

## **Incidence and prognostic importance of acute renal failure after percutaneous coronary intervention.**

Rihal CS, Textor SC, Grill DE, Berger PB, Ting HH, Best PJ, Singh M, Bell MR, Barsness GW, Mathew V, Garratt KN, Holmes DR Jr.

**B**ACKGROUND: In patients undergoing percutaneous coronary intervention (PCI) in the modern era, the incidence and prognostic implications of acute renal failure (ARF) are unknown. **METHODS AND RESULTS:** With a retrospective analysis of the Mayo Clinic PCI registry, we determined the incidence of, risk factors for, and prognostic implications of ARF (defined as an increase in serum creatinine [Cr] >0.5 mg/dL from baseline) after PCI. Of 7586 patients, 254 (3.3%) experienced ARF. Among patients with baseline Cr <2.0, the risk of ARF was higher among diabetic than nondiabetic patients, whereas among those with a baseline Cr >2.0, all had a significant risk of ARF. In multivariate analysis, ARF was associated with baseline serum Cr, acute myocardial infarction, shock, and volume of contrast medium administered. Twenty-two percent of patients with ARF died during the index hospitalization compared with only 1.4% of patients without ARF ( $P<0.0001$ ). After adjustment, ARF remained strongly associated with death. Among hospital survivors with ARF, 1- and 5-year estimated mortality rates were 12.1% and 44.6%, respectively, much greater than the 3.7% and 14.5% mortality rates in patients without ARF ( $P<0.0001$ ). **CONCLUSIONS:** The overall incidence of ARF after PCI is low. Diabetic patients with baseline Cr values <2.0 mg/dL are at higher risk than nondiabetic patients, whereas all patients with a serum Cr >2.0 are at high risk for ARF. ARF was highly correlated with death during the index hospitalization and after dismissal.

## **The role of transmyocardial laser revascularization in congestive heart failure**

**Nishida H, Kurosawa H, Endo M.**

**T**ransmyocardial laser revascularization (TMLR) has been approved as an indirect coronary revascularization measure through angiogenesis around created channels in patients who are not amenable to direct revascularization methods such as coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA). TMLR is less invasive and there are no contraindications in terms of left ventricular function. Therefore all patients who have untreatable lesions by CABG or PTCA with reversible ischemia are candidates for TMLR therapy. In a Japanese clinical trial, improvement of left ventricular function associated with relief of persistent angina and improved perfusion was seen in 54% of patients. Significant reduction of operative risk in adjunctive TMLR (combination of TMLR with CABG) compared with isolated CABG has been also demonstrated in a randomized trial. These results indicate the usefulness of adjunctive TMLR in multivessel-disease patients with left ventricular dysfunction. Because TMLR is a simple and less-invasive technique, combined use of TMLR with off-pump CABG or MIDCAB is also an attractive revascularization strategy in ischemic cardiomyopathy patients.

## **Do transmyocardial and percutaneous laser revascularization induce silent ischemia? An assessment by exercise testing.**

**Myers J, Oesterle SN, Jones J, Burkhoff D.**

**B**ACKGROUND: Transmyocardial and percutaneous laser revascularization (TMR, PTMR) may reduce angina and increase exercise tolerance in otherwise untreatable angina patients, although the mechanism is unknown and the placebo effect may be significant. One other proposed mechanism is cardiac denervation leading to silent ischemia. METHODS: Electrocardiograms obtained during symptom-limited exercise (ETT, modified Bruce protocol) at baseline and 12 months were analyzed (blinded core laboratory) from 182 patients randomized to TMR (n = 92) or medical therapy alone (MED(TMR), n = 90) and 219 patients randomized to PTMR (n = 109) or medical therapy alone (MED(PTMR), n = 110). RESULTS: Exercise duration increased 1 year after TMR or PTMR relative to medically treated patients (6.8 ± 3.4 min vs 8.6 ± 3.5 min for TMR; 7.3 ± 3.1 min vs 9.1 ± 3.6 min for PTMR, P <.05). At baseline, 20% of TMR and MED(TMR) subjects had ST depression >1.0 mm, >80% had angina during exercise, but only 3% had ST changes without chest pain (silent ischemia). This did not change after TMR. In the PTMR group, more subjects exercised to >1.0 mm ST depression (from 17% to 34%, P <.05), with no change in MED(PTMR), but the proportion with silent ischemia did not change in either group. CONCLUSION: Exercise tolerance improved after TMR and after PTMR. Relative to PTMR, TMR more effectively suppressed pain during exercise and ischemic ST depression. However, neither TMR nor PTMR induced significant silent ischemia. These results suggest that denervation may not be a significant factor contributing to angina relief after these procedures. The contribution of the placebo effect was not determined by these results.

