The effect of transmyocardial laser revascularization on angina symptoms and clinical results in patients with incomplete surgical revascularization

Tam cerrahi revaskülarizasyon yapılamayan hastalarda transmiyokardiyal lazer revaskülarizasyonu işleminin anjinal semptomlar ve klinik sonuçlar üzerine etkisi

Koray Ak, M.D., Selim Isbir, M.D., Ozgur Gursu, M.D., Sinan Arsan, M.D.

Marmara University, Faculty of Medicine, Department of Cardiovascular Surgery, Istanbul

Objectives: We evaluated the effect of transmyocardial laser revascularization (TMR) on angina symptoms and clinical results in patients in whom coronary artery bypass grafting (CABG) surgery was not sufficient to provide complete revascularization.

Study Design: This retrospective study included 45 patients who underwent CABG surgery with incomplete revascularization between 2003 and 2006. Of these, 35 patients (mean age 61.7 years) had CABG alone, while 10 patients (mean age 62 years) underwent TMR at the same session as an adjunct to CABG. All the patients were assessed by transthoracic echocardiography and myocardial perfusion scintigraphy at three months and after a mean follow-up period of 22.3±6.1 months. Anginal symptoms were assessed using the Canadian Cardiovascular Society (CCS) classification system.

Results: Preoperative variables were similar in both groups. All the patients were symptomatic preoperatively with mean CCS scores of 2.6±0.5 and 2.3±0.8 in the TMR and CABG-alone groups, respectively. The duration of cardiopulmonary bypass (CPB) was significantly longer in the TMR group (p=0.022). During weaning from CPB, the need for inotropic support was significantly less in the TMR group (10% vs. 48.6%; p=0.034). While there was no early mortality, late mortality occurred in three patients (1 in TMR, 2 in CABG-alone groups; p=0.329). At three months, 50% (n=5) of the TMR patients were asymptomatic, compared to 14.3% (n=5) in the CABG-alone group (p=0.016). Patients in the TMR group had significantly lower CCS angina scores at three months (1.2±0.6 vs. 2.2±0.7; p=0.001) and at the end of the follow-up (1±0.6vs. 2±0.7; p=0.001). There were no significant differences between the two groups with regard to the findings of myocardial perfusion scintigraphy and echocardiography.

Conclusion: Patients with incomplete surgical revascularization benefit from TMR in terms of decreased need for inotropic support during weaning from CPB and short-and mid-term relief of angina symptoms.

Key words: Coronary artery bypass; laser therapy/methods; myocardial revascularization/methods.

Amaç: Bu çalışmada, koroner arter baypas cerrahisi (KABC) ile tam revaskülarizasyon sağlanamayan hastalarda transmiyokardiyal lazer revaskülarizasyonu (TMR) uygulamasının anjinal yakınmalar ve klinik sonuçlar üzerindeki etkileri araştırıldı.

Çalışma planı: 2003-2006 yılları arasında KABC uygulanan ancak tam revaskülarizasyon sağlanamayan 45 hastaya ait veriler geriye dönük olarak incelendi. Bu gruptan 35 hastaya (ort. yaş 61.7) sadece KABC, 10 hastaya (ort. yaş 62) ise KABC ile eşzamanlı olarak TMR işlemi yapılmıştı. Hastalar üçüncü ayda ve ortalama 22.3±6.1 ay olan takip süresinin sonunda transtorasik ekokardiyografi ve perfüzyon sintigrafisi ile incelendi. Anjinal semptomlar CCS (Canadian Cardiovascular Society) sınıflamasına göre değerlendirildi.

