Catheter-Based Percutaneous Myocardial Laser Revascularization in Patients With End-Stage Coronary Artery Disease

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OBJECTIVES
This study evaluates the feasibility and safety of a catheter-based laser system for percutaneous myocardial revascularization and analyses the first clinical acute and long-term results in patients with end-stage coronary artery disease (CAD) and severe angina pectoris.

BACKGROUND
In patients with CAD and intractable angina who are not candidates for either coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA), transmyocardial laser revascularization (TMR) has been developed as a new treatment that results in reduced angina pectoris and increased exercise capacity. However, surgical thoracotomy is required for TMR with considerable morbidity and mortality.

METHODS
A catheter-based system has been developed that allows creation of laser channels in the myocardium from within the left ventricular cavity. Laser energy generated by a Holmium:YAG (Cardiogenesis Corporation, Sunnyvale, California) laser was transmitted to the myocardium via a flexible optical fiber capped by an optic lens. The optical fiber was maneuvered to the target area under biplane fluoroscopy through a coaxial catheter system permitting movement in three dimensions.

RESULTS
Thirty-four patients with severe CAD not amenable to either CABG or PTCA and refractory angina pectoris (Canadian Cardiologic Society [CCS] Angina Scale Class III–IV) were included in the study. Ischemic regions were identified by coronary angiography and confirmed by thallium scintigraphy. The percutaneous myocardial revascularization (PMR) procedure was successfully completed in all patients. In 29 patients, one vascular territory of the left ventricle and in 5 patients, two vascular territories were treated. Eight to fifteen channels were created in each ischemic region. Major periprocedural complications were limited to an episode of arterial bleeding requiring surgical repair. There was one death early after PMR, due to a myocardial infarction (MI) in a nontreated region. Clinical follow-up at 6 months (17 patients) demonstrated significant improvement of angina pectoris (CCS class before PMR: 3.0 ± 0.0, six months after PMR: 1.3 ± 0.8, p < 0.0001) and increased exercise capacity (exercise time on standard bicycle ergometry before PMR: 384 ± 141 s, six months after PMR: 514 ± 158 s, p < 0.05), but thallium scintigraphy failed to show improved perfusion of the laser treated regions.

CONCLUSIONS
Percutaneous myocardial revascularization is a new safe and feasible therapeutic option in patients with CAD and severe angina pectoris not amenable to either CABG or PTCA. Initial results show immediate and significant improvement of symptoms and exercise capacity but evidence of improved myocardial perfusion is still lacking. (J Am Coll Cardiol 1999;34:1663–70) © 1999 by the American College of Cardiology
first introduced by Mirhoseini et al. (1), may offer a new and effective treatment. In TMR, laser energy is used to create transmural channels from the epicardial surface to the ventricular chamber. The intention to provide additional perfusion channels to the ischemic myocardium needed revision soon after this form of treatment was introduced into clinical practice because nearly all channels were found to be occluded early after their creation (2–6). Today various other mechanisms are in debate, such as denervation, neoangiogenesis and placebo effects in order to account for the clinical improvement experienced by the majority of patients.

One major drawback of TMR is the need for thoracotomy in order to gain access to the epicardial aspect of the heart. Therefore, a catheter-based system has been developed that allows the controlled creation of laser channels into the myocardium from the ventricular chamber (7,8). This technique, termed “percutaneous myocardial revascularization” (PMR), utilizes a Holmium-YAG laser recently introduced in TMR (9), which allows the laser energy to be transmitted to the heart via optical fibers. The design of the system allows access to all aspects of the endocardial surface.

This study reports the acute and long-term results of the first patients treated with PMR.

