Transmyocardial and Endovascular Laser Revascularization AHM

Clinical Indications

- Transmyocardial laser revascularization (TMLR), open chest and thoracoscopic approaches, are considered medically necessary for the treatment of medically refractory, severe intractable angina that meet **ALL** of the following criteria
  - Anginal symptoms are caused by viable ischemic myocardium (as demonstrated by diagnostic study) not amenable to surgical revascularization therapies such as PTCA, stenting, coronary atherectomy or coronary bypass
  - Member has had maximal efforts to stabilize acute conditions such as severe ventricular arrhythmia, decompensated congestive heart failure or acute myocardial infarction
  - Severe New York Heart Association functional classification of angina pectoris -- Class III or IV
  - Symptoms of angina refractory to standard medical therapy, including drug therapy at the maximum tolerated or maximum safe dosages
  - The physician has been properly trained in the procedure and the laser used in performing the procedure has been approved by the FDA for the purpose for which it is being used
- TMLR, open chest and thoracoscopic approaches, is considered investigational for all other indications
- TMLR plus cell therapy with autologous bone marrow cells for the treatment of ischemic heart disease is considered investigational because of insufficient evidence of this approach
- Percutaneous transmyocardial laser revascularization is considered investigational for the treatment of refractory angina and all other indications because its effectiveness has not been established
- Excimer laser coronary angioplasty is considered investigational for all indications including treatment of individuals with acute myocardial infarction, and persons with depressed left ventricular ejection fraction, as well as treatment of atherosclerotic lesions that are causing stenosis or occlusion of native coronary arteries, vein grafts placed at coronary artery bypass surgery, or stainless steel intra-coronary stents
Evidence Summary

Background

- Refractory angina in coronary artery disease is defined as the persistence of severe anginal symptoms despite maximal conventional anti-anginal combination therapy. Furthermore, the option to use an invasive revascularization procedure such as percutaneous coronary balloon angioplasty or aortocoronary bypass grafting must be excluded on the basis of a recent coronary angiogram. This coronary syndrome, which represents end-stage coronary artery disease, is characterized by severe coronary insufficiency but only moderately impaired left ventricular function. About 70% of the cases demonstrate severe coronary triple-vessel disease with diffuse coronary atherosclerosis, have had one or more myocardial infarctions, and have undergone aortocoronary bypass grafting.

- Transmyocardial laser revascularization (TMLR) has emerged as a promising therapy for patients with end-stage coronary artery disease not amenable to other forms of therapy. TMLR is a surgical technique typically performed through a left thoracotomy, which uses a laser to bore 15 to 30 transmural channels from the epicardial to the endocardial surfaces through the left ventricular myocardium of the beating heart in an attempt to improve local perfusion to ischemic myocardial territories not being reached by diseased arteries. The precise workings of this technique are not certain. The original theory upon which the technique was based, that the open channels would result in increased perfusion of the myocardium, does not appear to be the major or only action at work. Several theories have been proposed, including partial denervation of the myocardium, or the triggering of the cascade of biological reactions that encourage increased development of blood vessels. There are reports in the medical literature of TMLR being performed through a thoracoscopic approach, and pilot studies are underway using a percutaneous, catheter-based system, which allows creation of channels from the endocardial surface of the left ventricle into the myocardium.

- Medicare began covering TMLR as of July 1, 1999 based on research at several medical centers indicating that this technique does offer relief of angina symptoms for a period of time in patients for whom no other treatment offering relief is available. Early results from nonrandomized and randomized controlled trials of TMLR show both a significant reduction in pain, a reduction in hospitalizations, and a resumption of some normal activities of daily living for most patients treated. HCFA concluded, therefore, that such studies offer sufficient evidence of medical effectiveness for TMLR as a late or last resort treatment of the symptomatology. It is important to note that this technique has not been shown to increase life expectancy, nor is it proven to affect the underlying cause of the
angina. With appropriate patient selection and perioperative management, TMLR is associated with a very low operative risk.

