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Evaluation of transmyocardial laser revascularization (TMLR) by gated myocardial perfusion scintigraphy

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TMLR is a novel treatment for patients with coronary artery disease. It comprises the creation of transmyocardial channels thought to improve myocardial perfusion. Gated Tc-99m sestamibi scintigraphy was used to evaluate changes in myocardial perfusion after TMLR. Twelve patients underwent TMLR using a carbon dioxide laser. Sestamibi scans were carried out following a standard protocol prior to and 1, 3, 6, and 12 months after TMLR. Both visual and semi-quantitative assessment showed improvement in 4 patients, deterioration in 2 patients, and no change in the remaining 6 patients each. However, visual and semi-quantitative assessment were concordant in 6 patients and discordant in 6 patients. In 3 of these, semi-quantitative assessment suggested a better outcome, and in 3 patients visual assessment gave better results. Our findings in a small group of patients suggest that about a third benefited from TMLR. Gated myocardial perfusion scintigraphy using technetium-99m sestamibi is suitable for visual evaluation of changes in the lased area over time, but does not allow semi-quantitative evaluation in the patient population typically treated with TMLR. Further investigations using optimized imaging protocols, including positron emission tomography and three dimensional image presentation, are warranted.

Key words: myocardial perfusion scintigraphy, sestamibi, ischemic heart disease, myocardial revascularization

INTRODUCTION

BOTH CORONARY ARTERY BYPASS GRAFTS (CABG) and percutaneous transluminal coronary angioplasty (PTCA) are well established interventional treatment modalities for patients with ischemic heart disease. CABG requires open heart surgery, whereas PTCA is performed after catheterization of the left heart. There are, however, some patients for whom neither of these two procedures is suitable, mainly for reasons of their distinct coronary pathology. Transmyocardial laser revascularization (TMLR) may present an alternative or adjunct treatment for these severely ill patients.

TMLR comprises the creation of tiny transmyocardial channels with a laser. Different types of lasers have been used in animals and man, namely carbon dioxide, holmium: yttrium-aluminium garnet (YAG), and argon. The mechanism by which myocardial perfusion might be increased by this procedure remains largely unclear. Theories about how TMLR improves myocardial perfusion include direct blood flow from the lased channels into the myocardial vascular plexus and neoangiogenesis caused by the laser-induced myocardial injury. There are conflicting reports regarding long-term patency of these channels.[1–4]

The aim of this study was to evaluate changes in regional myocardial perfusion after TMLR using gated technetium-99m sestamibi myocardial scintigraphy which seems to be highly suitable for this purpose as the tiny lased channels cannot be made visible by any means, namely coronary angiography or ultrasound.

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Table 1 Clinical details of patients included in the study

patient			medical history					coronary angiography				surgery		
initials	age	sex	hypertension	diabetes	hyperlipidemia	peripheral vascular disease	myocardial infarction	RCA	LAD	LCX	LVEF	CABG (vessel)	TMLR (territory)	number of holes
EW	64	f		+	+	+	ant × 3	50%	100%	60%	45%	—	LAD, LCX	34
MB	63	m	+		+			70%	70%	100%	60%	RCA, LCX	LAD	16
HF	67	m			+		ant & post	90%	100%	80%	68%	RCA	LAD, RCA	17
ER	76	m	+	+			ant & post	90%	75%	80%		RCA	LCX	11
LK	67	f	+	+	+	+	post × 3	90%	100%	50%	67%	RCA	LAD, LCX	21
EL	75	f	+	+			ant	50%	100%			—	LAD	12
RS	55	f	+					60%	50%		76%	RCA	LAD	8
RE	50	m		+	+				90%	70%	65%	RCA, LCX	LAD	8
WW	54	m	+				ant	100%	100%	100%	69%	RCA, LAD, LCX	LAD	11
EK	74	m	+	+		+		75%	100%		60%	RCA	LAD	11
IW	79	f						100%	100%	50%	58%	RCA	LAD	18
EP	61	m					ant × 2	100%	60%		68%	RCA	LCX	7