**METHODS**

**Patients.** Percutaneous myocardial revascularization was performed in 34 patients (26 men, 8 women) with severe disabling angina pectoris (Canadian Cardiologic Society [CCS] Angina Scale class III or IV) while receiving at least two antianginal medications at the maximum tolerated doses. Demographic and clinical data of the patients are given in Table 1. All patients had severe CAD on coronary angiography which was not amenable to either PTCA or CABG due to diffuse disease, complete occlusion, lack of graftable vessels or any combination thereof. Additional selection criteria were: 1) normal or only moderately impaired left ventricular performance (ejection fraction ≥35%), 2) stress induced myocardial perfusion defects on thallium-201 scintigraphy, and 3) wall thickness in the PMR target region >8 mm as determined by echocardiography. The “target region” was defined as the region of stress induced myocardial perfusion defects on thallium-201 scintigraphy which was not amenable to CABG or PTCA.

Patients were also excluded from PMR if they had unprotected left main coronary artery disease >50%, unstable angina pectoris or a change in antianginal medication within the last three months, myocardial infarction (MI) within the last three months, left ventricular thrombus, severe peripheral vascular disease that excluded femoral artery access, aortic stenosis that prohibited catheter access to the left ventricle or renal insufficiency with serum creatinine levels >2.5 mg/dl.

The study protocol was approved by the local ethics committee before initiation of the study. All patients gave written informed consent.

**CardioGenesis PMR System.** The design of the CardioGenesis PMR System (CardioGenesis Corporation, Sunnyvale, California) is shown in Figure 1A. The PMR guiding catheters are available with various angulations of the catheter tip. Guiding catheter and laser delivery catheter are freely movable against each other so that all areas within the left ventricular cavity can easily be reached. The laser energy is delivered through an optical fiber capped by a lens with a gold marker and an array of nitinol “petals” 3 mm from the tip (Fig. 1B). The purpose of these petals is to retard excessive advancement of the laser fiber into the myocardium and to stabilize the lens in the endocardial trabeculae.

**PMR procedure.** A 9 F sheath was introduced in the femoral artery for the PMR guiding catheter and a diagnostic 5 F coronary catheter was introduced in the contralateral femoral artery using standard Seldinger technique. Patients were heparinized with 10,000 IE intravenously. The guiding catheter was placed in the left ventricle after

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<th>Table 1. Clinical and Demographic Data of 34 Patients Treated With PMR</th>
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<td>Ejection fraction</td>
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<td><strong>Coronary angiography</strong></td>
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<td>1-Vessel disease</td>
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<td>Localization of ischemia</td>
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<td>Inferior wall</td>
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Abbreviations and Acronyms
- CABG = coronary artery bypass grafting
- CAD = coronary artery disease
- CCS = Canadian Cardiologic Society
- ECG = electrocardiogram
- LVEF = left ventricular ejection fraction
- MI = myocardial infarction
- n.s. = not significant
- PET = positron emission tomography
- PMR = percutaneous myocardial revascularization
- PTCA = percutaneous transluminal coronary angioplasty
- TMR = transmyocardial revascularization
- SPET = single photon emission tomography

CABG = coronary artery bypass grafts; CCS = Canadian Cardiologic Society Angina Scale; pat = patients; PTCA = percutaneous transluminal coronary angioplasty.
crossing the aortic valve with a standard 6 F pigtail catheter and connected to a heparin drip (1500 IE Heparin/500 ml saline). Left ventriculography and coronary angiography were performed in two orthogonal views using biplane imaging to visualize the target region for PMR and the corresponding coronary anatomy. These two views were not changed throughout the procedure. A transparent film was placed over a stored image on the video monitor and a "map" of the target region was traced. After correction for magnification, a distance of 1 cm was marked on the films. Then the laser delivery catheter containing the laser fiber was inserted and also connected to a heparin drip. The position of the laser catheter was assessed using biplane flouroscopy. After aiming the laser catheter towards the target region, the laser fiber was advanced until it made contact with the endocardial surface. A burst of two pulses of laser energy (2 Joules/pulse) was delivered, the laser fiber was advanced 2–3 mm and another burst of two pulses was delivered. Laser pulses were triggered by the electrocardiogram (ECG) signal during systole. The location of the laser channels was recorded in the two orthogonal views on the transparent films. Then the laser fiber was retracted and the catheter assembly repositioned to create the next channel. Care was taken to space channels at approximately equal distances of about 1 cm from each other by defining the position of the radio-opaque markers in orthogonal views. Channel numbers were limited by the 1 cm spacing requirement. Echocardiograms were performed during and immediately after the procedure in order to exclude perforation of the ventricular wall and ensuing pericardial tamponade. After the procedure, patients were observed for 24 h in the coronary care unit. Serial ECGs, cardiac enzyme levels and echocardiograms were obtained in the first 24 h after PMR.

