Case Reports

Transmyocardial Laser Revascularization

Anatomic Evidence of Long-Term Channel Patency

Denton A. Cooley, MD
O.H. Frazier, MD
Kamuran A. Kadipasaoglu, PhD
Seckin Pehlivanoglu, MD
Rhonda L. Shannon, MD
Paolo Angelini, MD

Transmyocardial laser revascularization, a new surgical technique, is being tested in patients with chronic obstructive coronary artery disease that is refractory to conventional revascularization techniques and to maximal medical therapy. During the operation, which is performed on the beating heart through a left thoracotomy, a high-energy CO_2 laser is used to bore transmural channels (1 mm in diameter) into the left ventricle. Each high-energy laser pulse is delivered during end diastole and transects the heart within 10 to 60 msec. The operation is based on the theory that blood will flow directly from the left ventricle into the channels and then into the myocardial vascular plexus. Restoring perfusion should alleviate ischemia in potentially viable myocardium and improve ventricular function.

Recently, one of our patients died 3 months after transmyocardial laser revascularization of causes unrelated to the operation. Histologic analysis enabled us to obtain, for the 1st time, anatomic evidence of patent laser channels. Routine staining of cardiac tissue with hematoxylin and eosin revealed multiple patent channels, running perpendicular to and interconnecting with the native vasculature. Although reactive fibrous scar tissue had caused narrowing of the original laser tract, the channels had endothelialized and they contained red blood cells. These findings suggest that the laser channels were functional. We report this interesting case and briefly discuss the anatomic and physiologic phenomena involved in establishing camerosinusoidal blood flow by use of transmyocardial laser revascularization. ***(Texas Heart Institute Journal 1994;21:220-4)***

Symptomatic coronary artery occlusive disease that is refractory to routine medical and interventional treatment continues to frustrate both cardiac surgeons and cardiologists. Recently, direct revascularization involving application of a high-energy CO_2 laser to create transmural channels in the left ventricular myocardium has been suggested as an alternative therapeutic technique.[1] Theoretically, these channels could establish blood flow from the left ventricular cavity to the myocardial vascular network.[2]

Early experiments in a canine model demonstrated the feasibility of this approach; the studies showed a significant increase in survival in dogs with transmural channels and ligated coronary arteries, and long-term channel patency was documented by microscopy.[2] Clinical studies of transmyocardial laser revascularization (TMLR) as an independent therapy began in 1990. Since then, subjective evidence of benefits has been reported,[3] and cineangiograms with marginal resolution have suggested the presence of patent channels.[4,5] In this clinical report, we present anatomic evidence of patent channels 3 months after TMLR.

Key words: *Laser surgery; myocardial ischemia; myocardial reperfusion; myocardial revascularization; ventricular function, left*

From: *The Cullen Cardiovascular Research Laboratories and the Departments of Cardiovascular Surgery, Pathology, and Adult Cardiology, Texas Heart Institute and St. Luke's Episcopal Hospital, Houston, Texas 77030*

Address for reprints: *Kamuran A. Kadipasaoglu, PhD, Texas Heart Institute, P.O. Box 20345, Houston, TX 77225-0345*

Case Report

In July 1993, a 56-year-old man with unstable angina was referred to our institution. Previously, the patient had undergone 2 coronary artery bypass operations: in 1983, saphenous vein grafts were placed to the left anterior descending, diagonal, and ramus branches; and a year later, bypass vein grafts were placed to the 1st and 2nd obtuse marginal branches of the circumflex artery. In 1988, the patient underwent percutaneous transluminal coronary angioplasty of the totally occluded dominant right coronary artery. In 1990, he underwent Simpson catheter atherectomy of a stenotic lesion in the left anterior descending bypass graft.

At the initial 1993 admission, cardiac catheterization revealed that the patient's native left anterior descending and circumflex arteries and all the bypass grafts

were totally occluded. A small ramus artery in the left coronary circulation was patent. The right coronary artery was mildly (50%) occluded at the proximal and middle segments, but distal runoff was good. Extensive right-to-left collateral circulation was observed. Left ventricular angiography showed mild apical hypokinesis and an ejection fraction of 48%. Because of the patient's recent history of progressive angina refractory to aggressive medical therapy, intervention was considered. After cineangiography showed evidence of poor distal coronary anatomy, the patient was offered the opportunity to enter the TMLR clinical trial.