RCA, right coronary artery; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery

Table 2 Myocardial perfusion of the lased area (as judged by visual and quantitative evaluation, see text for details) and LVEF before and 1, 3, 6, and 12 months after TMLR. Pre-treatment perfusion set to 100%

patient	overall evaluation		semi quantitative evaluation									LVEF (%)				
	visual	semi-quantitative	reference region	stress perfusion (%) 1	3	6	12	rest perfusion (%) 1	3	6	12	0	1	3	6	12
EW	no change	worse	RCA	83	83	53		98	65	66			30	22		
MB	better	better	RCA	97	118	120	124	79	88	96	93		47		36	80
HF	no change	no change	LCX		86	90	89		104	106	103			36	38	12
ER	no change	no change	LAD	107			103	108			83		53			36
LK	no change	worse	RCA	81	58	60	79	81	63	56	83		46	49	65	
EL	no change	better	LCX	100	94	86	88	121	123	114	107		55	30	50	
RS	better	no change	LCX	119	90	94	93	111	99	86	98	76	80	83	77	
RE	better	better	RCA	101	105	109	122	114	101	115	106	69	72	65	75	55
WW	worse	no change	RCA	98	93	104	103	98	101	93	101	46	51	62	55	56
EK	better	better	LCX	129	105	112	136	131	128	129	114		65	60	53	54
IW	no change	no change	LCX		96	116	85		94	110	94	57		55	64	60
EP	worse	no change	LAD	61	83	109		123	96	109			77	81	76	
mean				98	92	96	102	106	97	98	98	62	58	54	59	50
SD				19	15	22	19	17	20	22	10	13	16	20	15	21

METHODS

Patients. Twenty-one patients whose coronary pathology was unsuitable for CABG to at least one coronary territory underwent TMLR. Nine patients had to be excluded from the study: These consisted of two patients who died before their first follow-up and 7 patients in whom a base line scan could not be obtained. Clinical details of the 12 patients who remained in the study (5 women and 7 men, mean age 65 years) are given in Table 1. Fifty-four sestamibi scans could be obtained. One patient (EW, see Table 1) died between 6 and 12 months follow-up. Canadian Cardiovascular Society (CCS) classification and a nitrate score were recorded before TMLR and at each follow-up to assess clinical improvement. The study was approved by our ethics committee.

Transmyocardial laser revascularization. TMLR was performed during open heart surgery using an ECG gated carbon dioxide laser (The Heart Laser, PLC Systems Inc., Franklin, MA). The number of holes created was 8–34 (mean 15). Initial transmyocardial patency was checked with transesophageal echocardiography which shows gas bubbles in the left ventricle immediately after the laser is fired. The epicardial ends of the channels seal within a few minutes if the procedure is done within viable myocardial tissue. In the majority of patients, TMLR was performed