**Follow-up.** Follow-up visits were scheduled after three and six months. Follow-up consisted of assessment of clinical status, echocardiography, bicycle exercise test and thallium scintigraphy. Clinical status was assessed by recording the patient’s symptoms, medication and use of additional nitroglycerin to treat anginal attacks. Severity of angina was classified according to the CCS Scale. Use of additional nitrate to cover anginal attacks was recorded semiquantitatively as I = no additional nitrates, II = additional nitrates <1x/week, III = 1–2x/week, IV = >2x/week, V = 1–3x/day and VI = >3x/day. Exercise performance was assessed by symptom-limited bicycle ergometer test starting at 10 W with increments of 25 W every 3 min.

Myocardial perfusion was assessed by thallium scintigraphy following symptom-limited bicycle ergometry and after pharmacological stress by injection of 0.54 mg/kg body weight of dipyridamole, respectively. During physical exercise, the maximal level was limited by angina pectoris or dyspnoe; no patient attained the age-adjusted maximal heart rate. Single photon emission tomography (SPET) acquisition was performed 10 min and 4 h after injection by use of a dual-head camera (ADAC Laboratories, Milpitas, California). Data were reconstructed iteratively with attenuation correction. Relative count densities were determined in 14 wall segments: anterior, lateral, inferior and septal wall segments in an apical, a middle and a basal short axis slice, respectively and in two additional apical (anteroapical, inferoapical) segments. For follow-up studies count rates were related to that of an initially well perfused septal wall segment that was not directly affected by PMR. All scintigraphic studies were analyzed by a physician unaware of the timing of the study (i.e. before or after PMR).

**Statistical analysis.** Differences in angina pectoris severity (CCS classification) at baseline and three and six months after PMR, respectively, were compared using the sign-test. Differences in use of additional nitroglycerin, exercise duration in bicycle ergometry and left ventricular ejection fraction (LVEF) at baseline and three and six months after PMR, respectively, were compared using the Friedman-test and the Wilcoxon-test. Differences in CK-levels before and after PMR were compared using the Student t test. The global level of statistical significance was set at 5%. To allow for repeated comparisons, Bonferroni correction on all p values relating to repeated analysis was used.

A retrospective power calculation was performed to determine the power of the current sample size to detect clinically relevant differences in ejection fraction or thallium uptake (after stress or at rest, respectively) at a significance level of 5%. For ejection fraction, the power was 30% to
detect a difference in ejection fraction of 5%. The powers to recognize a difference of 5% for thallium uptake after stress or at rest were 19% and 36%, respectively. All statistical tests were performed using SPSS version 8.0 (SPSS Inc., Chicago, Illinois).

RESULTS

PMR procedure. The PMR procedure was successfully completed in all planned patients. In 27 patients only one region of the left ventricle was treated with PMR. The target region in these patients was the anterior wall in 11 patients, the lateral wall in 4 patients and the inferior wall in 12 patients. In seven patients, two regions of the left ventricle were treated with PMR, the anterior and lateral wall in four patients, the anterior and inferior wall in two patients and the lateral and inferior wall in one patient, respectively.

A mean of 10.4 ± 2.7 (range 8 to 15, median 10) laser channels were created in each region. Mean duration of the procedure was 51 ± 30 (range 13 to 150, median 48) min with procedure times declining from 97 ± 35 (range 65 to 150, median 80) min in the first five patients to 20 ± 6 (range 13 to 31, median 17) min in the last five patients as a result of the learning curve.

