Note: This is a two-article spread with a shared commentary. Please scroll down for the second article.

THERAPEUTICS

Transmyocardial revascularization increased exercise duration and reduced angina symptoms

Burkhoff D, Schmidt S, Schulman SP, et al., for the ATLANTIC Investigators. **Transmyocardial laser revascularisation compared with continued medical therapy for treatment of refractory angina pectoris: a prospective randomised trial.** Lancet. 1999 Sep 11;354:885-90.

QUESTION

In patients with medically refractory angina, does transmyocardial revascularization (TMR) increase exercise duration and reduce angina symptoms?

DESIGN

Randomized (allocation concealed*), blinded (outcome assessors),* controlled trial with 12-month follow-up.

SETTING

16 centers in the United States.

PATIENTS

182 patients (median age 63 y in the TMR group, 65 y in the medication-alone group; 91% women) who had Canadian Cardiovascular Society Angina (CCSA) scores of III or IV after maximum tolerated doses of ≥ 2 antianginal drugs, left ventricular ejection fraction ≥ 30%, reversible perfusion defects on dipyridamole thallium testing, and ≥ 1 region of protected myocardium. Exclusion criteria included myocardial infarction in the previous 3 months, severe symptomatic heart failure, history of clinically important ventricular arrhythmias or cardiac transplantation, or lack of fitness for surgery. Follow-up was 84% for change in exercise duration and 89% for change in CCSA scores.

INTERVENTION

Patients were allocated to TMR and continued medication (n = 92) or continued medication alone (n = 90). TMR consisted of a limited muscle-sparing left thoracotomy and the creation of transmyocardial laser channels (median 18 channels, 1 in each 1.0 to 1.5 cm^2) with a holmium: YAG (CardioGenesis Corp., Sunnyvale, CA, USA).

MAIN OUTCOME MEASURES

Change in exercise duration. Secondary outcomes included change in CCSA scores.

MAIN RESULTS

5 patients in the TMR group and 9 in the medication-only group died. Exercise duration was increased by a median of 65 seconds in the TMR group compared with a median 46-second decrease in the medical therapy group ($P < 0.001$). More patients in the TMR group than in the medical therapy group had a decrease of ≥ 2 CCSA classes {$P < 0.001$}† (Table).

CONCLUSION

In patients with medically refractory angina, transmyocardial revascularization was associated with a greater increase in exercise duration and a greater reduction in angina symptoms than was medication alone.

Source of funding: CardioGenesis Corporation.

For correspondence: Professor J.W. Jones, Department of Surgery, University of Missouri, 1 Hospital Drive, Columbia, MO 65212, USA. FAX 573-884-4585.

*See Glossary.

†*P* value calculated from data in article.

Transmyocardial revascularization (TMR) vs medical therapy for medically refractory angina‡

Outcome at 12 mo	TMR	Control	RBI (95% CI)	NNT (CI)
Reduction of ≥ 2 angina classes	61%	11%	457% (194 to 1001)	2 (2 to 3)

‡Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

COMMENTARY

These 2 studies by Burkhoff and Frazier and their colleagues provide evidence that TMR may be beneficial for patients with severe angina for whom traditional revascularization is not an option. TMR is a surgical procedure done by creating laser holes in the left ventricular free wall via a thoracotomy in patients who are not candidates for coronary artery bypass grafting or percutaneous intervention. Although the mechanism for this benefit is not clear, the premise is that TMR stimulates angiogenesis and thereby improves myocardial perfusion (1). Another proposed theory is that TMR causes myocardial denervation, allowing for relief of symptoms (2). Support for either of these mechanisms in clinical practice is limited at present.

