity of such procedures and the development of new laser tech-niques have been observed. TMLR does not require the use of extracorporeal circulation, and consequently the duration of the procedure itself and of the hospitalization thereafter is perceptibly shorter and the treatment costs significantly reduced.

This study demonstrated that the improvement of per-fusion during the first 6 months and a perceptible trend towards an increase in the number of viable nonischernie segments were related to a clinical improvement in angi-na, a reduction in the inducible myocardial ischemia, and greater stress tolerance. Exercise scintigraphy was used to identify the patients eligible for TMLR and was subsequently applied after sur-gery in order to determine the changes in myocardial per-fusion during the long-term follow-up period.

In the study performed by Horvath et al. [4], a signifi-cant improvement in perfusion was observed 3 months after surgery, with a further improvement after the fol low-ing 6 months. The author suggested that subjective clinical im-provement could not be explained solely by the improved perfusion. We observed a marked improvement in exercise toler-ance and alleviation of angina, though not necessarily related to the significant changes in myocardial perfusion. The amelioration of angina symptoms after TMLR may be related to a significant enhancement of regional blood flow to the zone of the ischemic myocardium which was preoperatively supplied via the physiologically most se-vere stenosis, as determined by coronary angiography Residual defects may not be functionally significant. As alreadv reported by Verani et al. it is unusual to see complete normalization of stress-induced defects after coronary revascularization. The same explanation could well apply to our results. We observed a greater improve-ment in exercise tolerance and amelioration of anginal symptoms as compared with the changes encountered after total rnyocardial perfusion.

Although the precise mechanisms, responsible for the beneficial effects of TMLR remain elusive, its success is based in theory on the assumption of an improved region-al blood flow to the ischemic myocardium. Anatomical evidence of channel patency was demonstrated in an ani-mal model and in humans . The results of physio-logical and anatomical studies in experimental animal models suggested, however, that blood did not necessarily flow through these channels.These findings would suggest that patients undergoing TMLR might not derive any perfusion benefit during the days following the procedure. The early improvement in angina may at least in part be due to sympathetic denerva-tion [5]. The late improvement is probably related to neoangiogenesis that appears during a later phase [6].

Laser-mediated vascular growth is a time-consuming process. and the earliest has been shown to occur 2—3 weeks after TMLR, with progressive increase thereafter . Evidence of neoangiogenesis and smooth muscle cell proliferation after TMLR was shown in animal models .In the present study, beneficial effects were evident by 3 months and persisted at 6 months. We also observed no increase in the number of infarcted segments. Very much in line with the findings of Donovan [7], we also assumed that TMLR did, in fact improve local perfusion to ischemic regions and did not creat regions of micriinfarction. The mechanism for improving local perfusion to ischemic regions has not as yet been well explained, although direct perfusion from channels and neovascularization are among the proposed hypotheses.

These results may lead to a more widespread acceptance of TMLR procedure in patients with refractory angina.

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E-mail: kardiochir@szpitaljp2.krakow.pl