Bulgular: İki grubun ameliyat öncesi verileri benzer bulundu. Hastaların tümü semptomatikti (CCS sınıfı TMR grubunda 2.6±0.5, sadece KABC grubunda 2.3±0.8). Kardiyopulmoner baypas (KPB) süresi TMR grubunda daha uzun idi (p=0.022). Ameliyat sonunda TMR grubunda düşük-orta doz inotrop desteğine daha az ihtiyaç duyuldu (TMR grubunda %10, sadece KABC grubunda %48.6; p=0.034). Erken mortalite hiçbir hastada gözlenmezken, üç hastada (TMR grubunda 1 hasta, sadece KABC grubunda 2 hasta; p=0.329) geç mortalite görüldü. Üçüncü ayda TMR grubundaki hastaların %50'si (n=5) asemptomatik iken, sadece KABC grubunda hastaların %14.3'ü (n=5) asemptomatikti (p=0.016). Anjinal semptomlarda düzelme TMR grubunda anlamlı derece daha fazla idi (CCS sınıfı 3. ay 1.2±0.6 ile 2.2±0.7; p=0,001 ve takip sonu 1±0.6 ile 2±0.7; p=0.001). Miyokart perfüzyon sintigrafisi ve ekokardiyografi ile kontrollerde iki grup arasında anlamlı fark görülmedi.

Sonuç: Tam cerrahi revaskülarizasyon sağlanamayan hastalarda TMR uygulaması KPB'den ayırma işlemi sırasında inotropik destek ihtiyacını, kısa ve orta dönemde anjinal yakınmaları azaltmaktadır.

Anahtar sözcükler: Koroner arter baypas; lazer tedavisi/yöntem; miyokart revaskülarizasyonu/yöntem.

Received: 13.01.2009 *Accepted:* 23.03.2009

Corresponding address: Dr. Koray Ak, Marmara Üniversitesi Tıp Fakültesi, Kalp ve Damar Cerrahisi Anabilim Dalı, Tophanelioğlu Cad., No: 13-15, 34640 Altunizade, İstanbul Tel: +90 - 216 327 10 10/715 e-mail: korayak@marmara.edu.tr

Recent developments in the medical treatment of atherosclerotic coronary artery disease (CAD) and increased success rate of interventional methods have resulted in a significant change in the patient profile undergoing coronary artery bypass grafting (CABG) surgery. The aging population is on the increase in developed countries. The recent increase in the aging population and comorbidities among patients who undergo CABS has resulted in a significant increase in the prevalence of widespread CAD which involves distal coronary artery bed. In their study, Mukherjee et al. [1] found 5% of patients who underwent coronary angiography to have CAD unsuitable for the percutaneous interventional technique and surgical revascularization. On the other hand, inability to perform complete revascularization in approximately 25% of patients who undergo coronary artery bypass surgery due to widespread CAD increases operative mortality as well as long-term mortality.[2-4] As a result, alternative treatment approaches are considered for the patients unsuitable for revascularization and in whom angina symptoms significantly affect quality of life.

Transmyocardial laser revascularization (TMR) administration is the leading alternative in the management of patients with persistent angina symptoms despite appropriate medical treatment and in patients who are unsuitable for complete revascularization. The laser procedure is applied alone or in combination with CABG. In 1995, Frazier et al. [2] demonstrated the positive effects of TMR on angina symptoms and myocardial perfusion. Results of this study were followed by an increased clinical use of TMR. Despite the positive effects of TMR on angina symptoms, myocardial perfusion and ventricular function in various experimental and clinical studies, no consensus has been reached on its clinical effectiveness.[5]

In this study we evaluated the short and long-term clinical effects of simultaneously administered TMR on angina symptoms in patients in whom coronary artery bypass grafting (CABG) surgery was not sufficient to provide complete revascularization due to widespread atherosclerotic CAD.

