Despite the advances that have occurred in coronary revascularization, there is a growing population of patients who are not candidates for either coronary artery bypass grafting (CABG) or conventional percutaneous coronary intervention (PCI). This population is heterogeneous and includes patients with diffuse coronary disease, comorbid conditions or multiple previous bypass operations resulting in no remaining suitable conduits. The majority of such patients present with severe angina despite maximum medical therapy. Additional management by revascularization is difficult because of diffuse disease not approachable by either CABG or PCI. The goal of therapy in such patients is to improve their quality of life and, if possible, to prolong it. The purpose of this article is to review the current status of novel techniques that are being developed to deal with this frustrating group of patients. Specifically, transmyocardial revascularization (TMR) is examined.

Transmyocardial revascularization. Transmyocardial revascularization is a therapeutic strategy designed to enhance myocardial perfusion by creating channels with laser energy directly in the ischemic myocardium.1–5 Clinical studies have reported angina relief in many of these patients, making this technique potentially promising.6–8 The mechanism of improvement is not entirely clear, but may be a combination of new vessel growth (angiogenesis), direct perfusion, or denervation.9,10 Also, a substantial placebo effect is possible. The surgical approach to TMR, however, has been limited by high perioperative mortality.6–8 The adaptation of the holmium: yttrium-aluminum-garnet (YAG) laser, which can create channels in the presence of the myocardial blood pool, makes a transcatheter approach possible.11–17 The percutaneous approach, by obviating thoracotomy and achieving the same objective, should make the procedure safer and more acceptable.

Clinical trials of TMR. Generally, to be a candidate for current TMR procedures, patients must meet the following criteria: 1) severe angina (functional class III or IV) despite optimal medical therapy; 2) poor candidate for catheter-based angioplasty due to high procedure risk or absence of acceptable target sites; and 3) poor candidate for surgical revascularization due to absence of acceptable target vessels and/or remaining surgical conduits.

Surgical TMR (Table 1), using an 85-W CO₂ laser, was applied in 1983 by Mirhoseini et al.4 to create transmyocardial channels as an adjunct to coronary artery bypass graft surgery in patients who could not be completely revascularized. These investigators reported less angina and greater myocardial perfusion in treated regions.3,4,16,17 Later, Frazier and Cooley5,6 used a similar surgical TMR approach with an 800-W CO₂ laser as “sole therapy” in 21 patients; they reported reduced angina, increased exercise capacity, and enhanced subendocardial perfusion by positron emission tomographic scans at 12 months.6 Similar favorable results were reported by Horvath and Cohn,2,7,8 who also used surgical laser TMR techniques. They studied 20 patients with angina refractory to medical therapy and evidence of reversible ischemia who were not candidates for angioplasty, bypass surgery or transplantation. However, they reported a mortality of 10% (2 out of 20 patients), and 3 additional deaths occurred post-discharge. Among survivors, a significant improvement in angina was observed (angina class decreased from 3.7 to 1.0 at 12 months; p < 0.001).

Preliminary results of a recent randomized trial to determine whether surgical CO₂ laser revascularization...
Table 1. Observational studies of surgical transmyocardial revascularization

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Patients</th>
<th>Laser Type</th>
<th>Perioperative Mortality (%)</th>
<th>Follow-up (months)</th>
<th>Angina Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooley(^6)</td>
<td>21</td>
<td>CO(_2)</td>
<td>9.5</td>
<td>12</td>
<td>Mean angina class reduced from 3.7 to 1.8</td>
</tr>
<tr>
<td>Horvath(^7)</td>
<td>20</td>
<td>CO(_2)</td>
<td>10</td>
<td>11</td>
<td>Mean angina class reduced from 3.7 to 1.0</td>
</tr>
<tr>
<td>Hovarth(^8)</td>
<td>200</td>
<td>CO(_2)</td>
<td>9</td>
<td>10</td>
<td>Improved by &gt; 2 classes in 75% of patients</td>
</tr>
<tr>
<td>Vincent(^9)</td>
<td>268</td>
<td>CO(_2)</td>
<td>10.8</td>
<td>12</td>
<td>82% angina class 0 or 1 at 12 months</td>
</tr>
<tr>
<td>Dowling(^10)</td>
<td>40*</td>
<td>holmium: YAG</td>
<td>12</td>
<td>3</td>
<td>Improved by &gt; 2 classes in 86% of patients</td>
</tr>
<tr>
<td>Allen(^11)</td>
<td>74</td>
<td>holmium: YAG</td>
<td>9</td>
<td>6</td>
<td>Improved by &gt; 2 classes in 85% of patients</td>
</tr>
<tr>
<td>Burkoff(^12)</td>
<td>92</td>
<td>holmium: YAG</td>
<td>1</td>
<td>12</td>
<td>Exercise tolerance improved; was better in surgical vs. medical graph</td>
</tr>
<tr>
<td>Allen(^13)</td>
<td>132</td>
<td>holmium: YAG</td>
<td>5</td>
<td>12</td>
<td>Improved by 2 classes in 76% vs. 32% in medical group</td>
</tr>
</tbody>
</table>

