Transmyocardial and Endovascular Laser Revascularization

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

I. Aetna considers open chest, and thoracoscopic approaches to transmyocardial laser revascularization (TMLR) medically necessary for the treatment of medically refractory, severe intractable angina (see Appendix for selection criteria).

Aetna considers open chest and thoracoscopic approaches to TMLR experimental and investigational for all other indications because its effectiveness for indications other than the one listed above has not been established.

II. Aetna considers the use TMLR plus cell therapy with adipose derived stromal cells or autologous bone marrow cells for the treatment of ischemic heart disease experimental and investigational because of insufficient evidence of this approach.

Policy History

Last Review
09/29/2020
Effective: 06/04/1997
Next Review: 02/11/2021

Definitions

Additional Information

Clinical Policy Bulletin
Notes
III. Aetna considers percutaneous TMLR experimental and investigational for the treatment of refractory angina and all other indications because its effectiveness has not been established.

IV. Aetna considers excimer laser coronary angioplasty experimental and investigational for all indications including treatment of individuals with acute coronary syndrome, 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.

See CPB 0599 - Autologous Skeletal Myoblast/Mononuclear also Bone Marrow Cell Transplantation (../500_599/0599.html).

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 aorto-coronary 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 1 or more myocardial infarctions, and have undergone aorto-coronary 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. It 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 non-randomized 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 peri-operative management, TMLR is associated with a very low operative risk.
Dallan and colleagues (2008) tested the hypothesis that TMLR combined with intra-myocardial 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 re-vascularization 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 dypiridamole. 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 can not 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 re-vascularization, 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: "current 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.

Guidelines from the Society of Thoracic Surgeons (Bridges, et al., 2004) state that "transmyocardial laser revascularization may be an acceptable form of therapy for selected patients: as sole therapy for a subset of patients with refractory angina and as an adjunct to coronary artery bypass graft surgery for a subset of patients with angina who cannot be completely revascularized surgically."

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 (FDA) for moderately calcified lesions,
studies indicated 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).

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.

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.

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.

**Excimer Laser for Coronary Artery Restenosis In-Stent Treatment**

Hirose and associates (2016) stated that treatment of in-stent restenosis (ISR) is associated with a high incidence of recurrence. These investigators evaluated the clinical safety and 6-month efficacy of ELCA before scoring balloon dilatation for the treatment of ISR. A total of 23 patients with ISR were included and treatment strategy of ISR was dependent on each operator; 12 patients among those were treated with ELCA before scoring balloon dilatation (ELCA group); and 11 patients were treated with scoring balloon alone (non-ELCA group). Acute procedural results were evaluated by quantitative coronary angiography (QCA) and frequency domain optical coherence tomography (FD-OCT). Follow-up angiography was performed in all patients and the incidence of recurrent ISR and target lesion revascularization (TLR) was determined at 6 months after initial ISR treatment. Procedural success was achieved in all patients. Baseline clinical and angiographic characteristics were similar between groups. Maximum dilatation pressure of scoring balloon was significantly lower in the ELCA group than in the non-ELCA group.
group (9.0 ± 3.1 versus 14.9 ± 4.3 ATM, p = 0.001). In follow-up angiography, the occurrence of TLR was similar between groups (16.7 versus 45.5 %, p = 0.09), but the late luminal loss was significantly lower in the ELCA group (0.7 ± 0.6 versus 1.3 ± 0.7 mm, p = 0.03). The authors concluded that ELCA was a safe and feasible technique for the treatment of ISR and associated with a relatively low recurrent restenosis in comparison with scoring balloon dilatation alone. The long-term effectiveness of this approach need to be established by well-designed studies.

Ambrosini and colleagues (2017) noted that stents reduce angiographic restenosis in comparison with balloon angioplasty. The rate of ISR, although less frequent than post-angioplasty restenosis, is becoming increasingly prevalent due to the recent exponential increase in the use of intracoronary stents. In a multi-centric, case-control study, these researchers evaluated angiographic and clinical outcomes of percutaneous transluminal coronary angioplasty (PTCA) in combination with the use of ELCA and drug-eluting balloon (DEB) in treatment of patients with ISR (n = 80). All patients underwent 9 months of clinical and a coronary angiography follow-up. This study showed clinical and angiographic long-term success in the 91 % of the patients. The incidence of myocardial infarctions (MI) and deaths was lower than the rate after plain balloon angioplasty within the stent. The authors concluded that the findings of this study showed that ELCA and DEB may be an alternative treatment for ISR.

