Thoracic and Cardiovascular Surgery

Transmyocardial Laser Revascularization as an Adjunct to Coronary Artery Bypass Grafting

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Many patients with angina related to coronary artery disease respond to medical management or can be completely revascularized using available percutaneous coronary interventions or coronary artery bypass grafting (CABG). There is evidence, however, to indicate that up to 25% of patients are incompletely revascularized following CABG and that incomplete revascularization is a significant independent predictor of early and late mortality and adverse events. Transmyocardial revascularization (TMR) is a surgical option for patients with debilitating angina due to coronary artery disease in areas of the heart not amenable to complete revascularization using conventional treatments. In randomized, 1-year controlled trials with long-term follow-up and in additional clinical experience, TMR performed adjunctively to CABG in patients who would be incompletely revascularized by CABG alone has yielded significantly improved clinical outcomes. Based on these published results, the Society of Thoracic Surgeons has issued a practice guideline recommending adjunctive TMR in this difficult patient group.
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Transmyocardial revascularization (TMR) is a surgical option that, when applied as sole therapy in selected patients who cannot be revascularized using conventional methods, has been shown in multiple randomized trials with 1-year follow-up to provide superior angina relief, decreased rehospitalizations, improved quality of life, and improved event-free survival compared with continued maximal medical management.[1-5] Among these trials, continued 3- to 5-year follow-up has shown sustained and significantly improved angina relief versus medical therapy,[6-8] with a survival benefit in one of these trials involving sicker Class IV patients randomized to TMR.[6] Considering its success as sole therapy, TMR has been evaluated in conjunction with coronary artery bypass grafting (CABG) in patients afflicted by diffuse coronary artery disease who would otherwise be incompletely revascularized by CABG alone.

Incomplete revascularization during CABG occurs in up to 25% of patients and is increasingly being recognized as an important predictor of perioperative adverse events.[9-12] Graham and associates[11] concluded that diffuse coronary artery disease is a powerful independent predictor of operative mortality (Fig. 1). Others have reported that incomplete revascularization is a significant independent predictor of operative mortality in the elderly[10,12] and represents a significant risk for late cardiac events.[9,12-14] In one series, the presence of diseased but nongrafted arteries posed a significant negative influence on event-free survival defined as the absence of death, recurrent angina, myocardial infarction, and the need for repeat CABG.[9] Moreover, it has been recently shown in a propensity-matched analysis that patients undergoing repeat CABG have a significantly increased incidence of incomplete revascularization with significantly poorer cardiac survival both early and late compared with patients undergoing first-time CABG.[15] Confirming these earlier findings, Kleisi and associates identified significantly reduced 5-year cardiac survival in patients incompletely revascularized versus patients for whom complete revascularization was achieved (75% versus 93%, $P < 0.001$).[16] This article will review the clinical science surrounding TMR performed adjunctively to CABG with an emphasis on the randomized controlled trials performed in this difficult patient group.

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Devices and Surgical Procedure

Two laser-based systems have been approved by the United States Food and Drug Administration to deliver TMR therapy to targeted areas of the left ventricle that cannot be revascu-

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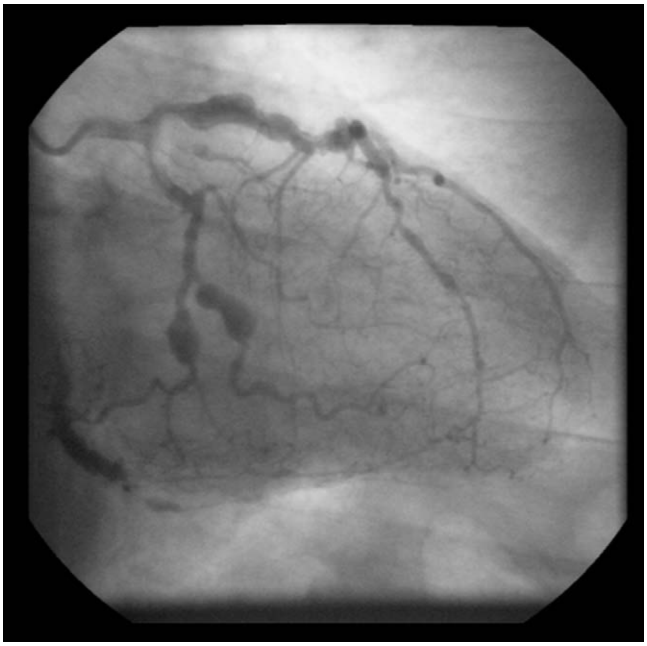