**A prospective, multicenter, randomized trial of percutaneous transmyocardial laser revascularization in patients with nonrecanalizable chronic total occlusions.**

**Stone GW, Teirstein PS, Rubenstein R, Schmidt D, Whitlow PL, Kosinski EJ, Mishkel G, Power JA.**

**O**BJECTIVES: We sought to evaluate the safety and efficacy of percutaneous transmyocardial revascularization (PTMR) in patients with refractory angina caused by one or more chronic total occlusions (CTOs) of a native coronary artery. **B**ACKGROUND: Previous unblinded, randomized trials of PTMR in patients with end-stage coronary artery disease and refractory angina have demonstrated significant relief of angina and increased exercise duration. Whether such benefits would be realized in blinded patients with less extensive coronary artery disease is unknown. **M**ETHODS: A total of 141 consecutive patients with class III or IV angina caused by one or more chronically occluded native coronary arteries in which a percutaneous coronary intervention (PCI) had failed were prospectively randomized, at 17 medical centers, in the same procedure, to PTMR plus maximal medical therapy (MMT) (n = 71) or MMT only (n = 70). Blinding was achieved through heavy sedation, dark goggles and the concurrent performance of PCI in all patients. **R**ESULTS: Baseline characteristics were similar between the two groups. A median number of 20 laser channels were created in patients randomized to PTMR. At six months, the anginal class improved by two or more classes in 49% of patients assigned to PTMR and in 37% of those assigned to MMT (p = 0.33). The median increase in exercise duration from baseline to six months was 64 s with PTMR versus 52 s with MMT (p = 0.73). There were no differences in the six-month rates of death (8.6% vs. 8.8%), myocardial infarction (4.3% vs. 2.9%) or any revascularization (4.3% vs. 5.9%) in the PTMR and MMT groups, respectively (p = NS for all). **C**ONCLUSIONS: In patients with class III or IV angina caused by nonrecanalizable CTOs, the performance of PTMR does not result in a greater reduction in angina, improvement in exercise duration or survival free of adverse cardiac events, as compared with MMT only.

## **Results of prospective randomized controlled trials of transmyocardial laser revascularization.**

**Horvath KA.**

Over 6,000 patients worldwide have undergone transmyocardial laser revascularization (TMR) for the treatment of myocardial ischemia due to end-stage coronary artery disease since 1990. Four prospective randomized controlled trials have reported their results in comparing TMR to maximum medical therapy. All of the trials demonstrated that TMR provided significant relief of angina when compared to medical management. Additional objective data in the form of exercise tolerance and myocardial perfusion scanning was used to support the symptomatic improvement. Recent reports of the failure of percutaneous transmyocardial laser revascularization (PMR) to provide angina relief greater than that seen in a placebo group underscore the need for better understanding of TMR. While all of these trials are similar, they are not identical and this review provides an update and comparison of the results.

## **Laser angioplasty and laser-induced thrombolysis in revascularization of anomalous coronary arteries.**

Shah R, Martin RE, Topaz O.

**A**cute coronary syndromes such as unstable angina and myocardial infarction are attributed to a pathophysiologic process that involves rupture of atherosclerotic plaque and subsequent thrombosis. Percutaneous intervention of anomalous coronary arteries in patients who present with acute coronary syndromes impose unique technical challenges related to the specific anatomic course and morphology of these vessels. Selection of appropriate guiding catheter configuration, choice of supportive guidewire, and proper delivery and activation of debulking devices and stents are important steps toward achieving adequate results. Excimer laser angioplasty is a debulking technology for removal of atherosclerotic plaque and associated thrombi. To date, application of laser angioplasty in anomalous coronary arteries is unreported. We herein present clinical data and discuss technical aspects related to performance of excimer laser angioplasty in three symptomatic patients with acute coronary syndrome, two having an anomalous right coronary artery and one with an anomalous circumflex artery. The delivery of laser energy in these cases resulted in rapid thrombolysis of an occlusive thrombus, successful debulking of the underlying atherosclerotic plaque, facilitation of adjunct balloon angioplasty and stenting, and ultimately, improved clinical condition.

**Magnetic resonance imaging demonstrates improved regional systolic wall motion and thickening and myocardial perfusion of myocardial territories treated by laser myocardial revascularization.**

Laham RJ, Simons M, Pearlman JD, Ho KK, Baim DS.