- Dallan and colleagues (2008) tested the hypothesis that TMLR combined with intramyocardial injection of autologous bone marrow cells (BMC) is safe, and may help increase the functional capacity of patient with refractory angina. A total of 9 patients (8 men, 1 woman, mean age of 6 +/- 5 years) with refractory angina for multi-vessel disease and previous myocardial revascularization procedures such as coronary artery bypass grafting (CABG)/percutaneous coronary intervention, and who not further surgical candidates due to the extension of the disease were enrolled. Transmyocardial laser revascularization (11 +/- 3 laser drills) was performed via a limited thoracotomy using a CO2 Heart Laser System. Autologous bone marrow cells were obtained immediately prior to surgery, and the lymphomonocytic fraction separated by density gradient centrifugation. During surgery, 5 ml containing approximately 1.9 +/- 0.3 x 10(8) BMC were delivered by multiple injections in the ischemic myocardium. Before (B) and 6 months (6M) after the procedure, patient underwent clinical evaluation and myocardial perfusion assessment by cardiac magnetic resonance imaging (MRI) during pharmacological stress with dipyridamole. No major complications or deaths occurred during the procedure. One patient died after 2 years (non cardiac cause). There was a reduction in the ischemic score as assessed by MRI from 1.64 +/- 0.10 (B) to 0.88 +/- 0.09 (6M) (p = 0.01). Clinically, there was a reduction in functional class of angina from 3.7 +/- 0.2 (B) to 1.3 +/- 0.2 (6M) (p < 0.0001). The authors concluded that in this initial experience, the combined strategy of TMLR plus cell therapy appeared to be safe, and may have synergistically acted to reduce myocardial ischemia, with clinically relevant improvement in functional capacity. Provided these data are confirmed in a larger, randomized, controlled trial with longer follow-up, this strategy could be used as a novel therapeutic option for treating patients with refractory angina. In this regard, Horvath (2008) stated that TMLR has been used as an adjunct to CABG. Combination CABG plus TMLR has resulted in symptomatic improvement without additional risk. Additional therapies to enhance the angiogenic response include combining TMLR with stem cell-based treatments, which appear to be promising future endeavors.

- Oesterle and colleagues (2000) reported their finding of percutaneous transmyocardial laser revascularization (PTMR), a catheter-based technique of TMLR, for refractory angina pectoris when bypass surgery or angioplasty is not possible. They concluded that PTMR was associated with increased exercise tolerance time, low morbidity, lower angina scores assessed by masked reviewers, and improved quality of life. Although there is controversy about the mechanism of action, and the contribution of the placebo effect cannot be quantified, this unmasked study suggests that PTMR provides some clinical benefits in the defined population of patients. Commenting on the study by Oesterle et al
(2000), Harbison and Kenny (2001) stated that PTMR is associated with a non-significant increase in mortality and a significant increase in non-anginal serious adverse events.

- Moreover, recent reports indicated that PTMR is ineffective in treating patients with refractory angina. Stone and associates (2001) reported that in a patient population at high risk for restenosis (n = 26), recently created PTMR channels are not protective against severe ischemia caused by acute vessel closure and that late symptomatic restenosis after percutaneous intervention (angioplasty) may still frequently occur despite PTMR in the same region.

- In a review on TMLR, Horvath (2002) noted that recent studies showed that PTMR failed to provide angina relief greater than that observed in placebo groups. In a prospective, multi-center, randomized trial of PTMR in patients with class III or IV angina caused by non-recanalizable chronic total occlusions, Stone and colleagues (2002) reported that the performance of PTMR in addition to maximal medical therapy (n = 71) does not result in a greater reduction in angina, improvement in exercise duration or survival free of adverse cardiac events, as compared with maximal medical therapy only (n = 70).

- Gatterer et al (2004) evaluated the short-term as well as long-term results of PTMR for patients with therapy refractory angina pectoris who are not amenable for angioplasty or bypass surgery. The authors concluded that while the angina class of the patients improved significantly, there was no significant change of myocardial perfusion but a trend to deterioration of left ventricular function after an average follow-up period of 7.7 months.