Lee and colleagues (2019) evaluated the effectiveness of ELCA to treat ISR due to peri-stent calcium-related stent under-expansion as assessed by OCT. These investigators studied 81 patients (81 lesions with ISR, stent under-expansion, and peri-stent calcium greater than 90°) who underwent OCT imaging both pre- and post-PCI and compared lesions treated with ELCA (n = 23) vs without ELCA (n = 58). The use of ELCA was associated with more calcium fracture (ELCA: 61 %, non-ELCA: 12 %, p < 0.01), larger final
minimum lumen area (ELCA: 4.76 mm² [3.25, 5.57], non-ELCA: 3.46 mm² [2.80, 4.13], p < 0.01), and a larger previously implanted stent area (ELCA: 6.15 mm² [4.83, 7.09], non-ELCA: 4.65 mm² [3.84, 5.40], p < 0.01). In the multi-variable model, ELCA use was associated with peri-stent calcium fracture (OR 46.5; 95% CI: 6.8 to 315.9, p = 0.01) that, in turn, was associated with final larger lumen and stent dimensions. Finally, contrast injection during ELCA was associated with multiple calcium fractures and fractures even in thicker calcium. The authors concluded that ELCA was effective for treating ISR with under-expansion by disrupting peri-stent calcium, facilitating better expansion of the previously implanted stent. The drawbacks of this study included that this was a retrospective observation study, and the number of patients was relatively small (n = 23 for ELCA treated subjects) precluding sub-group analysis especially the number of lesion treated with ELCA, likely causing selection bias.

Ichimoto and co-workers (2018) noted that ELCA has been used for the treatment of complex PCI such as ISR. However, little information was provided about the clinical outcomes after treatment with ELCA for ISR of drug-eluting stents (DES). These investigators examined the long-term clinical outcomes after PCI with ELCA for ISR of DES. A total of 81 consecutive patients with 87 lesions who underwent PCI for ISR of DES were included. Patients were classified into a PCI with ELCA group (23 patients with 24 lesions) and a PCI without ELCA group (58 patients with 63 lesions). The major adverse cardiac events (MACE) were evaluated. The mean duration of clinical follow-up was 29.8 ± 11.6 months. The incidences of diffuse restenosis and AHA/ACC type B2 or C lesion in the PCI with ELCA group were higher than in the PCI without ELCA group. Quantitative coronary angiography showed the acute luminal gain in the PCI with ELCA group was greater than in the PCI without ELCA group (1.64 ± 0.48 mm versus 1.26 ± 0.42 mm, p < 0.001). There were no significant differences in all-cause death, MI, or TLR between the 2 groups. Multi-
variative analysis due to a Cox proportional-hazards model showed that multi-vessel disease was an independent predictor of MACE (hazard ratio [HR] 3.05, 95% CI: 1.22 to 7.61, p = 0.02). The authors concluded that ELCA was effective as an atherectomy device for lumen enlargement and optimal lesion preparation. These researchers noted that even though ELCA was used for ISR of DES in significantly more complex lesions, the long-term clinical outcomes were favorable and similar.

In an editorial that accompanied the afore-mention study by Ichimoto et al (2018), Nakamura and associates (2018) stated that “Their findings suggest that ELCA is safe and effective at facilitating balloon or stent expansion by ablating in-stent intimal hyperplasia and improving optimal lesion preparation, especially in un-dilatable and under-expanded stents, although their study has several potential limitations, such as the absence of randomization to the treatment strategy, the small number of intravascular imaging used, and the retrospective nature of the study. We look forward to further studies in a larger number of patients and randomized trials”.

