A substantial number of patients present with medically refractory angina who are not candidates for angioplasty or bypass surgery. The creation of channels between the myocardium and the ventricular blood pool has been performed after thoracotomy with excellent relief of symptoms but has been associated with high perioperative mortality. We investigated the safety of a nonoperative, percutaneous technique for channel creation. Twenty-seven patients with angina and coronary anatomy not amenable to revascularization with coronary angioplasty or bypass surgery underwent percutaneous transluminal myocardial revascularization (PTMR). Energy from a Holmium:yttrium-aluminum-garnet (YAG) laser was directed through a fiber enclosed in a catheter to the ventricular myocardium creating channels between the blood pool and the myocardium. On average, 17 ± 4 channels were formed per patient. There were no procedure-related deaths, episodes of tamponade, or other complications except for an increase in creatine phosphokinase in 1 patient. Immediately after the procedure, there was no worsening of regional wall motion function in any patient, but rather improvement in some. All patients were discharged alive after a hospital stay of 1.8 ± 1.5 days. Mean Canadian Cardiovascular Society functional class declined from 3.6 ± 0.5 before the procedure to 0.65 ± 0.8 at 30 days after the procedure (p < 0.01). For 12 patients eligible for 6-month follow-up, mean functional class was 0.94 ± 0.97. At 6-month stress testing, 9 of these 12 had no electrocardiographic evidence of ischemia. Thus, PTMR can be performed safely in the cardiac catheterization laboratory with a complication rate lower than that reported in surgical series and with excellent near-term symptomatic relief. The long-term effect of PTMR on mortality and relief of angina as well as its safety and effectiveness compared with the surgical approach remains to be defined.

**METHODS**

**Study population:** This trial was conducted in part under the first Food and Drug Administration Investigational Device Exemption protocol for a human feasibility trial of PTMR, and was approved by the institutional review board of both institutions. The objective of the study was to evaluate the safety and feasibility of PTMR in patients with class III and IV angina not amenable to any other form of revascularization.

Between June 1997 and February 1998, 27 patients (16 in Batra Hospital, India, 11 at Washington Adventist Hospital, Maryland) were treated with PTMR as part of this phase I study. Patients were eligible for the study, if they: (1) had known coronary artery disease not amenable to percutaneous intervention or coronary artery bypass surgery (as determined by the cardiologist and a cardiovascular surgeon not involved in the direct care of the patient); (2) were in Canadian Cardiovascular Society functional class III or IV; (3) had inducible ischemia on exercise treadmill testing or had unstable angina defined as ischemic ST-segment depression at rest and requiring intravenous nitroglycerin; and (4) had a preprocedure echocardiogram demonstrating >9-mm wall thickness of the left ventricular region that was to be lased and an ejection fraction of >0.25.

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Patients were excluded from the study if they had decompensated congestive heart failure, sustained ventricular tachycardia, or ventricular fibrillation in the 2 weeks before the procedure, severe aortic stenosis with aortic valve area of < 1 cm², left ventricular aneurysm, or an abnormal aortic arch, which in the operator’s judgment, would not allow safe passage of the catheter.

**PTMR technique:** A 9Fr introducer was inserted into the femoral artery and an 8Fr introducer was inserted into the femoral vein using standard technique. Heparin 5,000 IU was administered intravenously to achieve an activated clotting time of at least 280 seconds. A 6Fr pigtail catheter was then advanced into the left ventricle and left ventriculography performed in the 30° right anterior oblique projection. A 45° left anterior oblique ventriculogram was also recorded if the area to be lasered was the posterolateral wall or a left lateral view if the anterior wall was to be lasered. A pigtail catheter was then exchanged for a 5- or 7-cm steerable PTMR catheter (Eclipse Surgical Technologies, Inc., Sunnyvale, California) over a 0.038-inch curved coated Amplatz extra stiff guidewire (Cook Inc., Bloomington, Indiana) shaped to conform to the left ventricular wall. The guidewire was removed and the PTMR catheter aspirated, flushed, and attached to a Touhy Borst Y-adapter. The other channel of the Y-adapter was continuously flushed with heparinized saline. The SlimFlex laser fiber (Eclipse Surgical Technologies, Inc.) was introduced into the PTMR catheter and advanced under flouroscopy into the left ventricular cavity. The PTMR catheter was then advanced to the apex of the left ventricle and deflected to position it against the wall to be lasered. The PTMR catheter and the SlimFlex laser fiber were then aligned and the distal marker band of the SlimFlex fiber advanced to a position slightly distal to the tip marker band of the PTMR catheter. The laser was set to deliver 3.5 W through the 1-mm diameter optical fiber in a series of 3 sequential pulses.