**O**BJECTIVES: This study was designed to investigate the use of magnetic resonance (MR) functional and perfusion imaging to evaluate laser myocardial revascularization (LMR). **B**ACKGROUND: Most clinical studies of LMR have shown improvements in angina class and exercise capacity, with minimal or absent improvements in myocardial perfusion and function. **M**ETHODS: Fifteen patients who underwent percutaneous Biosense-guided holmium:yttrium aluminum garnet LMR to areas of viable but ischemic myocardium were followed clinically and underwent functional and perfusion MRI at baseline, 30 days and 6 months. **R**ESULTS: The mean age was 64 ± 11 years; four patients were women. The ejection fraction was 47.4 ± 14.0%. Angina class at baseline was 3.4 ± 0.6 and improved to 2.5 ± 1.4 at six months ( $p = 0.054$ ). Exercise time at baseline was 298 ± 97 s and increased to 350 ± 95 s at 30 days and 365 ± 79 s at six months,  $p = 0.04$ . There were no significant changes in nuclear perfusion scans. Although MR determined that resting radial motion and thickening of the target wall were significantly less than normal at baseline ( $p < 0.001$ ), they improved significantly during follow-up (wall thickening: baseline, 30.6 ± 11.7%; day 30, 41.2 ± 13.3% and day 180, 44.2 ± 11.9%,  $p = 0.01$ ). The size of the underperfused myocardial area was 14.5 ± 5.4% at baseline and was reduced to 6.3 ± 2.8% at 30 days and 7.7 ± 3.7% at 6 months ( $p < 0.001$ ). **C**ONCLUSIONS: This small phase I, open-label, uncontrolled study of MR functional and perfusion imaging in patients undergoing Biosense-guided LMR suggests a beneficial effect of this treatment strategy on myocardial function and perfusion. The efficacy of Biosense-guided LMR is being evaluated in a large phase II, randomized, blinded placebo-controlled trial with an MRI substudy (DIRECT).

## **Myocardial perfusion after transcutaneous/percutaneous myocardial laser revascularization.**

**Wiemer M, Wielepp P, Butz T, Horstkotte D, Burchert W.**

**T**he effectiveness of transcutaneous and percutaneous myocardial laser revascularization in patients with endstage coronary artery disease and angina refractory to pharmacological therapy has been proved by various studies. Angiogenesis associated with an improvement of microcirculation and myocardial perfusion may be responsible for the reduction of angina and the improved physical performance. Myocardial perfusion studies published so far are compared to our own results utilizing positron emission tomography before and after percutaneous myocardial laser revascularization.

## Myocardial laser revascularization

1. Percutaneous laser revascularization in patients with chronic total occlusions.

Perin EC, DeMaio SJ, George B, O'Neill WW.

J Am Coll Cardiol. 2002 Dec 4;40(11):2062; author reply 2062-3.

2. The role of transmural laser revascularization in congestive heart failure.

Nishida H, Kurosawa H, Endo M.

Nippon Geka Gakkai Zasshi. 2002 Sep;103(9):588-93.

3. Do transmural and percutaneous laser revascularization induce silent ischemia?

Myers J, Oesterle SN, Jones J, Burkhoff D.

An assessment by exercise testing.

Am Heart J. 2002 Jun;143(6):1052-7.

4. A prospective, multicenter, randomized trial of percutaneous transmural laser revascularization in patients with nonrecanalizable chronic total occlusions.

Stone GW, Teirstein PS, Rubenstein R, Schmidt D, Whitlow PL, Kosinski EJ, Mishkel G, Power JA.

J Am Coll Cardiol. 2002 May 15;39(10):1581-7.

5. Results of prospective randomized controlled trials of transmural laser revascularization.

Heart Surg Forum.

Horvath KA.

2002;5(1):33-9; discussion 39-40.

6. Laser angioplasty and laser-induced thrombolysis in revascularization of anomalous coronary arteries.

Shah R, Martin RE, Topaz O.

J Invasive Cardiol. 2002 Apr;14(4):180-6.

7. Magnetic resonance imaging demonstrates improved regional systolic wall motion and thickening and myocardial perfusion of myocardial territories treated by laser myocardial revascularization.

Laham RJ, Simons M, Pearlman JD, Ho KK, Baim DS.

J Am Coll Cardiol. 2002 Jan 2;39(1):1-8.

8. Myocardial perfusion after transcatheter/percutaneous myocardial laser revascularization.

Wiemer M, Wielepp P, Butz T, Horstkotte D, Burchert W.

Z Kardiol 2002;91 Suppl 3:84-8

Am J Cardiol ,2001;87(7):861-7

## Quantitative analysis of myocardial perfusion changes with transmyocardial laser revascularization.

Burns SM, Brown S, White CA, Tait S, Sharples L, Schofield PM.