Total creatine kinase levels rose from 72 ± 21 U/l before PMR to 137 ± 45 U/l after PMR in 33 of the 34 patients (upper limit of normal 196 U/l). In one patient with peripheral artery disease there was a significant retroperitoneal bleeding from the 5 F femoral access site necessitating surgical repair. In this patient, total creatine kinase levels rose from 56 U/l before PMR to 1,236 U/l without significant rise in CK-MB levels probably as a result of skeletal muscle damage. A new left bundle branch block developed in one patient, and ST segment depression not corresponding to the treated region developed in another patient.

Patients were discharged from the hospital 3.5 ± 2.9 days (range 2 to 15 days, median 3 days) after the PMR procedure.

Adverse reactions. There was no periprocedural mortality in the patients treated with PMR. One episode of bleeding originating from the 5 F left femoral artery access site required surgical repair. Minor periprocedural complications were: 1) one temporary bundle branch block attributed to catheter pressure on the ventricular septum which resolved after change in catheter position, 2) one single episode of nonsustained polymorphic ventricular tachycardia also precipitated by mechanical contact with the ventricular wall, 3) one third degree atrioventricular block lasting 2–3 min; in this patient a temporary pacemaker was inserted, 4) in six patients a small pericardial effusion (<10 mm) developed within 24 h following the intervention. In all patients the pericardial effusion was not detectable immediately after the procedure; it did not create hemodynamic impairment and resolved spontaneously without further treatment, and 5) one episode of transient renal failure attributed to the use of contrast medium (creatinine levels rose from 220 mg/dl before PMR to 450 U/l after PMR).

Late results: three months after PMR. Twenty-five patients have completed follow-up 3 months after PMR treatment (Table 2). In these patients, severity of angina pectoris decreased from CCS class 3.1 ± 0.3 before PMR to 1.8 ± 0.8 after PMR (p < 0.001). Twenty-one patients reported improvement in their CCS class; four patients reported no change. Symptoms did not deteriorate in any of the patients. Use of additional nitroglycerin decreased from 4.7 ± 0.9 before PMR to 2.7 ± 1.4 after PMR (p < 0.001). Nineteen patients used less additional nitroglycerin after PMR; six patients reported no change in nitroglycerin use after PMR. No patient used more additional nitroglycerin than before PMR. Exercise time on bicycle ergometry rose from 373 ± 125 s before PMR to 470 ± 163 s after PMR (p < 0.05).

Left ventricular ejection fraction determined echocardiographically was 59% ± 12% before PMR and 60% ± 14% after PMR (not significant [n.s.]). In seven patients with initially impaired ventricular performance (LVEF <50%) LVEF was 43% ± 7% before PMR and 42% ± 13% after PMR (n.s.).

Three months after PMR, 201Tl scintigraphy was done only with pharmacological stress. Compared with the nonlasered septum, tracer uptake under stress was 74% ± 14% compared with 73% ± 11% before PMR (n.s.). Perfusion at rest after three months was 84% ± 10% compared with 88% ± 9% before PMR (n.s.).

Late results: six months after PMR. Follow-up data 6 months after PMR are available for 17 patients. Six months after PMR, patients reported angina pectoris of CCS class 1.3 ± 0.8 compared with 3.0 ± 0.0 before PMR (p < 0.001) and 1.7 ± 0.8 three months after PMR (n.s. vs. six months after PMR) (Fig. 2). Additional use of nitrates had decreased from 4.6 ± 0.9 before PMR to 2.9 ± 1.4 after three months (p < 0.001) and to 2.4 ± 1.4 six months after