Hashimoto and associates (2019) examined the impact of tissue characterization for ISR with OCT during ELCA in the DES era. The effect of ELCA for ISR according to differences in tissue characteristics is unclear. A total of 53 ISR lesions (7 bare metal stents [BMS] and 46 DES) were treated with an ELCA catheter. After ELCA, balloon dilatation with either the scoring or non-compliant balloons was conducted. The procedure was completed by applying a drug-coated balloon. Tissue characterization and lumen measurement with OCT were performed 3 times: before PCI, after ELCA, and after the procedure. Lesions were categorized into the homogenous, layered, and mixed groups. Follow-up angiograms were conducted 6 to 12 months following PCI. No significant differences in MLA were observed before PCI. A significant difference was observed in MLA following ELCA among the 3 groups (homogeneous group: 1.75 ± 0.84 mm², layered group:
1.72 ± 0.45 mm², mixed group: 2.24 ± 0.70 mm², p = 0.048).
Final MLA was larger in the mixed group than in the homogeneous group (p = 0.028). No significant difference was observed in binary re-stenosis in the follow-up angiogram (homogeneous group 55.5 %, layered group 33.3 %, mixed group 33.3 %; p = 0.311) and the TLR rate (homogeneous 30.0 %, layered 23.8 %, mixed 25.0 %; p = 0.923). The authors concluded that tissue characterization by OCT may predict the efficacy of ELCA and balloon angioplasty for ISR during the acute phase. These researchers stated that despite these differences observed in the acute phase, no clinical difference in the chronic phase was observed; further studies with a larger sample size are needed.

The authors stated that this study had several drawbacks. First, this was an observational, retrospective, single-center study. Only 53 lesions with 3 cohorts were evaluated. Thus, the study’s ability to detect significant correlates of effects with ELCA and OCT finding was limited. Second, there was no control group to evaluate the additional effect of ELCA in ISR treatment. Third, other potential confounders that could affect the result, such as the difference of the diseased stent (BMS or DES, the generation of DES, stent size, stent length), balloon size, and differences in the position of the coronary stent, were not evaluated. In fact, the homogenous group utilized a significantly smaller balloon size and stent used in the index procedure. Fourth, the risk factors contributing to ISR and TLR, such as the presence of antiplatelet therapy, ACS presentation, older age, diabetes mellitus, and multiple TLR, were not fully evaluated. In addition, these investigators stated that ELCA is designed to ablate the obstructive atherosclerotic plaque rather than creating deformation of the plaque as in balloon dilatation. This design is considered as a more rational therapeutic option for debulking before adjunctive balloon dilatation, in contrast to balloon dilatation alone for stent re-stenosis, as it is superior in dilating the lumen and stent areas. In fact, ELCA with an IVUS-based study for ISR in BMS was documented to be effective in the
Ablation of neointimal tissue in BMS. However, acute procedural results as well as long-term angiographic and clinical results of ELCA with balloon dilatation were not superior to balloon dilatation alone. Accordingly, ELCA was abandoned as a strategy for treating ISR. Moreover, according to the recent guidelines on myocardial revascularization, i.e., European Society of Cardiology Guideline, ELCA was not cited as useful for the treatment of ISR.

Furthermore, an UpToDate review on “Specialized revascularization devices in the management of coronary heart disease” (Cutlip, 2019) states that “The American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) guideline update concluded that there is no evidence that excimer laser coronary angiography (ELCA) improves late outcomes in lesions that can be safely treated with stenting or angioplasty alone”.

**Transmyocardial Laser Revascularization Plus Cell Therapy**

Konstanty-Kalandyk (2018) noted that refractory angina has limited effective therapeutic options and often contributes to frequent hospitalizations, morbidity and impaired quality of life (QOL). These researchers examined mid-term results of a bio-interventional therapy combining TMLR and intra-myocardial injection of adipose derived stem cells (ADSC) in patients with refractory angina not amenable to percutaneous or surgical revascularization. This study included 15 patients with severe refractory angina and anterior wall ischemia who were ineligible for re-vascularization strategies. Adipose tissue was harvested and purified, giving the stem cell concentrate. All patients underwent left anterior thoracotomy and TMLR using a low-powered holmium: yttrium-aluminum-garnet laser and intra-myocardial injection of ADSC using a combined delivery system. No deaths or major adverse cardiovascular
or cerebrovascular events were observed in the 6-month follow-up. Mean ejection fraction increased from 35% to 38%, and mean Canadian Cardiovascular Society Angina Score decreased from 3.2 to 1.4, with decreased necessity of nitrate usage; 73% of patients reported health improvement particularly regarding general health and bodily pain. Improvement in endocardial movement, myocardial thickening and stroke volume index (35.26 to 46.23 ml/m²) on cardiac MRI was observed in 3 patients who had repeat CMR imaging after 6 months. The authors concluded that the findings of this study suggested that interventional therapy combining TMLR with intra-myocardial implantation of ADSC may reduce symptoms and improve QOL in patients with refractory angina. Moreover, they stated that these early findings need further validation in large, multi-center RCTs.