Transmyocardial laser revascularization (TLR) is a technique of creating left ventricular transmural channels in patients with refractory angina. We aimed to measure perfusion changes quantitatively using technetium-99m methoxyisobutyl isonitrile. Perfusion scans were performed on 94 TLRs and in 94 control patients at rest and during exercise at assessment, and 3-, 6-, and 12-month follow-up. A serial set of scans allowed direct comparison of each patient over all visits. Bull's-eyes were divided into 5 anatomic regions and a 20-region model. Severity values were calculated for rest, stress, and each cardiac region using a threshold of 1 for analysis. Higher scores indicated greater severity of ischemia and lower perfusion. At 3-month follow-up, the severity was significantly worse during TLR than in control patients both during stress (0.172 +/- 0.003 and 0.161 +/- 0.003, respectively,  $p = 0.007$ ) and at rest (0.170 +/- 0.003 and 0.158 +/- 0.003, respectively,  $p = 0.002$ ). At 6 months, severity during stress was 0.176 +/- 0.003 with TLR and 0.162 +/- 0.003 in controls ( $p = 0.001$ ), with no significant difference at rest. At 12 months, there was no significant difference between TLR and control groups at stress and rest. Regional severity deteriorates during TLR compared with control patients anteriorly ( $p = 0.001$ ,  $p = 0.0016$ ,  $p = 0.005$  at 3, 6, and 12 months), apically ( $p = 0.005$ ,  $p = 0.0046$ ,  $p = 0.032$ , respectively), and laterally ( $p < 0.0001$ ,  $p = 0.001$ ,  $p = 0.002$ , respectively). An apparent improvement is observed in the inferoseptal region at 6- and 12-month follow-up—an area not lasered. Thus, TLR appears to produce deterioration in resting myocardial perfusion in lasered regions, and improvement in nonlasered regions, with no difference in exercise-induced myocardial ischemia compared with that in control patients.

Circulation , 2001;104(12 Suppl 1):I81-4

## Sustained angina relief 5 years after transmyocardial laser revascularization with a CO<sub>2</sub> laser.

Horvath KA, Aranki SF, Cohn LH, March RJ, Frazier OH, Kadipasaoglu KA, Boyce SW, Lytle BW, Landolfo KP, Lowe JE, Hattler B, Griffith BP, Lansing AM.

**BACKGROUND:** Although transmyocardial laser revascularization (TMR) has provided symptomatic relief of angina over the short term, the long-term efficacy of the procedure is unknown. Angina symptoms as assessed independently by angina class and the Seattle Angina Questionnaire (SAQ) were prospectively collected up to 7 years after TMR. **METHODS:** Seventy-eight patients with severe angina not amenable to conventional

revascularization were treated with a CO<sub>2</sub> laser. Their mean age was 61±10 years at the time of treatment. Preoperatively, 66% had unstable angina, 73% had had ≥1 myocardial infarction, 93% had undergone ≥1 CABG, 42% had ≥1 PTCA, 76% were in angina class IV, and 24% were in angina class III. Their average pre-TMR angina class was 3.7±0.4. RESULTS: After an average of 5 years (and up to 7 years) of follow-up, the average angina class was significantly improved to 1.6±1 (P=0.0001). This was unchanged from the 1.5±1 average angina class at 1 year postoperatively (P=NS). There was a marked redistribution according to angina class, with 81% of the patients in class II or better, and 17% of the patients had no angina 5 years after TMR. A decrease of ≥2 angina classes was considered significant, and by this criterion, 68% of the patients had successful long-term angina relief. The angina class results were further confirmed with the SAQ; 5-year SAQ scores revealed an average improvement of 170% over the baseline results. CONCLUSIONS: The long-term efficacy of TMR persists for ≥5 years. TMR with CO<sub>2</sub> laser as sole therapy for severe disabling angina provides significant long-term angina relief.

Circulation ,2001;104(12 Suppl 1):I115-20

Transmyocardial laser revascularization remodels the intrinsic cardiac nervous system in a chronic setting.

Arora RC, Hirsch GM, Hirsch K, Armour JA.

BACKGROUND: Prospective trials have demonstrated that transmyocardial laser revascularization (TMLR) imparts symptomatic relief to patients with refractory angina. Because peak clinical effectiveness of TMLR is usually delayed by several months, it has been proposed that ventricular denervation is one mechanism whereby TMLR imparts symptomatic relief. We have demonstrated that TMLR does not denervate the heart in the acute setting, nor does it modify the intrinsic cardiac nervous system (ICNS) in the acute setting. However, the long-term effects of TMLR on the ICNS remain unknown. METHODS AND RESULTS: A holmium:yttrium-aluminum-garnet laser created 20 channels through the anterolateral left ventricular free wall of 10 dogs. Four weeks later, the function of cardiac sensory inputs to the ICNS was studied by applying veratridine (7.5 micromol/L) to ventricular sensory fields. Chronotropic and inotropic responses elicited by cardiac sympathetic or parasympathetic efferent neurons stimulated electrically (10 Hz, 4 V, 4 ms) or chemically (nicotine 5 to 20 microgram/kg IV) were also assessed. Chemical activation of epicardial sensory neurites with veratridine elicited expected ICNS excitatory responses. Electrical stimulation of sympathetic and parasympathetic efferent neurons induced expected altered cardiac responses. In contrast, the responsiveness of the ICNS to systemically