\(^*\)all patients with ongoing unstable angina

YAG = yttrium-aluminum-garnet laser

Table 2. Observational studies of percutaneous transluminal myocardial laser revascularization

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of Patients</th>
<th>Laser System</th>
<th>30-Day Mortality</th>
<th>Pericardial Effusion or Tamponade</th>
<th>Minor CVA</th>
<th>Follow-up (months)</th>
<th>Angina Relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shawl(^14)</td>
<td>27</td>
<td>Eclipse</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>Mean angina class reduced from 3.6 to 0.97</td>
</tr>
<tr>
<td>Kaul(^15)</td>
<td>35</td>
<td>Eclipse</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>Mean angina class reduced from 3.6 to 1.08</td>
</tr>
<tr>
<td>Lauer(^16)</td>
<td>34</td>
<td>Cardiogenesis</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>Mean angina class reduced from 3.1 to 1.3</td>
</tr>
<tr>
<td>Oesterle(^17)</td>
<td>12</td>
<td>Cardiogenesis</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>Improved by &gt; 2 classes in 78%</td>
</tr>
<tr>
<td>Kornowski(^18)</td>
<td>32</td>
<td>Biosense</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>Increase in exercise testing from 440 to 505 seconds</td>
</tr>
</tbody>
</table>

Figure 1. (A) The 9 French coaxial guide catheter system facilitates retrograde passage into the left ventricle. (B) Seven French coring device through the 9 French guide catheter (C) using the vacuum extraction system by AngioTrax™.
is superior to medical therapy in patients not amenable to conventional revascularization techniques reported improved symptoms, quality of life, and some evidence of enhanced myocardial perfusion in the treated areas. Of the patients randomized to surgical TMR, 67% showed reduction of anginal class greater than 2 compared with 6% of the medically treated group. Hospitalization for unstable angina was markedly decreased (13% post-TMR versus 72% with medical therapy). Clinical efficacy, in the form of angina threshold, was decreased for as long as 2 years after the procedure. Nuclear studies, with analyses limited to the first 3 months, showed a less impressive 15% reduction in reversible defects in the TMR group versus a 7% increase in reversible defects in the control group. In a randomized prospective study, Allen et al. performed TMR using the surgical approach and holmium: YAG laser energy and reported significant improvement in angina class (85% vs. 18%, respectively) and decreased hospitalizations for angina in the TMR group compared with maximum medically treated patients at 6 months. Clinical benefit was sustained for up to 12 months.

Burkoff et al. randomized 182 patients with incomplete response to other therapies to TMR and continued medical therapy or continued medical therapy alone. TMR was significantly more effective than medical therapy alone in relieving symptoms.

Allen et al. randomized 275 patients with class IV angina not amenable to another form of revascularization to TMR and continued medical therapy or to continued medical therapy alone. The TMR patients had significantly better symptomatic outcome than other patients treated with medical therapy alone.

Percutaneous approach. The safety and efficacy of a non-surgical, less invasive, transcatheter approach has been reported in a few observational studies. Although clinical trials are in the early stages and randomized trial data are not yet available, preliminary results from these studies appear favorable (Table 2).

Percutaneous transluminal myocardial revascularization (PTMR) utilizes the approach adapted from other interventional catheterization procedures and employs catheter/fiber systems introduced through the femoral artery and fluoroscopically guided into the left ventricle. Channels (5 mm deep) are created from endocardium to myocardium, not penetrating the epicardium. The goal of catheter-based TMR is to provide channels created by the surgical approach without the need for thoracotomy or general anesthesia. In addition, the morbidity and mortality should be lower compared to surgical TMR, where periprocedural death is reported between 1–11% (Table 1).

Newer devices: Percutaneous myocardial channeling. Percutaneous myocardial channeling is a promising new technology. This procedure is performed through a 9 French guiding system (Figure 1A) with a 7 French electromechanical channeling device. This device creates channels in the left ventricular wall using a 7 French mechanical coring device (Figure 1B) with tissue extraction by vacuum (Figure 1C). Initial human experience has been reported by Shawl in 7 patients with coronary artery disease not amenable to either bypass graft surgery or percutaneous coronary intervention using this device. There were no complications and all patients were discharged within 48 hours.

Conclusion. Treatment of the inoperable coronary patient is one of the most difficult challenges facing the interventional cardiologist. For patients not amenable to coronary bypass, TMR (surgical or percutaneous) is a treatment option that appears to offer substantial anginal relief. The mechanism of benefit in these patients is not clearly delineated. A substantial placebo effect is possible, but revascularization and/or denervation may play a role. The potential for this technique as either a stand-alone procedure or as an adjunct to coronary bypass is under exploration.

REFERENCES