The authors stated that the main drawbacks of this study were the small sample size (n = 15) and lack of a control group, which limited the statistical rigor of the findings and questioned the efficacy results. However, the improvement in symptoms was accompanied by an improvement in myocardial function. Despite these drawbacks, this study provided an important opportunity to explore a new therapeutic option that has a great potential to improve the QOL.

Bockeria and colleagues (2019) examined the long-term results of TMLR using a CO2 laser in combination with intra-myocardial injection of autologous bone marrow stem cells (ABMSC) as an isolated procedure in patients with the end-stage coronary artery disease. This trial included 20 patients (90% men), with a mean age of 58.4 ± 8.7 years. To assess the long-term results, patients were examined in a hospital. The Minnesota Living with Heart Failure Questionnaire (MLHFQ) and the Seattle Angina Questionnaire (SAQ) were used. The evolution of laboratory and instrumental indices, as well as medical therapy, was assessed. The end-points of the study were death, acute myocardial infarction (AMI), repeated myocardial re-vascularization, recurrent hospitalizations due to
coronary artery disease (CAD), and stroke. The changes in angina functional class (FC) were also evaluated. The median of follow-up period was 54 (36 to 83) months. The analysis of the evolution of echocardiographic data showed the absence of statistically significant changes in the following parameters: left ventricular end-diastolic diameter (EDD) \( p = 0.967 \), end-systolic diameter (ESD) \( p = 0.204 \), end-diastolic volume (EDV) \( p = 0.852 \), end-systolic volume (ESV) \( p = 0.125 \), and left ventricular ejection fraction (LVEF) \( p = 0.120 \). Patients continued to regularly take the main groups of medications. Nitrate consumption was significantly reduced \( p < 0.001 \). Significant positive dynamics were observed in the changes in angina FC. At the baseline, all patients had angina III FC, in the long-term, 3 patients had II FC, 11 patients had I FC, and 6 patients had no angina. Clinical outcomes (mortality, recurrent MI, stroke) were absent during the follow-up period. There were 2 cases of repeated myocardial re-vascularization. Regression analysis revealed that SYNTAX score was associated with the clinical outcome "repeated re-vascularization". The authors concluded that TMLR in combination with intra-myocardial injection of ABMSC was a safe method to achieve a statistically significant anti-anginal effect and reduce the need for "nitrates", which in turn improved the QOL and reduced the frequency of hospitalizations due to CAD. The researchers stated that these results could be achieved with strict adherence to the certain indications for the intervention. The main drawbacks of this study were its small sample size \( n = 20 \) and the lack of a control, which limited the statistical rigor of the findings. These findings need to be validated by well-designed studies.

**Excimer Laser for Acute Coronary Syndrome**

Harima and colleagues (2018) tested a novel stent-less re-vascularization strategy using a combination of ELCA and drug-coated balloon (DCB) for patients with acute coronary syndrome (ACS). Consecutive ACS patients were planned to receive either a DCB application following ELCA without a
stent implantation or conventional re-vascularization with a coronary stent. The end-points were MACEs, defined as the composite of cardiac death, MIs, and TLR; target vessel revascularization (TVR); and angiographic outcome. Since a greater than expected number of patients allocated to the stent-less treatment arm eventually received a bailout stenting, the following 3 as-treated groups were compared; DCB with ELCA group (n = 60), stent with ELCA group (n = 23), and stent without ELCA group (n = 85). During a mean follow-up period of 420 ± 137 days, and with angiographic 6- and 12-month-follow-up rates of 96.7 %, 87 %, and 81.2 %, and 50 %, 65.2 %, and 45.9 %, respectively, the MACE rate did not differ across the groups (10 %, 4.3 %, and 3.5 %; p = 0.22) while an incidence of TVR was more common (15 %, 0, and 4.7 %; p = 0.02) and the diameter stenosis at 6-months of follow-up was greater (25.7 ± 18.2, 14.9 ± 13.1 and 16.2 ± 15.4 %; p = 0.002) in the DCB with ELCA group. The authors concluded that the stent-less re-vascularization strategy with DCB and ELCA was associated with a higher occurrence of re-stenosis in ACS patients.

