Transmyocardial Laser Revascularization: Is the Enthusiasm Justified?

NASSER HAYAT, M.D., PH.D., MOHAMED SHAFIE, D.M.,* MOHAMMED KAMEL GUMAA, M.B.B.CH., M.S.,* NAZIR KHAN, M.D.*

Department of Medicine, Faculty of Medicine, Kuwait University; *Chest Hospital, Cardiology Division, Safat, Kuwait

Summary

Background: Transmyocardial laser revascularization (TMLR) is advocated to offer relief of incapacitating angina for patients whose coronary vessels are poor targets for coronary artery bypass graft surgery (CABG) or balloon angioplasty and stenting. In spite of significant mortality and morbidity, the preliminary reports from centers performing the procedure were quite enthusiastic for a period of about 1 year following the procedure.

Hypothesis: The study aimed to determine mortality, morbidity, and long-term results of TMLR.

Methods: The study included 19 individuals with incapacitating angina not suitable for CABG or percutaneous balloon angioplasty. Patients were followed up clinically for death, myocardial infarction, heart failure, arrhythmia, and repeated hospital admissions for unstable angina or other conditions. Stress testing with radionuclide tracers was done following surgery in patients who were not unstable.

Results: Of 19 patients, 8 experienced significant morbidity. There was one hospital death. Four died within 17 months. Relief from angina of two classes or more was present in 15 of 18 patients (83.3%) for a variable time period. Mean time for anginal relief was 8.0 months (range 1–30 months). At last follow-up, only two patients with a hybrid procedure (both CABG and TMLR in the same sitting) had mild angina for 17 and 29 months, respectively. All others with a mean follow-up period of 21.2 months (range 6–53 months) developed unsta-

ble angina or had a large area of ischemia on stress radionuclide studies. Despite a high incidence of significant angina in patients after TMLR, hospitalization was reduced from an average of 42.6 days pre procedure in the year before to 21 days during the follow-up period post procedure.

Conclusion: Transmyocardial laser revascularization is associated with significant relief of angina pectoris in the majority of patients with severe diffuse coronary artery disease; however, this relief is short-lived in most. When mortality and morbidity are factored in, TMLR cannot be enthusiastically recommended.

Key words: coronary artery bypass surgery, transluminal coronary artery angioplasty, hybrid procedure, incapacitating angina

Introduction

Transmyocardial laser revascularization (TMLR) was conceived by Mirhoseini and Clayton as a way of relieving angina through drilling one millimeter punctures by a laser device into ischemic myocardium.¹ This was based on previous observation by Sen *et al.* and others, who found that experimentally ischemic myocardium was improved by direct acupuncture.² The goal was to offer relief of incapacitating angina for patients whose coronary vessels were poor targets for coronary artery bypass graft surgery (CABG). Candidates for TMLR would often have had previous revascularization procedures such as CABG or percutaneous transluminal coronary angioplasty (PTCA) and had recurrence of incapacitating symptoms.

The exact mechanism by which anginal relief is accomplished by TMLR is not known. Several mechanisms have been suggested to explain this phenomenon, such as direct perfusion in ischemic myocardium, trauma-induced angiogenesis, promotion of collaterals, damage to myocardial nerve fibers, or a combination of these.³ Unfortunately, the evidence is rather inconclusive.⁴ Nonetheless, preliminary reports from centers performing TMLR and the registry cases were quite enthusiastic about the 1-year results.^{5–8} Anecdotal reports carried these observations beyond 2 years.⁹ We report on 19 pa-

Address for reprints:

Dr. Nasser J. Hayat, M.D., Ph.D.
Associate Professor of Cardiology
Department of Medicine
Faculty of Medicine
P. O. Box 24923, Safat 13110
Kuwait

Received: March 17, 2000

Accepted with revision: July 5, 2000

tients who underwent TMLR in two recognized centers. Our follow-up results paint a picture of time-limited anginal relief in the background of significant mortality and morbidity.

Patients and Methods

Patients who were selected for TMLR were those who had angina at rest (class IV in The Canadian Cardiovascular Society "CCS" classification) or with minimal activity (class III). They needed frequent admissions to hospital for control of angina. Days of hospitalization were counted for every patient. The charts were reviewed for the clinical characteristics of the patients. Following cardiac catheterization, the films were reviewed by a panel of cardiologists and at least one surgeon. Once the individual patient was rejected as candidate for routine CABG, he or she was transferred to one of two centers for TMLR (Brigham & Women at Boston, Mass., USA, first 3 patients, and University Hospital at Marburg, Germany, 16 patients).

