THERAPEUTIC EFFECT OF TRANSMYOCARDIAL LASER REVASCULARIZATION IN PATIENTS WITH CHEST PAIN AND NORMAL CORONARY ANGIOGRAPHY (CARDIAC SYNDROME X)

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Abstract- Patients with syndrome X coronary disease represent a heterogeneous group of patients. Medical treatment with dilators and calcium channel blockers are not very effective. We evaluated the use of transmyocardial laser revascularization (TMLR) in treating 5 patients with this syndrome. Between May 2002 to December 2005, 5 patients with cardiac syndrome X (mean age of 49.7 years) underwent TMLR. All our cases were postmenopausal women. Mean class of Canadian class of angina was 3.4. Patients were none responding to maximum medical treatment. Angiograms showed small coronary arties with a large gap between branches which corresponded with severe ischemic on Thallium scan. We used Co2 laser between 35 to 45 joules of energy and we made 20 to 30 channels on the beating heart controlled by trans-esophagus echocardiography. Our patients were followed for 2.8 years. During follow up our patients remained asymptomatic and without any need medical treatment. Mean of Canadian class of angina after intervention was 1.8. Our patients returned to full activities. TMLR is an effective treatment in patients with syndrome X and coronary insufficiency.

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Key words: Calcium channel blocker, transmyocardial laser revascularization, trans-esophagus echocardiography

INTRODUCTION

Patients with cardiac syndrome X (CSX)-typical chest pain and electrocardiographic changes suggestive of myocardial ischemia despite normal coronary arteriograms–represent a diagnostic and therapeutic riddle. CSX is not associated with an increased mortality or an increased risk of cardiovascular events, but it often severely impairs quality of life and represents a substantial cost burden to the healthcare system.

This syndrome is predominantly seen in postmenopausal women (1). Prognosis is good regarding survival and left ventricular function in patients with CSX (2,3). American Heart Association/American College of Cardiology treatment guidelines are available for management of CSX in the context of the acute coronary syndrome (4). Advice on lifestyle changes and risk factor management–in particular aggressive lipid lowering therapy with statins should be considered vital components of any therapeutic strategy.

Recently, randomized controlled trials that compared the effects of surgical TMLR with those of maximal medical management were published (5-8). In these, TMLR was shown to significantly relieve angina, improve quality of life, increase exercise tolerance, and reduce hospital admissions. We collected data on 5 patients who underwent CO2 TMLR from 2 years ago and report on their clinical status and angina class postoperatively.

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MATERIALS AND METHODS

From May 2002 to December 2005, 5 consecutive patients with cardiac syndrome X underwent CO2 TMLR (Fig 1). The original selection criteria were that the patient (1) be in CCS angina class III or IV, (2) be >18 years old, (3) have an ejection fraction of >=20%, and (4) have evidence of reversible ischemia. With the patient under general anesthesia, transmural channels of almost equal to 1-mm diameter were created with a single pulse of the CO2 laser (peak power 850 W) through the myocardium of the left ventricle. Approximately 1 channel was created per square centimeter of myocardial surface. Complete transmural penetration by the laser was confirmed with intraoperative transesophageal echocardiography. All areas of reversible ischemia were targeted for treatment.

We obtained written informed consent from all patients

Analyses were performed with a 2-sided standard t test, and paired t test was used for normally distributed continuous variables. P <0.05 is considered to indicate statistical significance.

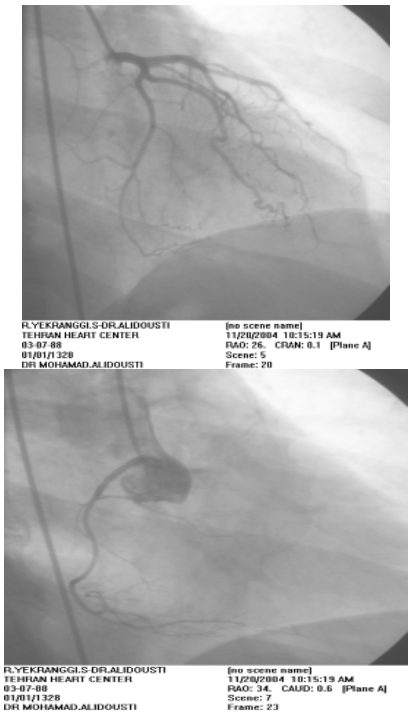

Fig. 1. Normal coronary angiography in patients with cardiac syndrome X.