Diagnostic Procedures

The patient gave informed written consent for TMLR according to an experimental protocol approved by the institutional review board. He then underwent further examination to evaluate baseline functional and perfusional status of the various left ventricular regions and to establish the potential viability of the dysfunctional segments.

Two-dimensional echocardiography with the infusion of low-dose dobutamine[6] (10 μg/kg/min) suggested the presence of hypokinetic but viable myocardium in the distal septal, basal inferior, anterior, and lateral walls. The global wall-motion score index, which was 1.9 at baseline, improved to 1.6 with dobutamine (scale: 1 = normokinesia; 4 = dyskinesia). Thallium-201 single photon emission tomography was performed at rest, and the results indicated that the anterolateral and inferior regions of the myocardium were ischemic, scarred, or both. Positron emission tomography was performed at rest with nitrogen-13 ammonia to measure left ventricular perfusion, and fluorine-18 fluorodeoxyglucose to assess left ventricular metabolism.[7] The results suggested the presence of a relatively small (2%-3% of left ventricular volume) nontransmural myocardial infarct, with a perfusion defect in the anterolateral and inferoapical regions of the myocardium, where metabolism was reduced but not absent. The presence of exercise-induced ischemia due to reduction in the coronary flow reserve was not evaluated because the patient's unstable angina precluded induction of stress by the dipyridamole handgrip test. The left ventricular ejection fraction was 42% before and 50% after low-dose dobutamine echocardiography, and 55% by multiple-gated acquisition imaging.

Operative Summary

With the patient under general anesthesia, the heart was approached from a left anterolateral thoracotomy through the 4th intercostal space. Multiple adhesions between the pericardium and the underlying epicardium were sharply divided. Transmyocardial laser revascularization was performed with the Heart Laser CO_2 system (Laser Engineering, Inc.; Milford, Massachusetts, USA), which has a peak output of 850 W. The laser was set to operate at a pulse energy of 35 J and a pulse duration of 44 msec. The delivery of each laser pulse was synchronized with the R wave on the electrocardiographic signal. A total of 30 pulses were delivered, approximately 1 cm apart from each other, to the anterior and the anterolateral aspects of the beating heart. Transmyocardial penetration of 25 pulses (81%) was confirmed by intraoperative transesophageal echocardiography on observation of intracavitary bubbles that were created when laser energy was converted into steam upon striking blood. Adequate hemostasis was achieved by external digital pressure or by placement of epicardial purse-string sutures. On completion of the laser procedure, a chest tube was placed for drainage, and the incision was closed in the routine manner.

Postoperative Course

After the operation, the patient experienced no complications and was discharged from the hospital on day 5. Aspirin and calcium channel blockers were prescribed. At that time, he was already able to walk 1/2 mile without problems.

One month later, the patient experienced tightness in his chest and dyspnea, and he was evaluated by his local cardiologist. He was able to exercise 7 minutes according to the Bruce protocol before having to stop because of dyspnea. At maximum exercise, the electrocardiogram showed "pseudonormalization" of the T wave and 1-mm ST segment depression in lead V6. Immediate poststress thallium and 3-hr delayed redistribution images showed apical scarring and anteroseptal ischemia.

At 3 months, the patient experienced angina at rest and sought treatment at a local emergency room. Cardiac catheterization revealed severe new stenoses in the proximal and middle segments of the right coronary artery. The inferior and apical regions of the myocardium were akinetic. In contrast, the anterior and anterolateral regions were normokinetic, and the left ventricular ejection fraction was 48%.

The patient was transferred to our hospital and underwent hemoperfusion-assisted balloon angioplasty of the right coronary artery.[8] Both stenoses in the right coronary artery were successfully dilated, but progressive cardiac failure with ST elevation, possibly due to distal microemboli, was observed. The patient, on continuous external cardiac massage, was taken to the operating room. A Fogarty embolectomy was performed in the right coronary artery, yielding whitish debris both proximally and distally; then a reversed autologous saphenous vein graft was placed to the right coronary artery. Despite intraaortic balloon support, the patient could not be

weaned from cardiopulmonary bypass and was pronounced dead. Consent for a limited autopsy (i.e., of the heart) was granted.