Table 2. Symptoms and Clinical Findings in 25 Patients Three Months After PMR

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<tr>
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<th>Baseline</th>
<th>After 3 Months</th>
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<tr>
<td>CCS class</td>
<td>3.1 ± 0.3</td>
<td>1.8 ± 0.8</td>
</tr>
<tr>
<td>Use of nitrates</td>
<td>4.7 ± 0.9</td>
<td>2.7 ± 1.4</td>
</tr>
<tr>
<td>Exercise capacity</td>
<td>373 ± 125</td>
<td>470 ± 163</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>59 ± 12</td>
<td>60 ± 14</td>
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<tr>
<td>Thallium uptake (stress)</td>
<td>74 ± 14%</td>
<td>73 ± 11%</td>
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<tr>
<td>Thallium uptake (rest)</td>
<td>84 ± 10</td>
<td>88 ± 9%</td>
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Use of nitrates was recorded on a semiquantitative scale (see Methods section). Exercise capacity denotes exercise time on standard bicycle ergometry. Ejection fraction was determined echocardiographically. Thallium uptake was determined as tracer uptake in the laser-treated regions compared with the nonlased septum (septum = 100%).

CCS = Canadian Cardiologic Society Angina Scale.
PMR (n.s. vs. three months after PMR) (Fig. 2). Ejection fraction did not change from 56% ± 11% before PMR to 57% ± 13% after three months and 57% ± 13% six months after PMR. Exercise time on bicycle ergometry rose from 384 ± 141 s before PMR to 509 ± 152 s after three months (p < 0.005) and to 514 ± 158 s after six months (n.s. vs. three months after PMR) (Fig. 3).

Tracer uptake compared with the non-lasered septum in 201Tl scintigraphy after pharmacological stress six months after PMR was 78% ± 14% compared with 75% ± 13% before PMR (n.s.) and 76% ± 12% three months after PMR (n.s.) (Fig. 4A). Tracer uptake six months after PMR after bicycle ergometry was 76% ± 11% compared with 79% ± 10% before PMR (n.s.) (Fig. 4B).

Perfusion at rest after six months was 89% ± 8% compared with 89% ± 9% before PMR and 91% ± 9% after three months (n.s.) (Fig. 4).

**Adverse events.** One patient with diffuse three vessel disease and previous CABG and PTCA who had undergone successful PMR treatment of the inferior wall was admitted to another hospital seven days after PMR with acute anterior MI and died in cardiogenic shock. One patient was readmitted to the hospital with congestive heart failure 6 weeks after PMR treatment. He felt well until one week before admission when he noticed an irregular pulse and progressive dyspnoe. Electrocardiogram disclosed atrial fibrillation with ventricular rates of about 130 beats/min. A normal sinus rhythm could not be restored, but control of ventricular rate with digitalis resulted in resolution of symptoms and the patient was discharged after five days. Another patient was hospitalized three weeks after PMR treatment also for congestive heart failure. In this patient with an ejection fraction of 35% before PMR, diuretic medication had been withdrawn by his primary care physician. After reinstition of diuretics the symptoms resolved.

**DISCUSSION**

In the majority of patients with CAD, symptoms of angina pectoris are treated effectively by angioplasty or CABG. However, in some patients the extent of CAD or diffuse involvement of the coronary arteries renders these patients unsuitable for PTCA or CABG, respectively. Furthermore other patients after multiple coronary interventions may
present with a situation where coronary morphology precludes further interventions. If medical therapy fails to control symptoms, quality of life is impaired in these patients by persisting angina pectoris and decreased exercise capacity as well as by the absence of a reasonable perspective for improvement in the future.

For these patients, transmyocardial laser revascularization was developed that creates well defined debris-free transmyocardial channels by use of laser energy from the epicardial surface to the ventricular cavity. Clinical studies consistently report a significant clinical benefit of the patients after PMR treatment resulting in less anginal symptoms, decreased use of additional nitrates and increased exercise capacity (9–13). Myocardial perfusion studies with $^{201}$Tl scintigraphy, however, still show equivocal results. Horvath et al. have reported improved perfusion in myocardial regions treated with TMR (14) while other studies could not find evidence of improved myocardial perfusion after TMR using $^{201}$Tl scintigraphy or positron emission tomography (PET) (13).