PATIENTS AND METHODS

This retrospective study included 45 patients who underwent CABG surgery with incomplete revascularization between November 2003 and June 2006. Of these, 35 patients (mean age, 61.7 years) underwent CABG alone during the May 2005 and June 2006 session, whereas 10 patients (mean age, 62 years) underwent TMR during the November 2003 and April 2005 session simultaneously with CABG. Inclusion criterion was the non-suitability for bypass due to anatomical defects (distal or severe widespread disease) in at least one main coronary artery (left anterior descending artery-LAD, circumflex and right coronary arteries) or its branches. All the patients had significant myocardial tissue viability before the surgery in the areas which were fed by nonrevascularized coronary arteries. Exclusion criteria were unstable angina pectoris, decompensated heart failure, severe left ventricular dysfunction (ejection fraction <30%), recent history of myocardial infarction (in the last 3 weeks), severe chronic obstructive pulmonary disease (FEV_1 <45%) and significant absence of myocardial tissue viability in the areas unsuitable for revascularization.

All the patients were assessed before surgery by transthoracic echocardiography, myocardial perfusion scintigraphy (SPECT), coronary angiography and left ventriculography. Myocardial viability in the areas of coronary anatomy unsuitable for revascularization was assessed by perfusion scintigraphy. In addition, transmyocardial laser revascularization was performed in the areas unsuitable for revascularization and in which myocardial viability was demonstrated by perfusion scintigraphy as assessed by coronary angiography and during surgery.

The surgical operation and postoperative care were performed by the same surgical team and anesthesiologist. Following general anesthesia, invasive arterial pressure monitorization was performed by right radial artery cannulation, while central venous route was provided by right internal jugular vein catheterization. The Swan-Ganz pulmonary artery catheter was used for hemodynamic monitorization in patients with unstable hemodynamics before the surgery and with early unstable hemodynamics and low cardiac output following the surgery. Median sterrnotomy was performed on all the patients for surgery. Cardiopulmonary bypass (CPB) was then performed by aortic and right atrial cannulation. Mild to moderate hypothermia (28-34 ºC) was created during bypass surgery. The myocardium was preserved by tepid blood cardioplegia inserted antegradely and topical cold exposure during aortic cross-clamping. Cardioplegia was maintained by an aortic root or saphenous vein grafting every 20 minutes. Retrograde cardioplegia was not performed on any of the patients. Bypass grafting by left internal mammary artery was used for LAD, whereas the great saphenous vein was used for the other coronary arteries. Pre-anastomosis coronary arteriotomy was performed through intact coronary arteries with no atherosclerotic plaques and calcification.

Transmyocardial laser revascularization (TMR Holmium Laser System, Cardiogenesis Corporation, Foothill Ranch, CA, USA) was performed following distal coronary anastomosis, before aortic cross-clamp removal (on-pump) or to the beating heart after aortic cross-clamp removal. The pump was in full flow to improve manipulations in the posterior wall of the beating heart during laser application and the left ventricle was completely drained. Ten laser pulses from the epicardium were dispersed for each channel through the myocardium. A mean of 25±10 channels were set at 1 cm intervals. Hemostasis of the epicardial channels was achieved by direct gas compression following protamine sulfate infusion or suturing of epicardial ends.