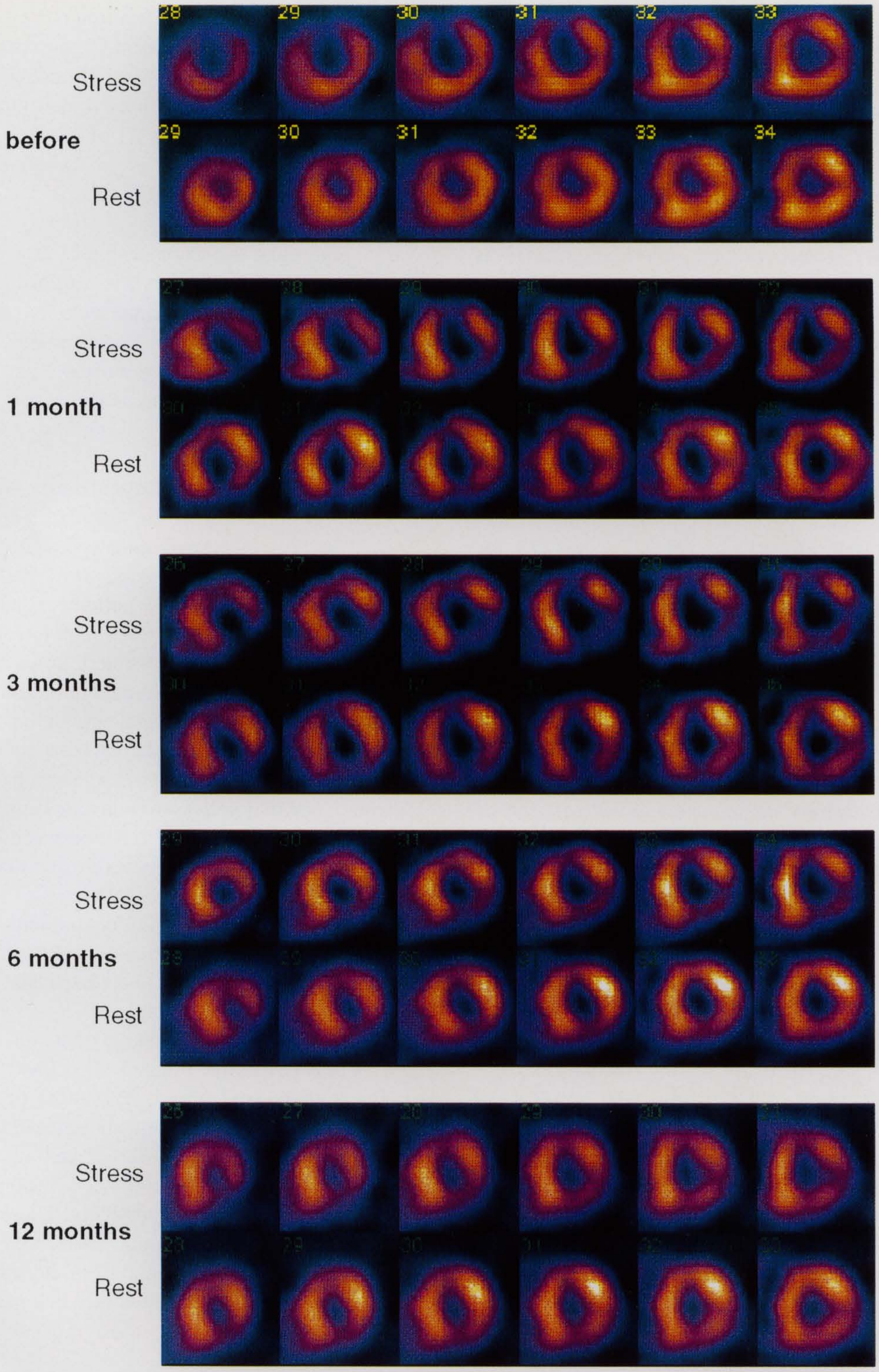

Fig. 1 Example of a patient (MB, see Table 1) before and after TMLR. Short axis slices after stress and at rest are shown. Inferoseptal segments were used as a reference. The perfusion of the lased area in the LAD territory seems to improve continuously. However, this patient apparently suffered a clinically silent posterior myocardial infarction during the follow-up period.

as an adjunct to CABG (to vessels supplying myocardial areas not affected by TMLR, with the exception of patients HF and WW, see Table 1). Two patients (EW and EL, see Table 1) had TMLR only.

Sestamibi scans. Technetium-99m sestamibi scans were carried out prior to and 1, 3, 6, and 12 months after

TMLR following a standard one-day protocol: The patients were asked to fast overnight. Cardiac medication with a short biological half-life was withdrawn 24 hrs prior to the investigation. This consisted of a stress test (as detailed below) with injection of 370 MBq Tc-99m sestamibi (methoxyisobutyl isonitrile; Cardiolite®, DuPont, Wilmington, DW), followed by the first scan 60 mins later. Immediately afterwards 800 MBq sestamibi were injected at rest and a second scan (ECG gated) was performed after 90 mins. Patients were encouraged to eat and drink after each sestamibi injection.