Most of the TMR procedures so far have been carried out with CO$_2$ laser systems. One of the drawbacks of these lasers is that the laser energy cannot be transmitted through optical fibers. The energy of the CO$_2$ lasers has to be delivered to the myocardium by use of a rather stiff mirror system so that CO$_2$ laser-based TMR can only be performed with open chest surgery. More recently, TMR has been carried out using excimer laser or Holmium: YAG laser systems (9) which allow the use of optical fibers for delivery of the laser energy.

To eliminate the need for open chest surgery, a catheter-based system has been developed that allows the creation of laser channels into the myocardium from the left ventricular chamber. This PMR system uses a Holmium: YAG laser (wavelength 2.1 $\mu$m) that allows the use of a fiber optic system to deliver the laser energy to the myocardium. The PMR system is designed to create laser channels with a maximal channel depth of 7 to 8 mm from the endocardial surface to the subendocardial and midmyocardial regions where the ischemia is located.

Safety and feasibility of the PMR procedure. Although there was initial concern that PMR may probably lead to creation of completely transmural channels and may result in pericardial effusion and pericardial tamponade, this study did not encounter episodes of pericardial tamponade. Small pericardial effusions were seen in some patients, not immediately after the PMR procedure but developing during the first 24 h after PMR. All these small pericardial effusions resolved spontaneously; no patient required pericardial drainage. These pericardial effusions were probably caused by a moderate inflammatory reaction to the creation of the laser channels similar to the small pericardial effusions that may develop after catheter ablation of ventricular tachyarrhythmias. If transmural channels had been created during PMR the pericardial effusions should have been detectable immediately after PMR and may have led to larger effusions causing pericardial tamponade. However, two episodes of significant pericardial effusions have been encountered in other institutions during PMR procedures (S. Oesterle, 1998, personal communications) in a total of more than 200 procedures. After pericardial drainage, both patients could be stabilized.

Biplane imaging was used for positioning of the laser catheter. However PMR can also be performed easily with only a single plane angiography unit. Before PMR, a coronary angiography was performed because of initial concern to avoid creating laser channels into the epicardial arteries. After some experience with the procedure, this coronary angiogram may not be absolutely necessary before PMR.

Assessment of efficacy: creation of laser channels and left ventricular function. Creatine kinase levels rose moderately after PMR. This indicates on one hand that PMR really creates laser channels into the myocardium. On the other hand, ventricular damage produced by PMR was only very limited which is also underlined by the fact that LVEF did not change, either immediately after PMR nor in the following months. Even in patients with impaired left ventricular function before PMR, the creation of laser channels did not lead to further deterioration of left ventricular function.

Assessment of efficacy: anginal symptoms and exercise capacity. Percutaneous myocardial revascularization relieved anginal symptoms and increased exercise capacity in most of the patients similar to TMR (10–12). This effect was seen three months after PMR with some patients experiencing further improvement of symptoms in the following three months. No patient reported deterioration of symptoms after PMR. However, it has to be noted that this clear and significant increase in exercise capacity does not necessarily prove increased myocardial perfusion. A psychologic effect caused by the intensive and repeated survey of the patients cannot be ruled out as a contributory factor for the increased exercise capacity and decreased use of additional nitrates seen in our patients.

Assessment of efficacy: myocardial perfusion. Myocardial perfusion assessed by $^{201}$Tl scintigraphy did not demonstrate improved perfusion after PMR but rather a tendency towards reduced tracer uptake after laser revascularization. Perfusion studies after TMR also do not report consistent results towards improved perfusion after TMR. Improved perfusion after TMR was found by Horvath et al. (12) but other studies could not demonstrate improved perfusion after TMR (13). In patients where TMR was performed together with CABG in the same patients, Diegeler et al. found improved perfusion in the myocardial areas treated with CABG but not in the regions treated with PMR (9). Indirect evidence of improved myocardial perfusion after TMR may be derived from studies using dobutamine stress...
echocardiography, where reduced ischemic wall motion abnormalities were found in laser treated regions (15).