- Leon et al (2005) reported the findings of a randomized, patient- and evaluator-blinded, placebo-controlled study in patients treated using PTMR. A total of 298 patients with severe angina were randomly assigned to receive low-dose or high-dose myocardial laser channels or no laser channels, blinded as a sham procedure. The primary end point was the change in exercise duration from baseline examination to 6 months. The incidence of 30-day death, stroke, myocardial infarction, coronary revascularization, or left ventricular perforation occurred in 2 patients in the placebo, 8 patients in the low-dose, and 4 patients in the high-dose groups (p = 0.12); 30-day myocardial infarction incidence was higher in patients receiving either low-dose or high-dose laser (9 patients) compared with placebo (no patients, p = 0.03). At 6 months, there were no differences in the change in exercise duration between those receiving a sham (28.0 s, n = 100), low-dose laser (33.2 s, n = 98), or high-dose laser (28.0 s, n = 98, p = 0.94) procedure. There were also no differences in the proportion of patients improving to better than Canadian Cardiovascular Society class III angina symptoms at 6 months. The follow-up visual summed stress single-photon-emission computed tomography scores were not significantly different from baseline in any group and were no different between groups. The modest improvement in angina symptoms assessed by the Seattle Angina Questionnaire also was not statistically different among the arms. The authors concluded
that treatment with PTMR provides no benefit beyond that of a similar sham procedure in patients blinded to their treatment status.

- An interventional procedure consultation document prepared for the National Institute for Health and Clinical Excellence (NICE, 2008) included the following provisional recommendations: "[c]urrent evidence on percutaneous laser revascularisation (PLR) for refractory angina pectoris shows no efficacy and suggests that the procedure may pose unacceptable safety risks. Therefore, this procedure should not be used." An interventional procedure consultation document by NICE on laser transmyocardial revascularization reached similar conclusions. The assessments noted that these procedures have not been shown to reduce mortality, and reductions in pain and improvements in quality of life in unblinded studies are likely to be placebo effects.

- In a meta-analysis, McGillion et al (2010) evaluated the effectiveness of PMLR versus optimal medical therapy for improving angina symptoms, health-related quality of life (HRQL), and exercise performance; the impact on all-cause mortality was also examined. A total of 7 trials (n = 1,213) were included. Primary analyses showed that at 12-month follow-up, those who had received PMLR had greater than or equal to 2 Canadian Cardiovascular Society class angina symptom reductions, odds ratio (OR) 2.13 (95 % confidence interval [CI]: 1.22 to 3.73), as well as improvements in aspects of HRQL including angina frequency, SMD = 0.29 (95 % CI: 0.05 to 0.52), disease perception, SMD = 0.37 (95 % CI: 0.14 to 0.61), and physical limitations, SMD = 0.29 (95 % CI: 0.05 to 0.53). Percutaneous transmyocardial laser revascularization had no significant impact on all-cause mortality. For secondary analyses, in which these researchers considered data from 1 trial that featured a higher-dose laser group, yielded no significant overall impact of PMLR across outcomes. The authors concluded that while PMLR may be effective for improving angina symptoms and related burden, further work is needed to clarify appropriate dose and impact on disease-specific mortality and adverse cardiac events.

- Excimer laser coronary angioplasty (ELCA) is one of the methods that fall within the spectrum of percutaneous coronary intervention (PCI) techniques. Coronary laser angioplasty is an alternative to coronary artery bypass surgery but not a replacement therapy for those patients considered unfit for surgery. In the majority of laser angioplasty cases, balloon angioplasty will also be required during the same procedure to achieve satisfactory results. Although the Spectranectics ELCA system is approved by the Food and Drug Administration for moderately calcified lesions, studies indicate an increased complication rate and lower success rate for these lesions. Thus, available evidence does not support laser technology as the most appropriate intervention.

- The American College of Cardiology/American Heart Association (ACC/AHA) 2005 guideline update for PCI (Smith et al, 2006) does not include ELCA in treatment recommendations. In a discussion of techniques associated with PCI, the authors stated
that despite the improvement in acute results observed for rotational atherectomy and excimer laser, there is no evidence that these approaches improve long-term outcomes in lesions that can be safely treated with balloon angioplasty or stenting alone. Furthermore, ELCA is not mentioned in a 2007 focused update of the 2005 guidelines (King et al., 2008).

- Excimer laser coronary angioplasty has also been studied as a treatment for patients with acute myocardial infarction, and in patients with depressed left ventricular ejection fraction. However, there is currently insufficient evidence to demonstrate the safety and effectiveness of ELCA for these indications.