All patients were followed up according to the same treatment protocol for the surgical procedures. Data obtained from the patients were routinely recorded and saved in our database. The following criteria were considered when deciding the need for inotropic support during weaning from cardiopulmonary bypass: *(i)* inadequate arterial pressure in the left ventricle (systolic arterial pressure <90 mmHg), despite normal values of systemic temperature (36-38 °C), intravascular fluid volume (central venous pressure 5-12 mmHg), and arterial blood gas (pO_2 80-100 mmHg, pCO_2 35-45 mmHg and pH 7.35-7.45); *(ii)* constant increase in central venous pressure (>15 mmHg); *(iii)* contraction defect in the right ventricular cavity or outward bulging due to retained inner volume; *(iv)* tendency to metabolic acidosis of arterial blood gases and constant increase in systemic lactate values. Initially, dopamine was preferred as the inotropic agent and inotropic support was described as low to middle (3-8 µg/kg/min dopamine) and high (>8 µg/kg/min dopamine or addition of a second inotropic agent or intraaortic balloon pump need). In addition, myocardial infarction (MI) during the surgery period was considered as a new electrocardiography finding or 3.5-fold increase in creatinine kinase MB isoenzyme. Low cardiac output was defined as high dose of inotropic and/or intraaortic balloon pump needed to achieve a systolic blood pressure of >90 mmHg and provide sufficient organ perfusion despite adequate intravascular volume replacement. Based on the RIFLE (Risk, Injury, Failure, Loss and End-stage kidney disease) classification, acute renal dysfunction was also defined as a 2-fold higher levels of serum creatinine following surgery compared to the preoperative levels or decrease in the glomerular filtration rate by >50%.[6] Early mortality was defined as death events occurring within the first month, while postoperative MI, low cardiac output and malignant ventricular arrhythmias were defined as undesirable major cardiac events. All the patients were followed up at the clinic on the 1st, 3rd, 6th months and 1st year after surgery and at the end of the follow-up period. The symptoms of the patients were assessed in the clinic. Beginning from the early period following surgery, all patients were given antiplatelet therapy (aspirin or clopidogrel or dual antiplatelet therapy), metoprolol, and atorvastatin. The decision for low molecular weight heparin and anticoagulation or dual antiplatelet therapy was made according to the distal vascular structure and quality of bypass grafts. All the patients were assessed by transthoracic echocardiography at three months and at the end of the follow-up period and by myocardial perfusion scintigraphy to assess myocardial perfusion.

Statistical analysis was performed by the SPSS (for Windows) 11.0 program. Continuous variables were stated as mean±standard deviation, whereas categorical variables were stated as percentage (%). Student T-test and Fisher's test were used for statistical comparison of continuous variables and categorical variables, respectively. A p value of less than 0.05 was considered as statistically significant.

RESULTS

The baseline characteristics of the patients are summarized in Table 1. No significant difference was found between the groups in terms of these preoperative data. All the patients were symptomatic before surgery. According to the Canadian Cardiovascular Society (CCS) classification, the mean angina class was 2.6±0.5 in the TMR group and 2.3±0.8 –in the CABG-alone group. A high comorbidity rate (diabetes mellitus, chronic obstructive pulmonary disease, peripheral artery disease and hypertension) was reported in all patients of both groups. Transmyocardial laser revascularization was performed at the posterolateral wall (nonrevascularized obtuse marginal branches) in 60% of the patients, at the inferior wall (nonrevascularized posterior descending artery and posterolateral branch) in 30%, and at the apical and anterolateral wall (nonrevascularized diagonal branches) in 10% of the patients.

Perioperative and postoperative early stage data are shown in Table 2. None of the groups showed early mortality. Duration of CPB was longer in the TMR group (p=0.022). There was no significant difference between the groups in respect of the number of distal coronary anastomosis (p=0.138). The left anterior descending artery was revascularized with the left internal mammary artery in all patients. A relatively lesser low to moderate dose of inotropic drug was needed in the TMR group during the weaning from cardiopulmonary

Table 1. Preoperative characteristics of the patients

	CABG + TMR (n=10)			CABG alone (n=35)			
	Number	Percentage	Mean±SD	Number	Percentage	Mean±SD	*p*
Age			62.0±4.1			61.7±4.7	0.980
Sex							0.829
Male	8	80.0		28	80.0		
Female	2	20.0		7	20.0		
Diabetes mellitus	5	50.0		9	25.7		0.190
Chronic obstructive pulmonary disease	4	40.0		17	48.6		0.602
Peripheral artery disease	2	20.0		5	14.3		0.481
Hypertension	3	30.0		9	25.7		0.391
History of cardiac intervention	2	20.0		5	14.3		0.481
PTCA/Stent	1			4			
CABG	-			1			
Ejection fraction (%)			49.0±7.3			50.2±7.5	0.636
Euroscore			4.5±2.0			4.1±1.8	0.658
CCS class			2.6±0.5			2.3±0.8	0.302
NYHA class			1.3±0.8			1.4±0.7	0.737