Surgical Procedure

Transmyocardial laser revascularization was performed via left lateral thoracotomy in nine patients. Patients who had combined CABG and TMLR (hybrid operation) were operated on by median sternotomy approach. The details of the operation have been well documented in other reports.¹⁰ Patients received 17 to 44 epicardial laser punctures.

Follow-Up

Patients were followed up in our center at different time intervals according to their symptoms. They were monitored for death, acute myocardial infarction, heart failure, arrhythmias, or other presenting clinical situation. Repeat hospitalization (counting the actual days spent in the hospital) for unstable angina or other conditions were noted. Angina was graded according to the CCS classifications. Stress testing with radionuclide tracers was done following surgery in patients who were not unstable (seven patients). Data were obtained from chart review and via telephone contact with some of the patients.

Results

Table I outlines the clinical characteristics of all 19 patients. Women comprised 42.1% or 8 of 19 patients (Tables I and II). In general, the patients had good systolic left ventricular function as demonstrated by mean ejection fraction of 54.5% and by absence of left ventricular failure in 18 of 19 patients pre TMLR. Class III angina was present in three patients and the rest were graded as being in class IV.

Following TMLR, one patient died suddenly on the post-operative Day 5. Of the remaining 18 patients 4 died (2 at 6 months and 1 at 17 months follow-up). The fifth death occurred in a patient who did not improve and who had CABG as a desperate measure following TMLR; she died 1 year after

TABLE I Patient characteristics and clinical outcome after TMLR

Patient No.	Age/sex	Diabetes	Hyper-tension	Hypercholesterolemia	Previous CABG	Previous PTCA	Anginal class	LVEF (%)	Length of follow-up after TMLR (months)	Improvement following TMLR (months)	Days in hospital		Anginal class post TMLR
											Pre TMLR	Post TMLR	
1	62 M	Y	Y	Y	Y	Y	IV	64	6	3	41	0 ^a	—
2	57 M	Y	N	N	Y	Y	IV	41	53	24	76	40	IV
3	59 M	N	Y	N	N	N	IV	73	38	12	10	0	III
4	61 F	Y	Y	Y	Y	Y	IV	50	6	0	40	68 ^a	—
5	69 F	Y	Y	N	Y	Y	IV	44	21	0	51	69 ^a	—
6	62 F	Y	Y	N	Y	N	IV	41	18	1	55	20 ^a	—
7	52 M	N	Y	Y	Y	Y	III	35	0	0	67	0 ^a	—
8	67 M	N	Y	Y	Y	N	III	48	29	14	98	39	I
9	49 F	Y	Y	Y	Y	N	IV	69	17	2	56	0	III
10	57 M	Y	Y	N	N	N	IV	53	34	1	14	13	IV
11	66 F	Y	Y	Y	N	N	IV	52	16	1	12	18	IV
12	64 M	N	Y	N	Y	Y	IV	64	21	0	75	60	IV
13	58 M	Y	N	Y	Y	Y	IV	45	9	9	92	0	II
14	70 F	Y	Y	Y	N	N	IV	72	18	3	27	20	IV
15	58 F	Y	N	N	N	N	III	53	34	30	8	26	III
16	77 F	Y	Y	N	N	N	IV	64	22	18	14	0	II
17	39 M	Y	Y	N	N	Y	IV	50	12	3	37	0	IV
18	55 M	Y	N	Y	Y	N	IV	59	11	6	23	5	IV
19	73 M	Y	Y	Y	N	N	IV	58	17	17	14	0	I

^a = Patient died.

Abbreviations: CABG = coronary artery bypass surgery, PTCA = percutaneous transluminal angioplasty, LVEF = left ventricular ejection fraction, TMLR = transmyocardial laser revascularization, Y = presence, N = absence.

TABLE II Summary of clinical characteristics of patients

	Number	(%)
Age	60.8	(range 39–77 years)
Male	11	(57.9)
Angina class III	3	(15.8)
Angina class IV	16	(84.2)
Previous PTCA	8	(42.1)
Previous CABG	11	(57.9)
Diabetes	15	(78.9)
Hypertension	15	(78.9)
Hyperlipidemia	10	(52.6)
LVEF (%)	54.5	(range 35–73)
Surgical procedure		
TMLR alone (%)	9	(48.4)
TMLR + CABG (%)	10	(52.6)

Abbreviations as in Table I.