- An assessment of ELCA by the Ludwig Boltzmann Institut (Johanssen, et al., 2010) found that the laser angioplasty has been reported as a debulking tool in highly calcified stenosis and in chronic total occlusions followed by a conventional balloon angioplasty/stenting. This systematic review included one randomized controlled trial with per randomization and per protocol analysis, and two case series without controls, reporting on a total of 444 patients. The assessment concluded that, due to limitations in the design of these studies, the evidence of effectiveness and safety is low. The report recommend against reimbursement for ELCA in Austrian hospitals.

- Niccoli et al (2013) stated that laser atherectomy might decrease procedural complications during PCI of degenerated saphenous vein grafts (SVGs) in case of unstable or thrombotic lesions because of its ability to de-bulk and vaporize thrombus. These investigators prospectively evaluated the safety and effectiveness of ELCA as a primary treatment strategy in consecutively unstable patients undergoing PCI of degenerated SVG lesions. A total of 71 consecutive patients with non-ST elevation acute coronary syndrome (mean age of 69 +/- 10 years, 66 men [89 %]) undergoing PCI of degenerated SVG were enrolled in a prospective case-control registry, using 2 different distal protection devices (DPDs; FilterWire EZ [Boston Scientific, Natick, MA; n = 24] and SpiderRX [Ev3, Plymouth, MN; n = 23]) or ELCA (n = 24) were included in this study.

- Primary end-points of the study were incidence of angiographic microvascular obstruction (Thrombolysis In Myocardial Infarction flow grade of less than 3 or Thrombolysis In Myocardial Infarction flow grade of 3 with myocardial blush grade 1 to 2) and incidence of type IVa myocardial infarction. Angiographic microvascular obstruction incidence tended to be less in ELCA-treated patients compared with DPD-treated patients (3 [13 %] versus 15 [32 %], p = 0.09). Type IVa myocardial infarction incidence was more in DPD-treated patients compared with ELCA-treated patients (23 [49 %] versus 5 [21 %], p = 0.04). The authors concluded that in patients with non-ST elevation acute coronary syndrome undergoing PCI of degenerated SVG, ELCA compared with DPD, is associated with a trend for better myocardial reperfusion and a
lesser incidence of peri-procedural necrosis. Moreover, they stated that controlled randomized controlled trials (RCTs) are needed to confirm these early observations.

- Fracassi et al (2013) noted that excimer laser utilization as an adjunctive device for PCI has increased in the last few years. Technical advancements have led to better results in terms of safety and effectiveness with a low complication rate. In particular, excimer laser for thrombus-containing lesions is able to achieve rapid thrombus removal and plaque de-bulking along with subsequent facilitation of stent angioplasty and a low rate of microvascular obstruction. Other indications for laser angioplasty embrace in-stent restenosis, chronic total occlusions, SVG lesions and new potential applications, such as stent expansion optimization and bi-furcation lesions. The authors concluded that as for other medical devices, however, excimer laser should be tested in future RCTs against current standard of therapy in order to better define its role for each of the indications summarized above.

- Lam and colleagues (2014) reported the successful management of under-expansion of a newly deployed coronary stent refractory to balloon dilatations. Direct stenting was performed for a lesion in the mid left anterior descending artery (without angiographically apparent heavy coronary calcification). The stent remained under-expanded despite repeated balloon dilatations including with high-pressure inflations. Subsequently, an excimer laser catheter was used in an attempt to vaporize the plaque by the accousto-mechanical effect of the rapidly exploding bubbles. The overall angiographic result was good after further balloon dilatation with ordinary pressure and full stent expansion was achieved. The authors concluded that management of under-expansion of a newly deployed stent is a potential indication of laser angioplasty

References


Appendix

The New York Heart Association (NYHA) functional classification of angina pectoris is as follows:
Class I- Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.
Class II- Patients with cardiac disease resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea, or anginal pain.
Class III- Patients with cardiac disease resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes fatigue, palpitation, dyspnea, or anginal pain.

Class IV- Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms of heart failure or the anginal syndrome may be present even at rest. If any physical activity is undertaken, discomfort is increased.

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