RESULTS

Intraoperatively, 20±8 channels (range, 13 to 44 channels) were created as confirmed with transesophageal echocardiography. There were no intraoperative deaths. The mean stay in the intensive care unit was 2 days, and the mean hospital stay was 6 days. 3 of the patients were in angina class IV and the remainders were in class III at baseline, for an average angina class of 3.7±0.4. At 1-year follow-up, the angina class distribution was markedly different, with 4 of the patients having no angina or being in CCS class I or II. Thallium scintigraphy after 6 months showed significant improvement in myocardial perfusion in 4 patients (Fig. 2a, b). The average angina class at 1 year was 1.5±1.1.

The average angina class at 2 years is 1.6±1.1, which is unchanged from the 1-year follow-up (P=NS).

4 of these patients had more than 2 angina class reduction. For the 5 parameters measured via the Seattle Angina Questionnaire, the long-term follow-up indicates significant improvement in exercise capacity, angina stability, angina frequency, treatment satisfaction, and disease perception. This improvement is reflected in a significant increase in Seattle Angina Questionnaire scores (P <0.001 versus baseline for all scores).

DISCUSSION

Patients with typical exertional chest pain and positive exercise tests usually have obstructive coronary artery disease, particularly when risk factors are present; approximately 20% of these patients have normal coronary arteriograms (2). Most cardiologists agree that, in addition to typical chest pain and ECG changes (or other evidence of a cardiac involvement such as myocardial perfusion abnormalities), the coronary angiogram could be completely normal (2, 3). Patients with systemic hypertension, left ventricular hypertrophy, and diabetes mellitus are excluded from CSX, as it is assumed that the cause for their angina is known. Patients with coronary artery spasm and those with objectively documented extracardiac causes for the pain (such as chest wall syndrome, psychological

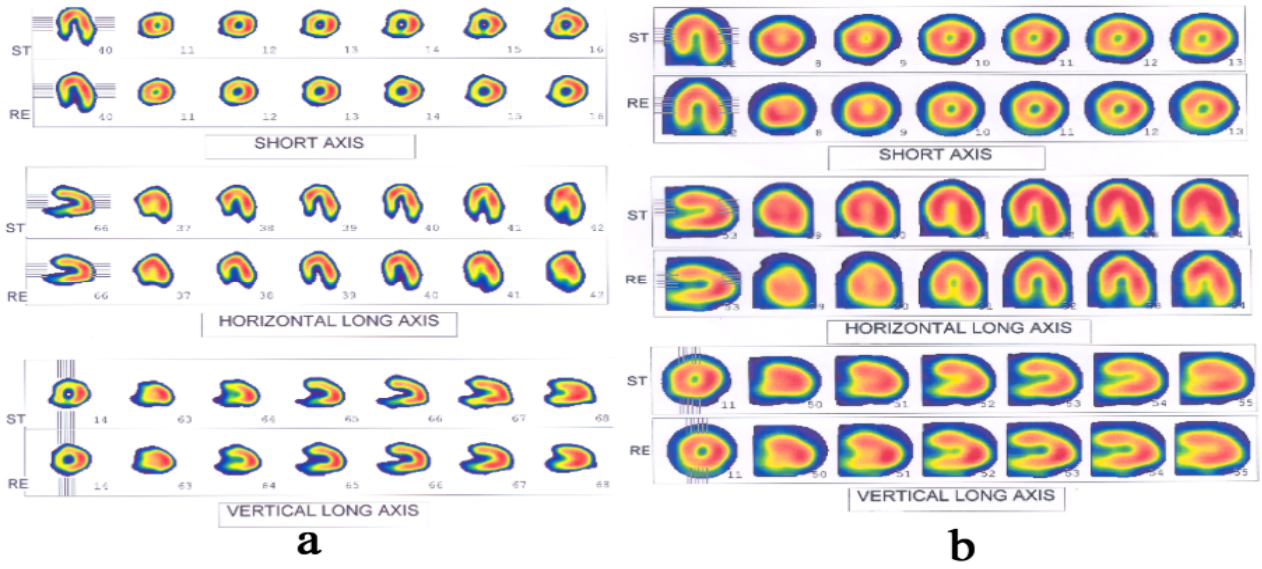

Fig. 2. a: Short and long axis 201-Thallium Scintigraphy images showing perfusion defects in the inferolateral wall of myocardium, **b:** Short and long axis 201-Thallium Scintigraphy images showing normal perfusion 6 months after TMLR in cardiac syndrome X.