Pathologic Evaluation

Patent laser channels could not be observed on gross internal inspection of the heart; several small depressed areas, however, were seen along the endocardial surface of the anterior and anterolateral left ventricle. Serial transverse sections obtained from this area were processed and embedded in paraffin according to routine histologic techniques, and multiple levels of each tissue block were stained with hematoxylin and eosin.

Nine endothelium-lined channels, oriented perpendicular to the epicardial surface, were identified on microscopy. These channels, approximately 20 to 75 μm in diameter, contained red blood cells and were surrounded by solid tracts of fibrous connective tissue (total width, 150-500 μm). Direct communications were observed between some of the channels and the ventricular cavity (Fig. 1) and native myocardial vessels (Fig. 2). Due to the processing technique used, none of the channels could be visualized along their entire length.

Other changes noted at postmortem examination included a resolving myocardial infarct (5-10 days old) in the posterior papillary muscle, multiple cholesterol emboli in the intramyocardial vessels of each ventricle, an old diffuse subendocardial left ventricular infarct, and severely obstructive atherosclerotic changes in the native cardiac arteries and in the grafts.

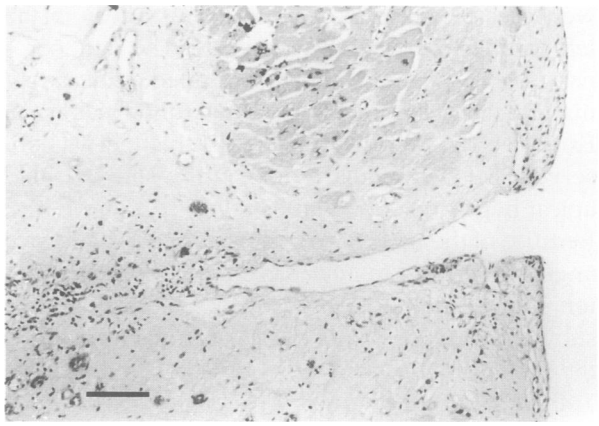


Fig. 1 *Laser channel connecting to the endocardial surface: original magnification 100x; bar = 70 μm.*

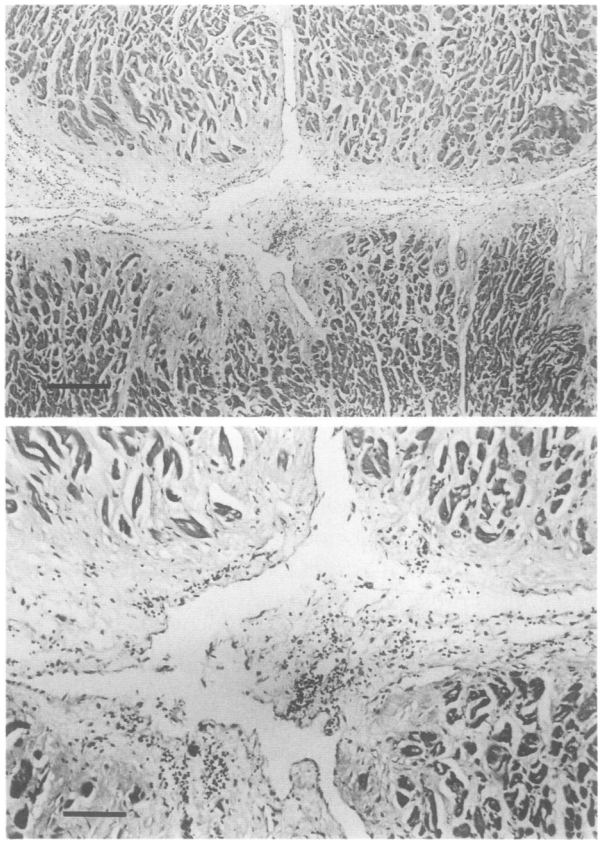


Fig. 2 *Laser channel (horizontal) connecting to intramyocardial vessels (vertical): **A**) original magnification 40x; bar = 150 μm; **B**) original magnification 100x; bar = 70 μm.*