The Angina Treatments: Lasers and Normal Therapies in Comparison (ATLANTIC) study found that both exercise duration and angina scores improved significantly in the TMR group but not in the medically treated group. However, these investigators found no improvement in myocardial perfusion by thallium testing in either group. The placebo effect cannot be underestimated in this cohort of patients who had end-stage coronary artery disease and were eagerly seeking relief for their chest discomfort. This effect is shown in the recent VEGF [vascular endothelial growth factor] in Ischemia for Vascular Angiogenesis (VIVA) trial (3), a blinded trial of intravenous VEGF given to a similar patient population. As in the TMR trials, the treatment group in the VIVA trial substantially improved in angina class and exercise time, but the placebo group also showed a similar improvement. Although the ATLANTIC study shows symptomatic improvement using TMR, the benefit of a placebo effect has not been ruled out.

The trial by Frazier and colleagues also compared TMR with maximal medical therapy. They again found a significant improvement in angina class in the TMR group but not in the medically

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Transmyocardial revascularization was effective in refractory angina and left ventricular free-wall ischemia

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 Sep 30;341:1021-8.

QUESTION

In patients with refractory angina and left ventricular free-wall ischemia that is not amenable to direct coronary revascularization, is transmyocardial revascularization (TMR) effective and safe for relieving angina?

DESIGN

Randomized (allocation concealed*), blinded (outcome assessor),* controlled trial with 12-month follow-up.

SETTING

12 centers in the United States.

PATIENTS

192 patients (mean age 61 y, 79% men) who had class III or IV (Canadian Cardiovascular Society) angina that was refractory to medical treatment, reversible ischemia of the left ventricular free wall, and coronary disease that was not amenable to coronary artery bypass grafting or percutaneous transluminal coronary angioplasty. Exclusion criteria were left ventricular ejection fraction < 20% or other major illness. Follow-up for relief of angina was 90% at 3 months, 81% at 6 months, and 73% at 12 months.

INTERVENTION

Patients were allocated to TMR (n = 91) or medical treatment (n = 101). TMR was done by creating transmural channels (1 channel/cm^2 of myocardial surface) approximately 1 mm in diameter with a single pulse of a carbon dioxide laser (peak power 850 W) through the left ventricle. 60 patients originally assigned to medical treatment crossed over to TMR because of unstable angina that required intravenous antianginal treatment for ≥ 48 hours in an intensive care unit.

MAIN OUTCOME MEASURES

Treatment success (reduction of ≥ 2 angina classes). Quality of life and cardiac perfusion were also evaluated in < 80% of surviving patients at 12 months.

MAIN RESULTS

TMR was better than medical treatment for relieving angina at 3 months (67% vs 20%, P < 0.001) and 6 months (67% vs 27%, P < 0.001).

CONCLUSION

In patients with refractory angina and left ventricular free-wall ischemia that is not amenable to direct coronary revascularization, transmyocardial revascularization was associated with an improvement in angina.

Source of funding: No external funding.

For correspondence: Dr. O.H. Frazier, Texas Heart Institute, P.O. Box 20345, Houston, TX 77225-0345, USA. FAX 713-794-6798. ■

*See Glossary.

COMMENTARY *(continued from page 84)*

treated group. However, an improvement in ischemic regions on single-photon-emission–computed tomography was seen in the TMR but not in the medically treated group. A confounding issue in this study is that the trial design allowed for crossover from medical therapy to TMR if patients had refractory angina, and approximately 60% of the medically treated group received TMR. These crossover patients received a similar benefit to those primarily randomized to TMR.

The difficulty with assessing whether TMR truly improves symptoms is that operators feel that they cannot ethically perform sham thoracotomy operations. The recent advent of creating similar laser myocardial channels by percutaneous technique will better lend itself to double-blind trials. Until such randomized, double-blind, controlled trials are done, a placebo effect cannot be excluded.

Brigitta C. Brott, MD
The Heart Group
Evansville, Indiana, USA

References

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2. **Hirsch GM, Thompson GW, Arora RC, et al.** Transmyocardial laser revascularization does not denervate the canine heart. Ann Thorac Surg. 1999;68:460-8.
3. **Henry TD, Annex BH, Axrin MA, et al.** Double blind, placebo controlled trial of recombinant human vascular endothelial growth factor—the VIVA trial [Abstract]. J Am Coll Cardiol. 1999;33:384A.