TABLE III Outcome after transmyocardial laser revascularization (TMLR)

	No.
Death	5
Morbidity	8
Hemorrhagic cardiac tamponade/pleural effusion	4
Wound infection	5
Large hematoma (thoracotomy site)	1
Decreased vision	1
Results of TMLR	
Did not improve	3
Improved ≤ 6 months	8
Improved > 6 months and < 12 months	1
Improved ≥ 12 months	6
Average time for anginal relief in all patients (months)	8.0
Average follow-up time after TMLR in 18 patients (months)	21.2
Average days spent in hospital before TMLR (19 patients)	42.6
Average days spent in hospital after TMLR (for 21.2 months follow-up)	21

CABG. Ten patients had a hybrid procedure and nine had only TMLR. One or more postoperative complications occurred in eight patients (Table III). In fact, these complications were noted early (in the first 30 days) and upon arrival from their operating centers. Prolonged antibiotic treatment for wound infection, evacuation of wound hematoma, and pleuro/pericardiocentesis kept some of the patients hospitalized after “successful” TMLR.

Fifteen patients had improvement in anginal grade by two classes or more for variable time periods. Mean time for anginal relief was 8.0 months (range 1–30 months). Our first patient had his TMLR in September 1995; he was symptom free for 2 years. After recurrence of angina, he has had two PTCAs

and repeat CABG. Only two patients in the hybrid group have had mild (CCS class I) angina for 17 and 29 months, respectively. Unstable angina was noted in seven patients. In five others, a large area of ischemia was detected by stress radionuclide studies. Mean follow-up time after TMLR was 21.2 months (range 6–53 months).

Following TMLR, hospitalization was reduced from an average of 42.6 days pre to 21 days post procedure. Hospitalization pre TMLR was counted in the year before procedure. However, admission post TMLR spanned a longer time period. If hospital days were normalized to 1 year, they would amount to 12 days per year. Average of single admission for unstable angina was 6 days. Thus, pre TMLR there were approximately seven admissions per year per patient or one every 7–8 weeks. Post TMLR admission amounted to 12 days per year per patient or approximately one admission every 6 months. Hospitalization decreased despite a high incidence of recurrence of significant angina (class III in three and IV in seven patients). Of the survivors, only four were recatheterized because of recurrence of unstable angina. Other patients refused further catheterization. Two patients underwent PTCA and two had repeat CABG. All deaths occurred at home. So far, we do not know of any cases of myocardial infarction, new heart failure, or arrhythmias. All surviving patients are on maximal antianginal treatment.

Discussion

When TMLR was introduced clinically in the early 1990s for patients with severe and diffuse coronary artery disease, it was hoped that it would prove to be beneficial and a definitive treatment option. In fact, our first patient had a spectacular outcome. This particular patient had had two previous CABGs and two successful attempts at PTCA. However, following all these measures he had developed unstable angina and was hospitalized for 2 months. His intravenous nitrates could not be stopped. He had an uneventful TMLR, and postoperatively he was well for 24 months. We thus embraced this new technique and indicated 18 others for TMLR, which was done as a sole intervention in nine and as a hybrid revascularization procedure in the remainder of the patients.

This retrospective report on the results of TMLR has two unique features: first, it constitutes consecutive patients from a nonoperating center (with neutral perspective), and second, it tracks the patients until emergence of symptoms (mean follow-up time of 21.2 months, which is longer than that stated in most reports). Counting the one hospital death and the two patients who died within 6 months of procedure failure, the mortality is in excess of 15%. The 30-day mortality rate in our patients (1 of 19, or 5.3%) is similar to that in other reports comprising larger numbers of patients.^{6, 8, 11} However at 6 months, more than 15% of our patients had died. The 1-year mortality reported by Frazier *et al.* is also 15%.⁶ We think that the excess mortality, at least in our small series, may be due to a higher percentage of patients with angina in class IV CCS (84%). Diabetes was present in 79% of our patients, which is