The following 4 criteria were used as a suggestion of laser energy delivery to the myocardial wall: (1) evidence of a couplet or at least 1 ventricular premature contraction with each laser pulse train, (2) evidence of laser fiber protruding through the PTMR catheter and touching the left ventricular wall, (3) audible tones of laser energy firing, and (4) the TMR 2000 laser system counter showing that 3 pulses had been delivered. Successful channel creation was judged likely if all of these criteria were met. In patients in whom a transesophageal echocardiogram was recorded, the production of bubbles at the time of laser activation in the left ventricular cavity also suggested delivery of laser energy.

Laser channels were made starting at the distal portion of the respective wall and then retracting toward the base of the same wall. The channels were created about 1 cm apart and the position of the catheter verified in both the right and left anterior oblique views before each laser activation. Once all the desired channels were created, the PTMR catheter and the laser fiber were removed. A 0.038-inch guide-wire was then advanced and the PTMR catheter exchanged for a pigtail catheter. Left ventriculography was performed in the same projection as before the procedure. After the procedure the patient was observed on a telemetry unit for 24 hours before discharge. All pre-PTMR medications were resumed after the procedure. A 2-dimensional echocardiogram was recorded within 24 hours of the procedure to evaluate the change in wall motion abnormality and also to look for any pericardial effusion. All patients had a 12-lead electrocardiogram and sequential creatine phosphokinase determination to assess for post-procedure myocardial necrosis. Left ventricular function was evaluated before and after the procedure with either transesophageal echocardiography (11 patients) or left ventriculography (16 patients). Thirty-day post-procedure vital status was also determined by clinic visit or by telephoning the patient’s primary physician. An exercise stress test was scheduled for each patient at 6 months.

**RESULTS**

Results are reported for all 27 consecutive patients. Baseline characteristics are listed in Table I. All patients were symptomatic before PTMR, with 10 in Canadian Cardiovascular Society functional class III and 17 in class IV. Before PTMR, 15 patients had positive ischemic exercise treadmill test results, and 12 with rest angina did not undergo exercise testing because of inability to wean from intravenous nitroglycerin. The patients were mostly men. A history of myocardial infarction was present in 55% and history of congestive heart failure in 4%. Prior coronary angioplasty had been performed in 63%, and 70% had prior coronary bypass surgery. A history of smoking was present in 26%, and 8% were current smokers. Three-vessel coronary artery disease was present in 74%, 2-vessel disease in 10%, and 1-vessel disease in

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>62 ± 8</th>
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<td>Men/women</td>
<td>25/2</td>
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*Table I Baseline Characteristics [n = 27]*/

| Functional class | Class III | 10 (37%) |
| Class IV         | 17 (63%)* |
| Ejection fraction (%) | 39 ± 10 |
| Diabetes mellitus | 7 (26%) |
| Hypertension† | 16 (59%) |
| Hyperlipidemia‡ | 12 (44%) |
| Smoking history | 7 (26%) |
| Family history of coronary artery disease | 10 (37%) |
| Previous myocardial infarction | 15 (55%) |
| Congestive heart failure | 1 (4%) |
| Previous coronary bypass | 19 (70%) |
| Previous coronary angioplasty | 17 (63%) |
| Previous bypass and/or angioplasty | 21 (78%) |

*Twelve patients with unstable angina on intravenous nitroglycerin.
†Hypertension was defined as a systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg or if patients were taking antihypertensive medications.
‡Hyperlipidemia was defined as a total cholesterol of ≥ 200 mg/dl and or a low-density cholesterol of ≥ 130 mg/dl, or if they were taking cholesterol-lowering medications.
16%. An average of 17 ± 4 channels were created by the laser. Procedural time from creation of the first to the last channel was 58 ± 26 minutes, with a fluoroscopic time of 15 ± 6 minutes. The energy was present at 3.5 W for each laser activation. Regional wall motions were unchanged or improved on repeat left ventriculography or by transesophageal echocardiogram immediately after the procedure. After the procedure, patients were successfully weaned off intravenous nitroglycerin. The average length of hospital stay for the 27 patients was 1.8 ± 1.5 days. There were no procedure-related deaths, pericardial effusions, or tamponade, and no deaths in the 30-day period after the procedure. One patient had an increase in the total creatine phosphokinase but the MB fraction was not determined. There was no electrocardiographic evidence of myocardial injury. There were no cerebrovascular accidents and there were no sustained supraventricular or ventricular arrhythmias.