CABG: Coronary artery bypass grafting surgery; TMR: Transmyocardial laser revascularization; PTCA: Percutaneous transluminal coronary angioplasty; CCS: Canadian Cardiovascular Society; NYHA: New York Heart Association

bypass (10% in the TMR group, 48.6% in the CABG-alone group; p=0.034). High dose of inotropic drug need was observed in only one patient in the TMR group (p=0.222). No significant difference was found between the groups in terms of in postoperative early stage variables (duration of ventilation, MI, low cardiac output, acute renal dysfunction, reperfusion arrhythmia and a 24-hour mediastinal drainage) (Table 2). In addition, there was also no significant difference between the groups in terms of hospitalization duration in the intensive care unit (ICU) and in the hospital.

The patients were followed up over a mean period of 22.3±6.1 months after surgery and the follow-up period was completed in all the patients. Late mortality due to sudden cardiac death was observed in one patient in the TMR group and 2 patients in

Table 2. Perioperative and postoperative early data of the patients

	CABG + TMR (n=10)			CABG alone (n=35)			
	Number	Percentage	Mean±SD	Number	Percentage	Mean±SD	
CPB (min)			47.1±6.2			41.1±6.5	**0.022**
Duration of aortic cross-clamp (min)			21.2±6.5			21.3±5.4	0.961
Inotropic support need during weaning from CPB							
Low to moderate dose	1	10.0		17	48.6		0.034
High dose	1	10.0		-			0.222
Number of grafts used			2.1±0.5			2.4±0.6	0.138
Perioperative myocardial infarction	2	20.0		7	20.0		0.829
Acute renal impairment	1	10.0		3	8.6		0.773
Supraventricular arrhythmia	1	10.0		1	2.9		
Reperfusion arrhythmia	1	10.0		3	8.6		
Duration of Ventilation (h)			11.5±3.9			11.1±5.2	0.804
Low cardiac output	-			1	2.9		
24-hour mediastinal drainage (ml)			450±80			435±65	0.605
Duration in ICU (h)			21.2±6.4			20.7±6.0	0.990
Duration of hospitalization (days)			6.2±0.9			6.6±1.0	0.252
CCS class (3rd month)			1.2±0.6			2.2±0.7	**0.001**
CCS class (end of follow-up)			1.0±0.6			2.0±0.7	**0.001**

CABG: Coronary artery bypass grafting surgery; TMR: Transmyocardial laser revascularization; CPB: Cardiopulmonary bypass; CCS: Canadian Cardiovascular Society; ICU: Intensive care unit.

CABG-alone group (p=0.329). 50% of the patients (n=5) in the TMR group were asymptomatic at three months after surgery during the follow-up period, whereas only 14.3% of the patients (n=5) were asymptomatic in the CABG-alone group (p=0.016). Among symptomatic patients, improvement in angina symptoms was significantly better in the TMR group at three months and at the end of follow-up period (Table 2). Myocardial perfusion scintigraphy repeated at three months after the surgery and at the end of the follow-up period demonstrated no significant change in myocardial perfusion of the TMR group compared to the other group. No significant difference between the groups was found in terms of mean ejection fraction based on echocardiography repeated at three months after the surgery and at the end of the follow-up period (At three months 47.3%±3.1 and 49%±6.4; p=0.216; at the end of the follow-up period 53.7%±4.1 and 50.5%±3.8; p=0.553 in TMR and CABG-alone groups, respectively).

DISCUSSION

The results of our study showed that simultaneous TMR was of critical importance for the eradication of angina symptoms in the short and mid-term (at 3rd and 22th months) in patients who underwent CABG and with incomplete surgical revascularization due to widespread CAD. During weaning from CPB, the need for inotropic support was significantly less in the TMR group. Laser application led to a slight increase in the duration of CPB. In our study we did not observe any effect of TMR on postoperative early outcomes and mortality rate. In addition, there was no positive effect of TMR on myocardial perfusion and ventricular function.