All patients but one (see below) were injected with 0.5 mg/kg dipyridamole (Persantin®, Boehringer Ingelheim, Germany) intravenously over 4 mins, with sestamibi being injected after another 2 mins. As a precaution against dipyridamole-induced hypotension, these patients were also exercised at 50 W for 6 mins, starting 2 mins after the onset of the dipyridamole infusion. One patient (RS, see Table 1) performed a bicycle stress test (25, 50, 75, and 100 W for 2 mins each with injection of sestamibi at peak exercise, followed by another 2 mins at 50 W). The amount of mechanical or pharmacological stress administered to each patient was kept constant during follow-up.

Scans were carried out using a triple-head gamma camera with focusing low-energy high-resolution collimators (Siemens Multispect III with CardioFocal collimators). Acquisition parameters were as follows: energy window 140 keV ± 15%, matrix 64 × 64, 120° rotation of each head, 40 views of 30 s each (non-gated)/30 views of 60 s each (gated), 8 frames per RR-interval, acceptance of pre-set RR-interval ± 20%. Reconstruction was performed with a filtered backprojection using a Butterworth filter (cutoff 0.7, order 9).

Quantification. The location of each lased channel was documented by the surgeon in a chart showing the epicardial surface of the heart and the coronary vessels. From this the location of the lased area in a bull's eye picture was estimated for each patient. According to coronary angiography, none of the patients had an aberrant coronary anatomy. A reference region of 2–4 bull's eye segments which were affected neither by TMLR nor CABG (except in patients MB, LK, RE, and WW who had severe three-vessel coronary disease where the reference region had to be placed in the territory of an RCA bypass graft) and remained visually unchanged throughout the study, was also determined individually. Bull's eyes were calculated for both exercise and rest sestamibi scan and normalized using the reference region as a standard. Changes in regional myocardial perfusion of the lased area over time could then be expressed as a percentage of the pretreatment perfusion level. Improvement was defined as an increase in perfusion of at least 10% in at least 2 follow-up scans either after stress or at rest. A decrease in perfusion of at least 10% in at least 2 follow-up scans after stress and at rest was regarded as deterioration.

Left ventricular ejection fraction (LVEF). This was calculated from end-systolic and end-diastolic short and long axis slices of the left ventricle using the Siemens' ICON software package.[5] Due to arrhythmias, LVEF could be determined in only 41 of the 54 scans (76%).

RESULTS

Visual reading of the scans (Table 2) showed that perfusion of previously ischemic myocardium increased in 4 patients and decreased in 2 patients. No changes were seen in 6 patients, 4 of whom had normal perfusion of the lased area, whereas the remaining 2 patients showed decreased perfusion after stress and at rest. In these two latter cases, a thallium-201 scan was performed and showed viable myocardium.

The results of the semi-quantitative assessment of myocardial perfusion of the lased area are detailed in Table 2. In 4 patients improvement could be seen, whereas 2 patients showed deterioration. No significant change was seen in the remaining 6 patients. Evaluation of the counts acquired in the reference regions (after adjusting for the activity injected) revealed, however, that these were not constant over time (data not shown).

Semi-quantitative and visual assessment were concordant in 6 patients and discordant in 6 patients. In 3 of these patients semi-quantitative assessment suggested a better outcome, and in 3 patients visual assessment gave better results. However, differences between semi-quantitative and visual assessment were never greater than one step on a "better-no change-worse" scale.

Changes in LVEF in individual patients (Table 2) did not seem to follow any particular pattern. Visual evaluation of regional wall motion of the lased area did not reveal any major changes over time.

