Transmyocardial holmium laser revascularization: feasibility of a thoracoscopic approach

Aldo Milano*, Stefano Pratali*, Marco De Carlo*, Andrea Pietrabissa#, Uberto Bortolotti#,*

*Department of Cardiac Surgery, University of Pisa Medical School, Pisa, Italy
#Department of General Surgery, University of Pisa Medical School, Pisa, Italy

Abstract

Objective: Creation of transmyocardial channels from the epicardium to the left ventricular cavity with the use of a laser is a modern approach in the treatment of patients with chronic ischemic heart disease unsuitable for coronary angioplasty or bypass grafting. We present the results of transmyocardial laser revascularization (TMLR) with a holmium laser as sole therapy in 22 patients operated on between November 1995 and February 1997. Methods: There were five females (23%) and 17 males (77%), with a mean age of 67 ± 7 years (range 53–74 years). Previous myocardial revascularization had been performed in 77% of the patients. Pre-operatively, 12 patients (55%) were in angina class III and ten (45%) in class IV (mean 3.5 ± 0.5); unstable angina was present in seven patients (32%). In 20 patients, TMLR was performed through a limited thoracotomy, while in two a thoracoscopic approach was used. Each patient received a mean of 33 ± 8 channels in 27 ± 13 min, while total operation lasted 130 ± 28 min. Results: There were no hospital deaths and no major post-operative complications. Mean hospital stay was 7 ± 3 days; the two patients undergoing thoracoscopic TMLR were discharged after 4 and 5 days, respectively. Two deaths were observed after 40 days and 4 months after TMLR, due to stroke and myocardial infarction. Mean follow-up of current survivors is 10 ± 6 months (range 3–15 months), with seven patients followed for over 12 months. At last follow-up, mean angina class is 1.9 ± 0.6 (P < 0.001). A significant increase in exercise tolerance and a reduction of the number of hospitalizations for angina were also observed. However, no significant changes in myocardial perfusion were observed. Conclusions: The present study demonstrates that: (1) TMLR with a holmium laser yields clinical improvement in the majority of patients with severe angina unsuitable for conventional surgical treatment, (2) gratifying results in terms of improved anginal status and exercise tolerance are achieved, despite the lack of significant changes in myocardial perfusion at early follow-up and (3) TMLR through a thoracoscopic approach is a feasible procedure.

Keywords: Coronary artery disease; Transmyocardial revascularization; Laser; Thoracoscopy

1. Introduction

Creation of transmyocardial channels with a laser is gaining increasing popularity as a means to improve myocardial perfusion in patients with coronary artery disease not suitable for coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA). Based on early experiments by Mirhoseini et al. [1,2] and following preliminary satisfactory results in humans [3–5], several clinical trials are currently undertaken to assess the efficacy of transmyocardial laser revascularization (TMLR). One such trial started in 1995 at our institution, where a holmium-yttrium-aluminum garnet (YAG) laser has been so far used for TMLR. The purpose of this study was to evaluate the safety and effectiveness of TMLR with a holmium laser and demonstrate the feasibility of this procedure through a thoracoscopic approach.

2. Materials and methods

2.1. Patient population

A clinical trial of TMLR as the sole therapy for otherwise
untreatable coronary artery disease was approved by our Ethical Committee. The inclusion criteria were the following: (1) presence of Canadian Cardiovascular Society (CCS) class III or IV angina, refractory to maximal medical treatment, (2) evidence of coronary artery disease not suitable for PTCA or CABG because of diffuse disease, small vessels or inadequate distal run-off, (3) left ventricular ejection fraction (EF) ≥ 30% and (4) documentation of myocardial ischemia and viability by 201Tl single-photon emission computed tomography (201Tl-SPECT) during exercise or pharmacological stress. The presence of myocardial ischemia in those patients who could not undergo a stress test was documented by electrocardiographic changes during the episodes of angina and by reversible perfusion defects at basal 201Tl-SPECT.

From November 1995 to February 1997, 22 patients were treated by TMLR after informed consent had been obtained. There were 17 males and five females, with a mean age of 67 ± 7 years (range 53–79 years). The main pre-operative characteristics are represented in Table 1. Sixteen patients had sustained a myocardial infarction, while in four (18%), two or more such episodes had occurred. Seventeen patients (77%) had undergone at least one previous CABG and eight (36%) one or more PTCA. Pre-operatively, 12 patients (55%) were in CCS class III and ten (45%) in class IV (mean 3.5 ± 0.5); unstable angina was present in seven patients (32%). Fifteen patients (68%) received multiple oral medications, consisting of a combination of \( \beta \)-blockers, calcium-channel blockers and nitrates. The seven patients (32%) with unstable angina required in addition intravenous administration of heparin and nitrates.

Pre-operative transthoracic 2D echocardiography showed a mean left ventricular ejection fraction (EF) of 46 ± 8% (range 30–60%). All patients underwent rest 201Tl-SPECT, 12 were stressed by exercise and three by dipyridamole infusion. Seven patients could not undergo a stress test because of their anginal status. A viability score was attributed to each segment of the left ventricular wall according to its degree of ischemia: fixed (0), partially reversible (1), totally reversible (2) and no ischemia (3). The interventricular septum, which was not treated by TMLR, was used as control.