Figure 1 Angiogram demonstrating diffuse coronary Artery disease, a condition that makes complete revascularization with CABG alone unlikely.

larized using conventional methods: the holmium:yttrium-aluminum-garnet (Ho:YAG) laser system (Cardiogenesis Corporation, Foothill Ranch, CA) and the carbon dioxide (CO_2) laser system (PLC Medical Systems, Franklin, MA). The Ho:YAG system uses a pulsed laser to deliver 6 to 8 W per laser pulse at a rate of 5 Hz through a 1-mm-diameter flexible fiberoptic bundle. The hand piece allows the surgeon to position and stabilize the embedded fiberoptic bundle against the epicardial surface. The CO_2 laser system is set to deliver 800 W in pulses 1 to 99 msec long at energies of 8 to 80 J to create 1-mm-diameter channels. Energy is delivered via an operator-set articulated arm and hand piece. The CO_2 system uses helium-neon laser guidance for proper epicardial positioning of the hand piece, and electrocardiographic (ECG) synchronization to fire on the R-wave of the ECG cycle when the ventricle is maximally distended and electrically quiescent. Transesophageal echocardiography is used to confirm transmural penetration. For both systems, laser channels are placed every centimeter squared in the distal two-thirds of the left ventricle, avoiding obviously scarred areas. After the placement of three to five channels, digital pressure is applied for 1 to 2 minutes to obtain hemostasis and allow for myocardial recovery. Epicardial ligation of a laser channel for persistent bleeding is rarely required. Adjunctive TMR with the Ho:YAG system may be performed with or without cardiopulmonary bypass (CPB). If CPB is used, it is preferred to place the TMR channels on an arrested heart just after initiating CPB. This facilitates the procedure and may reduce bleeding as compared with placing laser channels at the conclusion of CPB. During off-pump CABG cases, TMR is performed after bypass grafts are completed. Adjunctive TMR using the CO_2 system can be performed either before or after bypass grafts have been placed while the heart is beating.

Clinical Evidence

Despite this logical application of the technology by physicians, TMR therapy combined with CABG in selected patients has not been studied as extensively as sole therapy TMR; consequently, the benefit of combined therapy is supported by a smaller data set compared with that available for primary TMR. Moreover, the safety and effectiveness of adjunctive TMR have been more difficult to assess due to the influence of adjacent bypass grafts and lack of randomized control arms in some studies. Nonetheless, two prospective randomized, controlled trials (RCTs) have been conducted for combined CABG with TMR in patients who would be incompletely revascularized using CABG alone, and patients from each of these trials have been followed long term. These trials (primary evidence), nonrandomized studies (secondary evidence), and observational or retrospective studies (tertiary evidence) are discussed below.

Primary Evidence

Two multicenter, prospective, controlled trials involving 312 randomized patients evaluated TMR performed adjunctively to CABG in comparison to CABG alone in patients with diffuse disease who would be incompletely revascularized by CABG alone (Allen and coworkers, $N = 263$[17]; Frazier and coworkers, $N = 49$[18]).

In a prospective, controlled trial conducted at 24 US centers, Allen and associates randomized 263 patients who would be incompletely revascularized by CABG alone due to one or more ischemic areas not amenable to bypass grafting to adjunctive TMR ($N = 132$) or CABG alone ($N = 131$). At a mean age of 64 years, patients had a mean ejection fraction of 0.51; 60% of patients had a previous myocardial infarction, and 26% had undergone a prior CABG surgery. Patients were blinded to treatment through 1 year. Significantly reduced operative mortality was observed following adjunctive TMR compared with CABG alone (1.5% versus 7.6%, $P = 0.02$), although the Parsonnet-predicted mortality risk was comparable (6.3%, adjunctive TMR versus 6.6%, CABG alone, $P = 0.80$). Adjunctive TMR required reduced postoperative inotropic support (30% versus 55%, $P = 0.0001$) and afforded increased 30-day freedom from major adverse cardiac events (97% versus 91%, $P = 0.04$). Improvements in angina and exercise treadmill scores at 1 year were similar between groups. Compared with CABG-alone patients, adjunctive TMR patients had significantly increased 1-year survival (95% versus 89%, $P = 0.05$) and freedom from major adverse cardiac events, prospectively defined as death or myocardial infarction (92% versus 86%, $P < 0.05$).

More recently, a 5-year follow-up of this work has been reported.[19] Whereas both randomized groups experienced significant improvement in CCS angina class based on blinded, independent (nonsurgeon) assessment during follow-up, adjunctive TMR patients had significantly lower