administered nicotine was obtunded. CONCLUSIONS: Although chronic TMLR does not affect cardiac afferent or extracardiac efferent neuronal function, it does remodel the ICNS so that its responsiveness to a known potent chemical agonist (ie, nicotine) becomes obtunded. Remodeling of the ICNS may account in part for the delayed symptomatic relief that TMLR imparts to patients with refractory angina.

Am J Med , 2001;111(5):341-8

Transmyocardial CO<sub>2</sub> laser revascularization improves symptoms, function, and quality of life: 12-month results from a randomized controlled trial.

Spertus JA, Jones PG, Coen M, Garg M, Bliven B, O'Keefe J, March RJ, Horvath K.

**PURPOSE:** To describe differences in health status (symptoms, physical function, and quality of life) between continued medical management and transmyocardial revascularization with a carbon dioxide laser in patients with severe, symptomatic, inoperable coronary artery disease. **SUBJECTS AND METHODS:** This prospective, multicenter trial randomized 98 patients to transmyocardial revascularization and 99 to continued medical therapy. Health status was assessed with the Seattle Angina Questionnaire and the Short Form-36 at baseline and at 3, 6, and 12 months. A new analytic technique, the benefit statistic, was developed to facilitate interpretability of disease-specific health status assessments over time. **RESULTS:** Of the 99 patients assigned to medical therapy, 59 (60%) subsequently underwent transmyocardial revascularization. By an intention-to-treat analysis, patients initially randomized to transmyocardial revascularization had 44% of their angina eliminated versus 21% for the medical treatment group (difference = 23%; 95% confidence interval [CI], 11% to 34%). Differences in the benefits of transmyocardial revascularization on physical limitations (33% vs 11% in the medical arm [difference = 23%; 95% CI, 15% to 31%]) and quality of life (47% vs 20% in the medical arm [difference = 26%; 95% CI, 18% to 35%]) were similarly large. These benefits were apparent at 3 months and sustained throughout the 1 year of follow-up. An efficacy analysis that excluded patients who crossed over from the medical treatment to transmyocardial revascularization arm suggested greater treatment benefits. **CONCLUSIONS:** Transmyocardial revascularization may offer a valuable palliative alternative to patients with severe limitations in health status for whom no standard revascularization options exist.

Circulation ,1999 ;100: 135-140

### Cardiac Sympathetic Denervation After Transmyocardial Laser Revascularization

Thabet Al-Sheikh, Keith B. Allen, Susan P. Straka, David A. Heimansohn, Richard L. Fain, Gary D. Hutchins, Stephen G. Sawada, Douglas P. Zipes, and Erica D. Engelstein

**Background-**Transmyocardial laser revascularization (TMR) has been shown to improve refractory angina not amenable to conventional coronary interventions. However, the mechanism of action remains controversial, because improved myocardial perfusion has not been consistently demonstrated. We hypothesized that TMR relieves angina by causing myocardial sympathetic denervation.

**Methods and Results-**PET imaging of resting and stress myocardial perfusion with [13N]ammonia (NH<sub>3</sub>) and of sympathetic innervation with [11C]hydroxyephedrine (HED) was performed before and after TMR in 8 patients with class IV angina ineligible for CABG or PTCA. A mean of 50±11 channels were created in the left ventricle (LV) with a holmium:YAG laser. A semiautomated program was used to determine NH<sub>3</sub> uptake and HED retention in the LV. Perfusion and innervation defects were defined as the percentage of LV with tracer uptake or retention >2 SD below normal mean values. All patients experienced improvement in their angina by 2.4±0.5 angina classes after surgery, P=0.008. Sympathetic innervation defects exceeded resting perfusion defects in all patients before TMR (34.6±27.3% for HED versus 9.4±10.8% for NH<sub>3</sub>, P=0.008). TMR did not significantly affect resting or stress myocardial perfusion but increased the extent of sympathetic denervation in 6 of 8 patients by 27.5±15.9%, P=0.03. In the remaining 2 patients, both sympathetic denervation and stress perfusion defects decreased after surgery.

**Conclusions-**TMR causes decreased myocardial HED uptake in most patients without significant change in resting or stress myocardial perfusion, suggesting that the improvement in angina may be at least in part due to sympathetic denervation.