Assessment of efficacy: mortality and morbidity after PMR. Mortality and morbidity rates were low in these first patients treated with PMR compared with TMR where mortality rates of 10% in the first 30 days following TMR were reported (11,12). However, one patient died in cardiogenic shock because of an anterior MI one week after PMR in the inferior wall. This patient had severe three vessel CAD and had undergone bypass surgery four years before PMR. The saphenous vein grafts to the left anterior descending and the circumflex artery were patent with moderate atherosclerotic lesions; the bypass to the right coronary artery was occluded. Perfusion imaging before PMR did not show stress induced ischemia in the anterior wall, so PMR was performed only in the inferior wall. If the anterior wall had been considered at risk angiographically, a percutaneous coronary intervention or another bypass operation would have been discussed. Percutaneous myocardial revascularization is not considered to have the ability to protect against acute MI. Transmyocardial revascularization also does not convey much protection against acute coronary symptoms in patients with severe CAD.

In the course of this study, a clear learning curve was seen with procedure times of about 30 to 40 min for the last patients. This shows that PMR is a rapid procedure with little discomfort for the patients compared with TMR. The time required to perform PMR is only moderately longer than the time needed for balloon angioplasty or angioplasty using other devices.

Mechanisms. Despite considerable research efforts, the pathophysiological mechanisms responsible for the effect of myocardial laser revascularization still remain poorly understood. Initially it was postulated by Mirhoseini et al. (16) that these channels may possibly function as conduits to allow perfusion of the ischemic myocardium with oxygenated blood from the left ventricular cavity probably similar to the perfusion via sinusoids seen in reptilian hearts (17). Although patent laser channels after TMR have been reported (10,18), the initial concept has been questioned by many authors who found occluded laser channels at various time points after TMR (2–5,19). In animal studies, Kwong et al. (20) showed that laser treatment leads to local denervation of the myocardium which may be responsible for the acute clinical benefit seen in patients treated with TMR. On the other hand, histological evidence of perichannel angiogenesis after TMR has been found that may contribute to the long-term benefit of TMR (3,6,18,21). However, this study could not demonstrate improved perfusion in the laser treated myocardial areas. One explanation could be that 201Tl scintigraphy is not sensitive enough to show improved perfusion in rather small areas of the left ventricular wall. Positron emission tomography allows the study of smaller volumes of the myocardium and may show improved perfusion in small areas treated with PMR. After TMR improved perfusion of subendocardial regions of the myocardium compared with subepicardial regions was reported in one study using PET analysis (10), but this analysis has been questioned and others could not find improved perfusion of laser treated regions using PET (13). On the other hand it cannot be excluded that the therapeutic effect of laser revascularization is not due to improved perfusion. Finally, it cannot be ruled out that part of the clinical improvement after TMR is simply due to a “placebo effect” of the procedure itself.

Study limitations. One limitation of this pilot study is the lack of a randomized control group. After the results of this study, randomized studies have been started in Europe and the U.S. to compare the effect of PMR with conventional medical therapy in patients with end-stage CAD.

Canadian Cardiologic Society classification and data of nitroglycerin use were based on patient questioning. Therefore, a placebo effect or bias cannot be ruled out for these data. 201Tl scintigraphy is probably not sensitive enough to demonstrate changes in myocardial perfusion after PMR. Studies with PET may allow more accurate quantification of myocardial perfusion before and after PMR.

Long-term studies after PMR are still lacking so that a beneficial effect of PMR on long-term mortality and survival still remains to be shown.

Conclusions. Percutaneous myocardial revascularization is a new safe and feasible therapeutic technique for patients with CAD and severe angina pectoris not amenable to either CABG or PTCA. Initial results indicate clinical benefit to the patients with improvement of symptoms and increased exercise capacity, but evidence of improved myocardial perfusion still remains to be demonstrated.

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