Surgical TMR is an intervention approved by the US American Food and Drug Administration (FDA) and has been included in guidelines for the treatment of atherosclerotic heart disease presenting with widespread CAD. Two types of the laser application are recognized by the FDA. The Holmium: YAG (Ho:YAG) and carbon dioxide (CO_2) laser. The other laser technique is the Excimer laser which is currently used in Europe but has not yet gained approval by FDA. No consensus has been reached on the clinical effectiveness of transmyocardial laser revascularization. Clinical practice is based on the hypothesis of opening transmyocardial channels and feeding the myocardium via these channels. Several clinical and histological studies have showed that epicardial channels remained open in the early stages; however they were occluded in the long term.[7,8] It has been suggested that open epicardial channels in the early stages and increased myocardial perfusion may decrease perioperative mortality particularly in patients with left ventricular dysfunction and reduced energy storage.[9] In addition, coronary artery vasodilation associated with sympathetic nerve denervation may result in increased coronary blood flow in the areas unsuitable for revascularization.[5] Al-Sheikh et al.[10] revealed post-TMR myocardial sympathetic nerve denervation by means of positron emission tomography. Myocardial angiogenesis is another mechanism of action of TMR which is currently commonly discussed. Horvath et al.[11] demonstrated that TMR increased the gene expression of vascular endothelial growth factor (VEGF) and levels of VEGF mRNA.

On the other hand, several studies have suggested that postoperative TMR resulted in negative effects of TMR on early myocardial performance. Hughes et al.[12] demonstrated increased myocardial fluid during the early stages following the TMR procedure, with subsequent systolic and diastolic dysfunction. In addition, Kadipasaoglu et al.[13] reported decreased cardiac index, and increased risk of myocardial ischemia and ventricular arrhythmias after TMR. In our study the patients had mild preoperative left ventricular dysfunction and there was no significant difference between the groups in terms of postoperative early arrhythmia and low cardiac output. The need for inotropic support during weaning from CPB in patients who underwent transmyocardial laser revascularization was lower. Similarly, Allen et al.[9] examined 263 patients with incomplete surgical revascularization in a prospective, randomized study and found the need for postoperative inotropic support to be significantly lower in patients with CABG + TMR (n=132) compared to CABG alone (n=131) (30% vs 55%; p=0.0001). We suggest that the decreased need of inotropic support may be associated with open transmyocardial channels in the early period and coronary vasodilatation.

Osswald et al.[3] showed that incomplete surgical revascularization was another major factor which increases perioperative mortality particularly in the elderly. Allen et al.[9] reported that simultaneous TMR decreased the perioperative mortality rate significantly in patients with incomplete surgical revascularization (1.5% to 7.6%; p=0.02). In the same study it was reported that major undesirable cardiac events decreased significantly in patients who underwent TMR compared to the other patients (91% to 97%; p=0.04) and the postoperative 1-year life expectancy was significantly higher in patients who underwent TMR. In addition, in a prospective and randomized study including 49 patients with incomplete surgical revascularization, Frazier et al.[14] reported that simultaneous TMR with CABG significantly decreased postoperative mortality (9% to 33%). Revascularization and mortality rates were found to be lower in the TMR group compared to the other group during 1-year and 4-year follow-up period.[14,15] However, several studies have been conducted which show no effect of TMR on 1-year life expectancy in patients with incomplete surgical revascularization.[16,17] In our study, no significant effect of TMR on early mortality and major postoperative undesirable cardiac events and late mortality could be shown.