At 1 month, of the 27 patients, all of whom were in functional class III or IV, before the procedure, 5 were in class I, 3 were in class II, and 9 were in class 0. No patient had class III or IV angina 1 month after the procedure. The mean functional class at entry was 3.63 ± 0.5 and it declined to 0.65 ± 0.8 at 30 days. For 12 patients with functional class available at 6-month follow-up, the mean anginal class was 0.94 ± 0.97.

Six-month follow-up exercise treadmill test data were available in 12 of the 27 patients. Of these, 9 had no electrocardiographic evidence of ischemia or chest pain on treadmill stress testing. Also, of the 12 patients admitted with unstable angina who were unable to wean off intravenous nitroglycerin, 6-month follow-up data are available in 6. Four of these 6 had no electrocardiographic evidence of ischemia during treadmill stress testing.

DISCUSSION

This study is the first to report percutaneously introduced catheter-based transmyocardial revascularization and it demonstrates that PTMR using the holmium-YAG laser can be performed safely in the catheterization laboratory. The absence of any peri-procedural (30 day) deaths in this group of patients contrasts with the high perioperative mortality reported in patients undergoing laser transmyocardial revascularization via thoracotomy. In addition, as reported in the surgical series, most of our patients had immediate symptomatic improvement.

Mechanism: Despite extensive investigation, the mechanism of transmyocardial revascularization is still unknown. Initial studies postulated that patent channels would provide continuous blood flow similar to endocardial perfusion in normal alligator hearts. However, data are conflicting as to the long-term patency of these laser channels. Another interesting possibility is the stimulation of angiogenesis by laser-induced injury, thus leading to increased myocardial perfusion. Another intriguing mechanism to explain the acute symptomatic relief, as was observed in our cases, is damage of myocardial nerve fibers, resulting in an anesthetic effect.

The reason for the absence of mortality and the near absence of significant periprocedural complications with the transcatheter technique may relate to the markedly lower physiologic and structural trauma resulting from the catheter approach. This would be particularly important in patients who are not completely revascularized, yet are subjected to major surgical stress. The elevation of creatine phosphokinase in 1 of the patients was likely due to the lasing process, although this cannot be said with certainty. However, there were no significant clinical sequelae, associated with the enzyme elevation.

Comparison with prior studies: Previous reports have documented both immediate- and long-term angina relief after surgical transmyocardial revascularization. Frazier et al reported 21 patients who underwent surgical PTMR. In this series there was a reduction in Canadian Cardiovascular Society functional class from 3.70 ± 0.7 to 1.70 ± 0.9, and there was a persistent 6-month effect. In these patients, there was no improvement in perfusion on thallium scintigraphy, but significant improvement in ejection fraction. Early mortality (<10 days) occurred in 2 of 21 patients. Horvath et al reported 200 patients undergoing surgical PTMR at 8 hospitals in the United States. Patients had baseline and 3-, 6-, and 12-month follow-up stress perfusion studies. Perioperative mortality was 9%. Angina class was significantly improved at all follow-up visits for this patient cohort and there was a significant reduction in the number of perfusion defects in the treated left ventricular free wall. In their series, Cooley et al reported a significant 12-month improvement in anginal class (3.7 ± 0.4 to 1.8 ± 0.6) and an improvement in perfusion by positron emission computed tomography scan.

Study limitations: This is a small, uncontrolled, study with only short-term follow-up. Each of the reported patients will be followed at 6 and 12 months, with clinical assessment and stress perfusion studies. The relative effectiveness and safety of the percutaneous versus the surgical, approach requires a direct, randomized trial. However, current data make a compelling case for careful investigation of the percutaneous approach.

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