disturbances, and esophageal spasm) are also excluded (2).Despite intense investigation over the past 30 years regarding the pathogenesis of CSX, many fundamental questions remain unanswered. Microvascular angina (reduced coronary microvascular dilatory responses and increased coronary resistance) (9) has been consistently found in CSX patients and suggested as a cause for regional myocardial blood flow abnormalities and heterogeneous myocardial perfusion. Endothelial dysfunction, with reduced bioavailability of endogenous NO and increased plasma levels of endothelin-1 (ET-1), may explain the abnormal behavior of the coronary microvasculature in CSX (10-12). Transient myocardial perfusion defects have been reported in areas supplied by arteries showing endothelial dysfunction (10) and increased levels of ET-1 correlated with impaired coronary microvascular dilator responses in patients with chest pain and normal coronary arteries (13). Given the high prevalence (approximately 70% in most series) of postmenopausal women in the CSX population, estrogen deficiency has been suggested as a pathogenic agent acting via endothelium-dependent and endothelium-independent mechanisms (14, 15). Myocardial Ischemia is objectively documented in only a minority (approximately 25%) of patients (2, 3). Because many authors question the role of myocardial ischemia in CSX based on its good prognosis, the poor response to nitrates in many cases, the normal results of stress echocardiography, and the absence of objective markers of ischemia in many CSX patients, non-ischemic mechanisms have been proposed to explain the occurrence of CSX, including autonomic nervous system dysfunction (16, 17) and increased pain perception (18). Increased pain perception is common in patients with CSX, but the reason remains elusive (16-18). CSX patients have high rates of psychiatric morbidity (19); approximately 30% have a treatable psychiatric disorder and another 30% have psychological problems. Physical training improves pain threshold and endothelial function and delays the onset of exertional pain in patients with typical chest pain and normal coronary arteries (20).

TMLR is designed to treat patients with severe disabling angina due to end-stage coronary disease. Both experimentally and clinically CO_2 laser for TMLR was first demonstrated by us (21-26). The short-term ability of TMR to provide angina relief has been previously demonstrated (5-8). These previous reports from randomized controlled trials demonstrate significant symptomatic relief,

improved exercise tolerance, and improved quality of life for laser-treated patients versus patients who continued their maximal medical therapy. A significant decrease in the number of reversible or ischemic myocardial defects without an increase in the number of fixed or infarcted areas has been demonstrated with the CO2 laser in comparisons of TMLR-treated patients both with their baseline values and with patients randomized to medical management (5, 6). Further evaluation using other objective measures, such as Dobutamine stress echocardiography (27) and CINE and contrast-enhanced MRI, (28) shows an improvement in myocardial function and a decrease in myocardial ischemia without an increase in myocardial infarction in patients treated with CO2 TMLR.

Significant short-term angina relief at 1 year was also documented with the Ho:YAG device (29, 30), but there is a significant difference in the laser tissue interaction between the CO2 and Ho:YAG lasers. The CO2 laser is able to create a transmural channel with a single pulse and with minimal collateral damage. The Ho:YAG laser requires multiple pulses to create a channel, and with each pulse, an explosion occurs at the tissue level. This increases the collateral damage and creates a photoacoustic effect in which shock waves of energy are transmitted through the myocardium. In addition, the Ho:YAG laser energy is delivered via fiber. This fiber is manually advanced through the myocardium during Ho:YAG TMR. This report documents the follow-up period for TMR with CO2 laser in patients with CSX.

The follow-up of patients with severe disabling angina and normal coronary angiography treated with CO2 TMR reveals sustained angina relief over 2 years postoperatively.

Conflict of interests

The authors declare that they have no competing interests.

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