According to the Society of Thoracic Surgeons (STS) Transmyocardial Laser Revascularization Guidelines, angina pectoris refractory to conventional therapies is included in Class I indication, whereas it is included in Class IIa indication when performed with simultaneous CABG.[18] In our study, we found a significant improvement in angina symptoms in patients with TMR 3 months after surgery and at the end of the follow-up period (mean of 22 months) compared to the other patients (p=0.001; Table 2). On the other hand, Allen et al.[19] demonstrated that simultaneous TMR resulted in a decrease in the degree of angina during 5-year follow-up period compared to CABG alone (0.4±0.7 to 0.7±1.1; p=0.05). In our study we observed that 85.8% of the patients who underwent CABG 3 months after surgery had various degrees of angina symptoms. In addition, Sergeant et al.[20] reported that early recurrence of angina symptoms following CABG may be caused particularly by incomplete surgical revascularization, avoidance of using internal the mammary artery for grafting, atherosclerotic CAD with an aggressive prognosis and the degree of the preoperative angina symptoms. In our study all patients had incomplete surgical revascularization and both groups had severe angina symptoms before surgery (mean CCS approximately 2.5). On the other hand, several studies have demonstrated that the improvement in angina symptoms following TMR was temporary and that sympathetic nerve denervation due to laser application resolved within two years.[21]

Although many studies have shown the benefits of transmyocardial laser revascularization on angina symptoms, the effect on myocardial perfusion is still controversial. The major limitation in assessing the effects of TMR on myocardial perfusion is the presence of open bypass grafts in those patients.

We consider that the limitations of our study which included the small sample size, difference in the numbers of the patients between both (10/35) and the short mean follow-up period (22 months), may mask the effects of TMR particularly on late postoperative major undesirable cardiac events and mortality. Therefore, further studies including a larger sample size and longer follow-up period are required. Moreover, a certain time period is required for the training of TMR application. TMR performed on some of the cases during this training period might may also have affected our study results. Furthermore, whether lower level of angina symptoms in TMR group compared to the other group results from the benefits of the application or a placebo effect is controversial. This is because in the study, the patients were preoperatively informed about the laser application in the TMR group. This may have affected the psychological state of the patients positively and hence decreased their complaints related to angina symptoms.

In conclusion, simultaneous TMR decreases the need for inotropic support during weaning from CPB in patients who underwent CABG and with incomplete surgical revascularization. We suggest that decreased need for inotropic support might have benefits in reducing postoperative mortality and undesirable events including postoperative hemodynamic effects and low cardiac output particularly in patients with left ventricular dysfunction. TMR plays an important role in the control of early and mid postoperative angina symptoms. However, further clinical and molecular studies are required to assess the effects of TMR on early and late postoperative clinical outcomes and myocardial perfusion.

REFERENCES

1. Mukherjee D, Bhatt DL, Roe MT, Patel V, Ellis SG. Direct myocardial revascularization and angiogenesis-how many patients might be eligible? Am J Cardiol 1999;84:598-600.
2. Frazier OH, Cooley DA, Kadıpaşaoğlu KA, Pehlivanoğlu S, Lindenmeir M, Barasch E, et al. Myocardial revascularization with laser. Preliminary findings. Circulation 1995;92:58-65.
3. Osswald BR, Blackstone EH, Tochtermann U, Schweiger P, Thomas G, Vahl CF, et al. Does the completeness of revascularization affect early survival after coronary artery bypass grafting in elderly patients? Eur J Cardiothorac Surg 2001;20:120-5.
4. Bell MR, Gersh BJ, Schaff HV, Holmes DR Jr, Fisher LD, Alderman EL, et al. Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery. A report from the Coronary Artery Surgery Study (CASS) Registry. Circulation 1992;86:446-57.