The median CCS classification improved from 3 (range 2–4) before TMLR to 2 (range 1–4) at 1 and 3 months, and to 1 (range 1–4) at 6 and 12 months post treatment, respectively. The median nitrate score changed from 3 (range 1–4) before TMLR to 0 (range 0–2) at 1 month, 1 (range 0–3) at 3 and 6 months, and 2 (range 0–4) at 12 months post treatment, respectively. There was no clear association between these clinical scores and regional myocardial perfusion obtained from the sestamibi scans.

An example of a sestamibi study in a patient who had TMLR of the LAD territory (MB, see Table 1) is shown in Figure 1.

DISCUSSION

Transmyocardial laser revascularization is under investigation as an adjunct or alternative treatment to CABG and PTCA. However, little is known about the mechanism by which TMLR may improve myocardial perfusion.

Myocardial perfusion scintigraphy gives a picture of the distribution of myocardial blood flow and allows semi-quantitative evaluation of regional myocardial perfusion. Therefore, it seems to be well suited to assess TMLR-induced changes in myocardial perfusion over time.

In 12 patients who had TMLR, mostly as an adjunct to CABG, visual assessment showed that TMLR was beneficial in a third of the patients. Our results are in accordance with those of Horvath et al.[6] who found in a group of 20 patients that those with ischemia in the lased area received the greatest benefit. Cooley et al.[7] found a mean increase in subendocardial/subepicardial perfusion ratio of $20 \pm 9\%$ in 11 patients one year after TMLR. It is reasonable from a pathophysiological point of view that TMLR should improve subendocardial perfusion more than subepicardial, but it seems doubtful whether TMLR should be evaluated by changes in subendocardial/subepicardial perfusion ratio which may overstress the resolution of a gamma camera. Frazier et al.[8] reported 15 patients with no change in regional myocardial perfusion measured with thallium-201 scintigraphy, but described an increase in subendocardial/subepicardial perfusion ratio of 14% after 3 months and 21% after 6 months with PET. In an American multicenter trial with 200 patients improved perfusion after TMLR was found.[9] On the other side, Lutter et al.[10] reported no change in myocardial perfusion measured by hybrid PET and Nagele et al.[11] found reduced myocardial perfusion after TMLR.

The finding that visual and semi-quantitative assessments were discordant in half the cases may be related to several inherent difficulties of this kind of study:

a) reliability of the reference region

Visual evaluation of the reference regions showed constant perfusion over time. Semi-quantitative evaluation of the counts acquired in the reference regions revealed, however, that these were not constant over time. This may be related to either the biokinetics of the tracer, or general problems with quantifying single photon emitters, or both. A way round this obstacle would be to use positron emitting tracers which allow determination of absolute myocardial perfusion (e.g. ammonia-13 or rubidium-82).

b) patient population with mainly three-vessel coronary disease

It is mostly these severely ill patients in whom TMLR is going to be applied.[12,13] In four of our patients, multiple CABGs made it impossible to find a reference region that was not affected by bypass grafts. Furthermore, it may be postulated that the perfusion of the reference region does not necessarily remain constant during a one-year follow-up period in these severely ill patients.

c) identification of the exact location of the lased area in a bull's eye chart

This could be overcome in part by presenting the results of the sestamibi scans in a three dimensional projection and thus making it directly comparable to the chart in which the surgeon marks the location of the lased channels.

For these reasons, we conclude that visual rather than semi-quantitative evaluation gives a better reflection of regional myocardial perfusion in this study.

Our findings in a small group of patients suggest that a third benefited from TMLR. Gated myocardial perfusion scintigraphy using technetium-99m sestamibi is suitable for visual evaluation of changes in the lased area over time, but does not allow semi-quantitative evaluation in the patient population typically treated with TMLR. Further investigations using optimized imaging protocols, including positron emission tomography and three dimensional image presentation, are warranted.

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