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Perioperative morbidity and mortality after transmyocardial laser revascularization: incidence and risk factors for adverse events

G. Chad Hughes, Kevin P. Landolfo, James E. Lowe, Robin B. Coleman, Carolyn L. Donovan

**OBJECTIVE** The purpose of this study was to describe the incidence and spectrum of perioperative cardiac and noncardiac morbidity and mortality after transmyocardial laser revascularization (TMR) and to identify predictors of these adverse clinical events.

**BACKGROUND** Clinical studies have demonstrated the efficacy of TMR for relieving angina pectoris, although no study to date has specifically addressed the associated perioperative morbidity and mortality.

**METHODS** Between October 1995 and August 1997, 34 consecutive patients with end-stage coronary artery disease (CAD) underwent isolated TMR. The majority of patients (94%) had class III or IV angina pectoris, and two patients (6%) had unstable symptoms preoperatively. Patient records were reviewed for fatal and nonfatal adverse cardiac and noncardiac events.

**RESULTS** Perioperative death occurred in two patients (5.9%) due to cardiogenic shock complicating acute myocardial infarction. Perioperative cardiac morbidity occurred in 16 patients (47.1%); noncardiac morbidity was seen in 12 patients (35.3%). Preoperative unstable angina was the only variable predictive of perioperative death ( $p = 0.005$ ). Cardiac ( $p = 0.005$ ) and noncardiac ( $p < 0.001$ ) morbidity rates were significantly higher for the initial 15 patients undergoing the procedure. Other predictors of perioperative complications included lack of postoperative treatment with a furosemide infusion ( $p = 0.04$ ) and preoperative unstable angina ( $p = 0.05$ ).

**CONCLUSIONS** Perioperative mortality in patients undergoing isolated TMR is low. Transmyocardial laser revascularization patients are at higher risk for adverse perioperative cardiac and noncardiac events, likely reflecting the lack of immediate benefit from the procedure in the setting of severe CAD. These patients merit vigilant surveillance for adverse events and aggressive medical management in the perioperative period

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Catheter-based percutaneous myocardial laser revascularization in patients with end-stage coronary artery disease.

Lauer B, Junghans U, Stahl F, Kluge R, Oesterle SN, Schuler G

**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.

#### Summary

1. Procedural success: 100%
2. Major periprocedural complications: one arterial bleeding requiring surgical repair.
3. One death early after PMR, due to a myocardial infarction (MI) in a nontreated region.
4. Six-month F/U: 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,  $p<0.05$ )
5. No improvement in thallium scintigraphy

Lancet , 1999 ;354(9182):885-90

Transmyocardial laser revascularisation compared with continued medical therapy for treatment of refractory angina pectoris: a prospective randomised trial. ATLANTIC Investigators. Angina Treatments-Lasers and Normal Therapies in Comparison.

Burkhoff D, Schmidt S, Schulman SP, Myers J, Resar J, Becker LC, Weiss J, Jones JW

**BACKGROUND:** Transmyocardial revascularisation (TMR) is an operative treatment for refractory angina pectoris when bypass surgery or percutaneous transluminal angioplasty is not indicated. We did a prospective randomised trial to compare TMR with continued medication. **METHODS:** We recruited 182 patients from 16 US centres with Canadian Cardiovascular Society Angina (CCSA) score III (38%) or IV (62%), reversible ischaemia, and incomplete response to other therapies. Patients were randomly assigned TMR and continued medication (n=92) or continued medication alone (n=90). Baseline assessments were angina class, exercise tolerance, Seattle angina questionnaire for quality of life, and dipyridamole thallium stress test. We reassessed patients at 3 months, 6 months, and 12 months, with independent masked angina assessment at 12 months. **FINDINGS:** At 12 months, total exercise tolerance increased by a median of 65 s in the TMR group compared with a 46 s decrease in the medication-only group (p<0.0001, median difference 111 s). Independent CCSA score was II or lower in 47.8% in the TMR group compared with 14.3% in the medication-only group (p<0.001). Each Seattle angina questionnaire index increased in the TMR group significantly more than in the medication-only group (p<0.001). **INTERPRETATION:** TMR lowered angina scores, increased exercise tolerance time, and improved patients' perceptions of quality of life. This operative treatment provided clinical benefits in patients with no other therapeutic options.

Figure. Distribution of CCSA scores by independent assessors

J Thora Cardiovasc Surg, 2000; 119(3):540-9

Transmyocardial laser revascularization combined with coronary artery bypass grafting: a multicenter, blinded,

prospective, randomized, controlled trial.