much higher than that in other published series;⁶⁻⁸ that undoubtedly contributed to excess mortality and morbidity. A recent randomized trial comparing survival at 12 months for patients undergoing TMLR versus medical treatment indicated better survival in the medically treated patients, but the difference was statistically not significant.¹¹ In the same report, significant anginal relief at 12 months (two classes of CCS) was present in only 25% of patients undergoing TMLR. In our series, only 16% (3 of 19) had mild angina at the end of follow-up. In a series reported by Milano *et al.* with no operative mortality, there were two deaths at 4 months following TMLR with Holmium laser (12.5%).¹² Angina relief at mean follow-up of 10 ± 4 months was moderate. However, there was no statistically significant difference in segments of myocardium with fixed or reversible ischemia whether lased or not. Others reported lack of objective improvement in cardiac perfusion measurements.^{4,7} In fact, the report by Burkoff *et al.* showed excess myocardial infarction and heart failure in the TMLR cohort.⁸ Other reported morbidities in larger series have included ventricular tachycardia and hypotension.^{7,8} In the patients whom we followed, not only was there excess morbidity (44%), but anginal relief was of limited duration (mean 8.0 months). More than 25% of patients required repeat catheterization, two had CABG, and two had repeat PTCA. For a procedure that was thought to be definitive, a disappointing result is that some patients have had to undergo further revascularization procedures with their attendant costs. The only benefit we have observed is the noticeable reduction of rehospitalization, which could partially be explained by the demise of the most symptomatic patients. Better medical treatment and the placebo effect of sternotomy/thoracotomy may have contributed to further reduction of repeat hospitalization. We should not discount some beneficial effect of the procedure.

Conclusion

Transmyocardial laser revascularization is associated with significant anginal relief in 15 of 18 (83.3%) high-risk patients; however, this relief is short-lived in the majority of patients. When mortality and morbidity of the procedure are factored in, TMLR cannot be enthusiastically recommended.

References

1. Mirhoseini M, Clayton MM: Revascularisation of the heart by laser. *J Micro Surg* 1982;2:253-260
2. Sen PK, Udawadia TE, Kinare SG, Parulkar GB: Transmyocardial acupuncture: A new approach to myocardial revascularisation. *J Thorac Cardiovasc* 1965;50:181-189
3. Kornoski R, Hong MK, Leon MB: Current perspectives on direct myocardial revascularization. *Am J Cardiol* 1998;81(7A):44E-48E
4. Abramov D, Bhatnagar G, Tamariz M, Guru V, Goldman BS: Current status of transmyocardial laser revascularisation: Review of the literature. *Can J Cardiol* 1999;15(3):303-310
5. Horvath KA, Cohn LH, Cooley DA, Crew JR, Frazier OH, Giffith BP, Kadipasaoglu K, Lasing A, Mannting F, March R, Mirhoseini MR, Smith C: Transmyocardial laser revascularisation: Results of a multicenter trial with transmyocardial laser revascularisation used as sole therapy for end stage coronary artery disease. *J Thorac Cardiovasc Surg* 1997;113(4):645-654
6. Frazier OH, March RJ, Horvath KA, for the transmyocardial carbon dioxide laser revascularization study group: Transmyocardial revascularization with a carbon dioxide laser in patients with end-stage coronary artery disease. *N Engl J Med* 1999;341:1021-1028
7. Allen KB, Dowling RD, Fudge TL, Schoettle GP, Selinger SL, Gangahar DM, Angell WW, Petracek MR, Shaar CJ, O'Neil WW: Comparison of transmyocardial revascularization with medical therapy in patients with refractory angina. *N Engl J Med* 1999;341:1029-1036
8. Burkoff D, Schmidt S, Schulman SP, Myers J, Resar J, Becker LC, Weiss J, Jones JW: 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. *Lancet* 1999;354:885-890
9. Cooley DA, Frazier OH, Kadipasaoglu KA, Pehlivanoglu S, Shannon RL, Angelini P: Transmyocardial laser vascularization: Anatomic evidence of long term channel patency. *Tex Heart Inst J* 1994;21:220-224
10. Cooley DA, Frazier OH, Kadipasaoglu KA, Lindenmeir MH, Pehlivanoglu S, Kolff W, Wilansky S, Moore WH: Transmyocardial laser revascularization: Clinical experience with twelve months follow-up. *J Thorac Cardiovasc Surg* 1996;111:791-799
11. Schofield PM, Sharples LD, Caine N, Burns S, Tait S, Wistow T, Burton M, Wallwork J: Transmyocardial laser revascularisation in patients with refractory angina. A randomised controlled trial. *Lancet* 1999;353:519-524
12. Milano A, Proctali S, Taratarini G, Marrioti R, Decarlo M, Patient G, Boni G, Bortolotti U: Early results of transmyocardial revascularisation with a holmium laser. *Ann Thorac Surg* 1998;65:700-704