Discussion

After Wearn and colleagues[2] described the myocardial microanatomy, several attempts were made to reestablish blood supply to ischemic segments of the heart by perfusion of the sinusoidal vascular plexus.[9,10] In 1965, Sen[11] proposed the creation of needle-puncture transmural channels that would perfuse the myocardium by joining the ventricular cavity with the conduits of the plexus. Several techniques were developed along these lines, including intramyocardial implantation of T tubes,[12] boring,[13] and needle acupuncture.[14] None of these techniques, however, proved successful: acute thrombosis, fibrous scarring, or both caused the channels to close.[15]

In 1982, Mirhoseini[1] proposed drilling transmyocardial channels with a laser apparatus. During the last decade, experiments conducted with various low-energy lasers on cardioplegically arrested animal hearts have produced controversial results.[16,17] The technology necessary to perform the operation on a beating heart has only recently become available. Unlike previous systems, the currently used CO_2 laser system produces single high-energy pulses (maximum, 69 J/pulse) that can transect the entire thickness of the myocardium during contraction (pulse duration, 1-99 msec), without interfering with the electrical activity of the heart. Recently,

Mirhoseini[3] reported that a few human subjects receiving TMLR treatment with such a system experienced clinical improvement, as evidenced by a reduction in angina and improvement in quality of life. Even though left ventricular angiography 3 months after TMLR did not reveal the neochannels in our patient, this report offers the 1st histologic documentation of long-term channel patency as indirect evidence of improved myocardial perfusion in human subjects undergoing TMLR.

Histologic evidence both of patent, endothelium-lined tracts within the laser-drilled channels and of connections between the ventricular cavity and the native intramyocardial sinusoids at 3 months are necessary to document revascularization by TMLR. Endothelialization would minimize the contact activation of intrinsic humoral mechanisms and would improve interfacial hemocompatibility,[18] and camerosinusoidal connections would promote the continuity of flow through these channels. The resulting reduction in the potential for thrombogenicity and for hemostagnation would then contribute to channel patency.

Whether functional phasic collapse occurs in the described neochannels is not known; however, some degree of systolic compression in the subendocardial areas is highly probable, except in the presence of local severe hypokinesia (or dyskinesia), which is expected to return to normal after TMLR. It seems essential to understand that TMLR cannot be expected to augment myocardial flow from an aortic source and that the conditions for the neochannels to function are 1) that they maintain connection with the ventricular cavity; 2) that they interconnect with the intramyocardial arteriolar/capillary network; and 3) that the new blood flow drains into the coronary venous system due to a positive pressure gradient. The left ventricular pressure is indeed higher than the right atrial pressure during the whole cardiac cycle, but the intramyocardial pressure is an important modulator of the driving gradient in the neocircuit. The relative magnitude of left ventricular pressure and intramyocardial pressure throughout systole remains controversial. Undoubtedly, the experimental technique chosen to measure intramyocardial pressure affects the accuracy of the measurement. When pressure is measured with catheter-tipped micromanometers[19] or with closed-tip, fluid-filled catheters,[20] intramyocardial pressure is invariably higher than left ventricular pressure during systole. In contrast, when measurements are obtained with collapsible conduits that are vented distally to the atmosphere, the intraventricular pressure is higher than the intramyocardial pressure throughout systole, even though the driving gradient of the endocardium is lower than that of the epicardium.[21] The latter view is supported by our observation that, during surgery, arterial blood spurts from the neochannels.

Another factor that may influence the effectiveness of TMLR is the density of the native microvasculature at the time of intervention. An abundance of vessels should increase the probability of establishing immediate communications between the laser channels and the sinusoids. This would augment the distal runoff, lower the back-pressure, and accelerate the blood flow inside the channel. Transmyocardial laser revascularization would therefore be more appropriate for treating chronic ischemia than for treating acute ischemia, since the ischemic myocardium responds to hypoxia by promoting the development of collateral vessels or by enlarging pre-existing collaterals and sinusoids.[22] The hibernating and the collateral-dependent anatomy in the current patient population seems to be ideally suited for studying the effects of TMLR.

Currently, transmyocardial laser revascularization is an investigational procedure, and clinical studies at the Texas Heart Institute are being conducted under an Investigational Device Exemption approved by the United States Food and Drug Administration.