Allen KB. Dowling RD. DelRossi AJ. Realyvasques F. Lefrak EA. Pfeffer TA. Fudge TL. Mostovych M. Schuch D. Szentpetery S. Shaar CJ

**Objective:** We sought to assess the safety and efficacy of transmyocardial revascularization combined with coronary artery bypass grafting in patients not amenable to complete revascularization by coronary bypass alone. **Methods:** A total of 263 patients whose standard of care was coronary artery bypass grafting and who had one or more ischemic areas not amenable to bypass grafting were prospectively randomized to receive coronary bypass of suitable vessels plus transmyocardial revascularization to areas not graftable (n = 132) or coronary bypass alone with nongraftable areas left unrevascularized (n = 131). Group preoperative demographics and operative characteristics were similar. **Results:** The operative mortality rate after coronary bypass/transmyocardial revascularization was 1.5% (2/132) versus 7.6% (10/131) after coronary bypass alone (P = .02). Patients undergoing both coronary bypass and transmyocardial revascularization required less postoperative inotropic support (30% vs 55%, P = .0001) and had a trend toward fewer insertions of intra-aortic balloon pumps (4% vs 8%, P = .13) than did patients having coronary bypass alone. Multivariable predictors of operative mortality were coronary artery bypass alone (odds ratio, 5.3; 95% confidence interval, 1.1-25.7; P = .04) and increased age (odds ratio, 1.1; 95% confidence interval, 1.0-1.2; P = .03). One-year Kaplan-Meier survival (95% vs 89%, P = .05) and freedom from major adverse cardiac events defined as death or myocardial infarction (92% vs 86%, P = .09) favored the combination of coronary bypass and transmyocardial revascularization. Baseline to 12-month improvement in angina and exercise treadmill scores was similar between groups. **Conclusions:** In a prospective, randomized, multicenter trial, transmyocardial revascularization combined with coronary artery bypass grafting in patients not amenable to complete revascularization by coronary bypass alone was safe; however, angina relief and exercise treadmill improvement were indistinguishable between groups at 12 months of follow-up. Operative and 1-year survival benefits observed after adjunctive transmyocardial revascularization require confirmation by a larger validation study, which is ongoing.

Fig. 1. One-year Kaplan-Meier intent-to-treat survival estimates.

Fig. 2. Mean angina class at baseline (2.8 vs 2.9,  $P = .5$ ) was similar between patients undergoing CABG/TMR and those undergoing CABG alone. Three months after the surgery, both groups experienced a similar significant reduction in angina class (0.4 vs 0.4,  $P = 1.0$ ). At 12 months of follow-up, angina class remained significantly improved and was similar between groups (0.5 vs 0.6,  $P = .2$ ).

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Short- and intermediate-term clinical outcomes from direct myocardial laser revascularization guided by biosense left ventricular electromechanical mapping.

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**Background:** Direct myocardial revascularization (DMR) has been examined as an alternative treatment for patients with chronic refractory myocardial ischemic syndromes who are not candidates for conventional coronary revascularization.

**Methods and Results:** We used left ventricular electromagnetic guidance in 77 patients with chronic refractory angina (56 men, mean age  $61 \pm 11$  years, ejection fraction  $0.48 \pm 0.11$ ) to perform percutaneous DMR with an Ho:YAG laser at 2 J/pulse. Procedural success (laser channels placed in prespecified target zones) was achieved in 76 of 77 patients with an average of  $26 \pm 10$  channels (range 11 to 50 channels). The rate of major in-hospital cardiac adverse events was 2.6%, with no deaths or emergency operations, 1 patient with postprocedural pericardiocentesis, and 1 patient with minor embolic stroke. The rate of out-of-hospital adverse cardiac events (up to 6 months) was 2.6%, with 1 patient with myocardial infarction and 1 patient with stroke. Exercise duration after DMR increased from  $387 \pm 179$  to  $454 \pm 166$  seconds at 1 month and to  $479 \pm 161$  seconds at 6 months ( $P = 0.0001$ ). The time to onset of angina increased from  $293 \pm 167$  to  $377 \pm 176$  seconds at 1 month and to  $414 \pm 169$  seconds at 6 months ( $P = 0.0001$ ). Importantly, the time to ST-segment depression ( $\geq 1$  mm) also increased from  $327 \pm 178$  to  $400 \pm 172$  seconds at 1 month and to  $436 \pm 175$  seconds at 6 months ( $P = 0.001$ ). Angina (Canadian Cardiovascular Society classification) improved from  $3.3 \pm 0.5$  to  $2.0 \pm 1.2$  at 6 months ( $P < 0.001$ ). Nuclear perfusion imaging studies with a dual-isotope technique, however, showed no significant improvements at 1 or 6 months.

**Conclusions:** Percutaneous DMR guided by left ventricular mapping is feasible and safe and reveals improved angina and prolonged exercise duration for up to a 6-month follow-up.

Figure 2. Exercise (ETT) time results at baseline (B/L) and 1 month (1M) and 6 months (6M) after percutaneous DMR (P <0.001 for 1- and 6-month time points versus baseline).