Appendix

Selection Criteria for Transmyocardial Laser Revascularization

1. 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; and

2. Member has had maximal efforts to stabilize acute conditions such as severe ventricular arrhythmia, decompensated congestive heart failure or acute myocardial infarction; and
3. Severe New York Heart Association functional classification of angina pectoris – Class III or IV (see note below); and

4. Symptoms of angina refractory to standard medical therapy, including drug therapy at the maximum tolerated or maximum safe dosages; and

5. 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.

The New York Heart Association (NYHA) functional classification of angina pectoris is as follows:

Table: New York Heart Association (NYHA) Functional Classification of Angina Pectoris

<table>
<thead>
<tr>
<th>Class</th>
<th>Class Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>Patients with cardiac disease but without resulting limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or anginal pain.</td>
</tr>
<tr>
<td>Class II</td>
<td>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.</td>
</tr>
<tr>
<td>Class III</td>
<td>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.</td>
</tr>
<tr>
<td>Class IV</td>
<td>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.</td>
</tr>
</tbody>
</table>

**CPT Codes / HCPCS Codes / ICD-10 Codes**

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;.</em></td>
</tr>
<tr>
<td></td>
<td><em>Transmyocardial laser revascularization (TMLR):</em></td>
</tr>
<tr>
<td></td>
<td><em>CPT codes covered if selection criteria are met:</em></td>
</tr>
<tr>
<td>33140</td>
<td>Transmyocardial laser revascularization, by thoracotomy</td>
</tr>
<tr>
<td>33141</td>
<td></td>
</tr>
<tr>
<td>I20.1</td>
<td>Angina pectoris</td>
</tr>
<tr>
<td>I20.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Transmyocardial laser revascularization plus cell therapy with adipose derived stromal cells or autologous bone marrow cells:</em></td>
</tr>
<tr>
<td></td>
<td><em>CPT codes not covered for indications listed in the CPB:</em></td>
</tr>
<tr>
<td>38206</td>
<td>Blood-derived hematopoietic progenitor cell harvesting for transplantation, per collection; autologous</td>
</tr>
<tr>
<td>38232</td>
<td>Bone marrow harvesting for transplantation; autologous</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>---------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>38241</td>
<td>Hematopoietic progenitor cell (HPC); autologous transplantation</td>
</tr>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I21.01 - I25.9</td>
<td>Chronic ischemic heart disease</td>
</tr>
<tr>
<td>I21.A1</td>
<td>Myocardial infarction type 2</td>
</tr>
<tr>
<td>I21.A9</td>
<td>Other myocardial infarction type</td>
</tr>
</tbody>
</table>

**Excimer laser coronary angioplasty:**

**CPT codes not covered for indications listed in the CPB:**

**Excimer laser coronary angioplasty - No specific code:**

**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I21.01 - I25.9</td>
<td>Chronic ischemic heart disease</td>
</tr>
<tr>
<td>I21.A1</td>
<td>Myocardial infarction type 2</td>
</tr>
<tr>
<td>I21.A9</td>
<td>Other myocardial infarction type</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

3. Allen KB, Dowling RD, Heimansohn DA, et al. Transmyocardial revascularization utilizing a


40. Institute for Clinical Systems Improvement (ICSI). Transmyocardial laser therapy for severe refractory
angina. ICSI Technology Assessment Report.


https://aetnet.aetna.com/mpa/cpb/100_199/0163.html


57. March RJ. Transmyocardial laser revascularization with the CO2 laser: One year results of a randomized,


https://aetnet.aetna.com/mpa/cpb/100_199/0163.html


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0163
Transmyocardial and Endovascular Laser Revascularization

There are no amendments for Medicaid.

updated 09/29/2020