5. Bahçıvan M, Keçeligil HT, Kolbakır F. Transmiyokardiyal lazer revaskülarizasyon. Anadolu Kardiyol Derg 2008;8:58-64.
6. Kuitunen A, Vento A, Suojaranta-Ylinen R, Pettilä V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. Ann Thorac Surg 2006;81:542-6.
7. Gassler N, Wintzer HO, Stubbe HM, Wullbrand A, Helmchen U. Transmyocardial laser revascularization. Histological features in human nonresponder myocardium. Circulation 1997;95:371-5.
8. Burkhoff D, Fisher PE, Apfelbaum M, Kohmoto T, DeRosa CM, Smith CR. Histologic appearance of transmyocardial laser channels after 4 1/2 weeks. Ann Thorac Surg 1996;61:1532-4.
9. Allen KB, Dowling RD, DelRossi AJ, Realyvasques F, Lefrak EA, Pfeffer TA, et al. Transmyocardial laser revascularization combined with coronary artery bypass grafting: a multicenter, blinded, prospective, randomized, controlled trial. J Thorac Cardiovasc Surg 2000;119:540-9.
10. Al-Sheikh T, Allen KB, Straka SP, Heimansohn DA, Fain RL, Hutchins GD, et al. Cardiac sympathetic denervation after transmyocardial laser revascularization. Circulation 1999;100:135-40.
11. Horvath KA, Chiu E, Maun DC, Lomasney JW, Greene R, Pearce WH, et al. Up-regulation of vascular endothelial growth factor mRNA and angiogenesis after transmyocardial laser revascularization. Ann Thorac Surg 1999;68:825-9.
12. Hughes GC, Shah AS, Yin B, Shu M, Donovan CL, Glower DD, et al. Early postoperative changes in regional systolic and diastolic left ventricular function after transmyocardial laser revascularization: a comparison of holmium:YAG and CO_2 lasers. J Am Coll Cardiol 2000;35:1022-30.
13. Kadıpaşaoğlu KA, Sartori M, Masai T, Cihan HB, Clubb FJ Jr, Conger JL, et al. Intraoperative arrhythmias and tissue damage during transmyocardial laser revascularization. Ann Thorac Surg 1999;67:423-31.
14. Frazier OH, Boyce SW, Griffith BP, Hattler BG, Kadıpaşaoğlu KA, Lansing AM, et al. Transmyocardial revascularization using a synchronized CO_2 laser as adjunct to coronary artery bypass grafting: results of a prospective randomized multicenter trial with 12-month follow-up [Abstract]. Circulation 1999;100 (18 Suppl 1):248.
15. Frazier OH, Tuzun E, Eichstadt H, Boyce SW, Lansing AM, March RJ, et al. Transmyocardial laser revascularization as an adjunct to coronary artery bypass grafting: a randomized, multicenter study with 4-year follow-up. Tex Heart Inst J 2004;31:231-9.
16. Peterson ED, Kaul P, Kaczmarek RG, Hammill BG, Armstrong PW, Bridges CR, et al. From controlled trials to clinical practice: monitoring transmyocardial revascularization use and outcomes. J Am Coll Cardiol 2003;42:1611-6.
17. Stamou SC, Boyce SW, Cooke RH, Carlos BD, Sweet LC, Corso PJ. One-year outcome after combined coronary artery bypass grafting and transmyocardial laser revascularization for refractory angina pectoris. Am J Cardiol 2002;89:1365-8.
18. Bridges CR, Horvath KA, Nugent WC, Shahian DM, Haan CK, Shemin RJ, et al. The Society of Thoracic Surgeons practice guideline series: transmyocardial laser revascularization. Ann Thorac Surg 2004;77:1494-502.
19. Allen KB, Dowling RD, Schuch DR, Pfeffer TA, Marra S, Lefrak EA, et al. Adjunctive transmyocardial revascularization: five-year follow-up of a prospective, randomized trial. Ann Thorac Surg 2004;78:458-65.
20. Sergeant P, Lesaffre E, Flameng W, Suy R, Blackstone E. The return of clinically evident ischemia after coronary artery bypass grafting. Eur J Cardiothorac Surg 1991;5:447-57.
21. Schneider J, Diegeler A, Krakor R, Walther T, Kluge R, Mohr FW. Transmyocardial laser revascularization with the holmium:YAG laser: loss of symptomatic improvement after 2 years. Eur J Cardiothorac Surg 2001;19:164-9.