Figure 3. Angina class (CCS) at baseline (B/L), 2 weeks (2W), and 3 months (3M) and 6 months (6M) after percutaneous DMR (P <0.0001 for 3- and 6-month time points versus baseline).

Ann Thorac Surg , 2000; 69(2):655-62

Myocardial laser

revascularization: the controversy and the data.

Bridges CR

The clinical and experimental data relevant to the theoretical mechanisms and clinical results of laser myocardial revascularization are reviewed. Both transmural and percutaneous approaches are considered. Both types result in a reduction in anginal symptoms in patients refractory to conventional therapy and are likely to act through common pathways. The proximate mechanisms for the transmural revascularization effect most likely relate to myocardial inflammation, secondary stimulation of growth factors, and denervation of the myocardium.

PMR

1. Quantitative analysis of myocardial perfusion changes with transmural laser revascularization.

Burns SM, Brown S, White CA, Tait S, Sharples L, Schofield PM.

Am J Cardiol 2001 Apr 1;87(7):861-7

2. Sustained angina relief 5 years after transmural laser revascularization with a CO<sub>2</sub> laser.

Horvath KA, Aranki SF, Cohn LH, March RJ, Frazier OH, Kadipasaoglu KA, Boyce SW, Lytle BW,

Landolfo KP, Lowe JE, Hattler B, Griffith BP, Lansing AM.

Circulation 2001 Sep 18;104(12 Suppl 1):I81-4

3. Transmural laser revascularization remodels the intrinsic cardiac nervous system in a chronic setting.

Arora RC, Hirsch GM, Hirsch K, Armour JA.

Circulation 2001 Sep 18;104(12 Suppl 1):I115-20

4. Transmural CO<sub>2</sub> laser revascularization improves symptoms, function, and quality of life: 12-month results from a randomized controlled trial.

Spertus JA, Jones PG, Coen M, Garg M, Bliven B, O'Keefe J, March RJ, Horvath K.

Am J Med 2001 Oct 1;111(5):341-8

5. Cardiac Sympathetic Denervation After Transmyocardial Laser Revascularization

Thabet Al-Sheikh, Keith B. Allen, Susan P. Straka, David A. Heimansohn, Richard L. Fain, Gary D. Hutchins, Stephen G. Sawada, Douglas P. Zipes, and Erica D. Engelstein  
Circulation 1999 100: 135-140.

6. Perioperative morbidity and mortality after transmyocardial laser revascularization: incidence and risk factors for adverse events

G. Chad Hughes, Kevin P. Landolfo, James E. Lowe, Robin B. Coleman, Carolyn L. Donovan  
Journal of the American College of Cardiology, 33:4:1021-1026

7. Cardiac Sympathetic Denervation After Transmyocardial Laser Revascularization

Thabet Al-Sheikh, Keith B. Allen, Susan P. Straka, David A. Heimansohn, Richard L. Fain, Gary D. Hutchins, Stephen G. Sawada, Douglas P. Zipes, and Erica D. Engelstein  
Circulation 1999 100: 135-140.

8. Catheter-based percutaneous myocardial laser revascularization in patients with end-stage coronary artery disease.

Lauer B, Junghans U, Stahl F, Kluge R, Oesterle SN, Schuler G  
J Am Coll Cardiol 1999 Nov 15;34(6):1663-70

9. Transmyocardial laser revascularisation compared with continued medical therapy for treatment of refractory angina pectoris: a prospective randomised trial. ATLANTIC Investigators. Angina Treatments-Lasers and Normal Therapies in Comparison.

Burkhoff D, Schmidt S, Schulman SP, Myers J, Resar J, Becker LC, Weiss J, Jones JW  
Lancet 1999 Sep 11;354(9182):885-90

10. Transmyocardial laser revascularization combined with coronary artery bypass grafting: a multicenter, blinded, prospective, randomized, controlled trial.

Allen KB, Dowling RD, DelRossi AJ, Realyvasques F, Lefrak EA, Pfeffer TA, Fudge TL, Mostovych M, Schuch D, Szentpetery S, Shaar CJ  
J Thora Cardiovasc Surg 2000; 119(3):540-9

11. Short- and intermediate-term clinical outcomes from direct myocardial laser revascularization guided by biosense left ventricular electromechanical mapping.

Kornowski R, Baim DS, Moses JW, Hong MK, Laham RJ, Fuchs S, Hendel RC, Wallace D, Cohen DJ, Bonow RO, Kuntz RE, Leon MB.  
Circulation 2000; 102(10):1120-5

12. Myocardial laser revascularization: the controversy and the data.

Bridges CR  
Ann Thorac Surg 2000; 69(2):655-62