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References

1. Mirhoseini M, Muckerheide M, Cayton MM. Transventricular revascularization by laser. Lasers Surg Med 1982;2:187-98.
2. Wearn JT, Mettier SR, Klumpp TG, Zschiesche LJ. The nature of the vascular communications between the coronary arteries and the chambers of the heart. Am Heart J 1933; 9:143-64.
3. Mirhoseini M, Cayton MM, Shelgikar S. Transmyocardial laser revascularization. J Am Coll Cardiol 1994;23(Suppl 1A): 416A.
4. Mirhoseini M, Cayton MM, Shelgikar S, Fisher JC. Clinical report: laser myocardial revascularization. Lasers Surg Med 1986;6:459-61.
5. Mirhoseini M, Cayton MM. Direct myocardial revascularization: preliminary experience. In: Abela GS, ed. Lasers in cardiovascular medicine and surgery: fundamentals and techniques. Boston: Kluwer Academic Publishers, 1990:385-95.
6. Cigarroa CG, deFilippi CR, Brickner ME, Alvarez LG, Wait MA, Grayburn PA. Dobutamine stress echocardiography identifies hibernating myocardium and predicts recovery of left ventricular function after coronary revascularization. Circulation 1993;88:430-6.
7. Gould KL. Clinical cardiac positron emission tomography: state of the art. Circulation 1991;84(Suppl II):I-22-36.

8. DiSciascio G, Angelini P, Vandormael MG, Brinker JA, Cowley MJ, Dean LS, et al. Reduction of ischemia with a new flow-adjustable hemoperfusion pump during coronary angioplasty. The Coronary Hemoperfusion Ischemia Prevention Study (CHIPS) Investigators. J Am Coll Cardiol 1992; 19:657-62.
9. Beck CS. The development of a new blood supply to the heart by operation. Ann Surg 1935;102:801-13.
10. Vineberg AM. Development of an anastomosis between the coronary vessels and a transplanted internal mammary artery. Can Med Assoc J 1946;55:117-9.
11. Sen PK, Udwadia TE, Kinare SG, Parulkar GB. Transmyocardial acupuncture: a new approach to myocardial revascularization. J Thorac Cardiovasc Surg 1965;50:181-9.
12. Massimo C, Boffi L. Myocardial revascularization by a new method of carrying blood directly from the left ventricular cavity into the coronary circulation. J Thorac Cardiovasc Surg 1957;34:257-64.
13. Wakabayashi A, Little ST Jr, Connolly JE. Myocardial boring for the ischemic heart. Arch Surg 1967;95:743-52.
14. Sen PK, Daulatram J, Kinare SG, Udwadia TE, Parulkar GB. Further studies in multiple transmyocardial acupuncture as a method of myocardial revascularization. Surgery 1968;64: 861-70.
15. Pifarré R, Jasuja ML, Lynch RD, Neville WE. Myocardial revascularization by transmyocardial acupuncture: a physiologic impossibility. J Thorac Cardiovasc Surg 1969;58:424-31.
16. Whittaker P, Kloner RA, Przyklenk K. Laser-mediated transmural myocardial channels do not salvage acutely ischemic myocardium. J Am Coll Cardiol 1993;22:302-9.
17. Hardy RI, Bove KE, James FW, Kaplan S, Goldman L. A histologic study of laser-induced transmyocardial channels. Lasers Surg Med 1987;6:563-73.
18. Trachtenberg JD, Ryan US. Endothelial cells and biomaterials. In: Greco RS, ed. Implantation biology. Host response and biomedical devices. Boca Raton, FL: CRC Press, Inc., 1994: 81-112.
19. Sabbah HN, Stein PD. Relation of intramyocardial and intracavitary pressure to regional myocardial asynergy in the canine left ventricle. Am Heart J 1983:105:380-6.
20. Pifarré R. Intramyocardial pressure during systole and diastole. Ann Surg 1968;168:871-5.
21. Baird RJ, Manktelow RT, Shah PA, Ameli FM. Intramyocardial pressure: a study of its regional variations and its relationship to intraventricular pressure. J Thorac Cardiovasc Surg 1970;59:810-23.
22. Fujita M, Ohno A, Wada O, Miwa K, Nozawa T, Yamanishi K, et al. Collateral circulation as a marker of the presence of viable myocardium in patients with recent myocardial infarction. Am Heart J 1991;122:409-14.