### 2.2. Characteristics of the laser

All patient underwent TMLR using a holmium:YAG crystal lasing medium (Eclipse Surgical Technologies, Sunnyvale, CA) operating at a wavelength of 2.1 \( \mu \text{m} \) (mid-infrared spectrum). The system delivers 5 pulses/s, with a pulse length of 250 \( \mu \text{s} \) and a power of 6–8 W. With this system there is no need for electrocardiographic synchronization. The laser beam is conducted through a flexible optical fiber with a 1 mm tip (‘CrystalPoint’), thus allowing creation of 1 mm myocardial channels. An even more flexible optical fiber (‘CrystalFlex’) allows to reach the posterior left ventricular wall by means of a special right-angled instrument (‘J grip’) acting as a guide.

### 2.3. Surgical procedure

#### 2.3.1. Thoracotomic approach

Under general anesthesia the patient is intubated with a single-lumen catheter and monitored in a routine fashion. Operation is performed on the patient’s beating heart through a limited left antero-lateral thoracotomic incision on the bed of the fifth rib. The pericardium is opened anterior to the phrenic nerve and suspended. Major epicardial coronary vessels are identified as well as previous venous or arterial grafts. Transmyocardial channels are created from the epicardium to the endocardium into the left ventricular cavity, mainly in those areas identified as ischemic, but also in contiguous areas for a more complete treatment. The density of channels is about 1/cm\(^2\), with approximately 35 channels drilled for each patient. Penetration of the laser probe into the left ventricular chamber can be easily felt by the surgeon, being also indicated by a change of the acoustic pattern of the system, rendering routine echocardiographic confirmation unnecessary. Bleeding resulting from the channel is easily controlled by digital compression and epicardial sutures are almost never required.

#### 2.3.2. Thoracoscopic approach

The patient is anesthetized and intubated in the standard manner and placed in 30° right lateral decubitus. A 25° angled telescope is advanced through a 10-mm port placed in the sixth intercostal space at the posterior axillary line of the left hemithorax. Left lung volume is reduced as appropriate to allow access to the thoracic cavity, while maintaining a positive intrapleural pressure of 6 mmHg by CO\(_2\) insufflation. Under direct visualization two additional ports are subsequently inserted: one of 10 mm in the seventh intercostal space at the anterior axillary line and the other of 5 mm in the fourth intercostal space at the mid-axillary line (Fig. 1). A standard endoscopic technique is used throughout the procedure to visualize the myocardium and to posi-

### Table 1

Pre-operative data

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. patients</th>
<th>Male:female</th>
<th>Mean age (range)</th>
<th>Diabetes mellitus</th>
<th>Arterial hypertension</th>
<th>Renal failure</th>
<th>Dyslipidemia</th>
<th>Mean CCS angina class</th>
<th>Unstable angina</th>
<th>Previous myocardial infarction</th>
<th>Previous PTCA</th>
<th>Previous CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>22</td>
<td>17:5</td>
<td>66.9 ± 6.9 (53–79)</td>
<td>9</td>
<td>12</td>
<td>6</td>
<td>15</td>
<td>3.5 ± 0.5</td>
<td>7</td>
<td>20</td>
<td>8</td>
<td>17</td>
</tr>
</tbody>
</table>

CCS, Canadian Cardiovascular Society; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass grafting.
tion the optical fiber. A long pericardial incision is created anterior to the left phrenic nerve with the use of graspers and coaxially curved scissors. When present, pericardial adhesions are dissected so as to clearly visualize the areas of the left ventricular wall to be treated. The superior and inferior edges of the pericardial window are suspended by interrupted stitches pulled outside through the anterior thoracic wall. The anterior and lateral epicardial surfaces of the left ventricle are reached by the optical fiber delivered via the working channel of Olsen’s cholangiograsper or directly via a trocar port (Fig. 2). The base and the posterior aspect of the left ventricle are treated with the CrystalFlex fiber, with the aid of the ‘J grip’ (Fig. 3). Hemostasis is achieved by local compression exerted by a peanut pledget holder inserted and retracted inside a reducer tube. At the end the pericardial incision is partially closed by approximating the edges with few interrupted stitches. A pleural aspiration drain is left and removed 24 h later after pulmonary re-expansion.

2.4. Peri- and post-operative care

During operation, after opening the chest and before beginning TMLR, a lidocaine infusion is started, to prevent ventricular arrhythmias. Volume losses are replaced with crystalloid solution, since the amount of bleeding is usually negligible. Antiarrhythmic treatment is continued throughout the first post-operative night, together with furosemide administration to avoid myocardial edema; inotropic drugs are administered if necessary. The patient is extubated and discharged to the ward as soon as possible. Pre-operative oral medications are restarted on the first post-operative day and maintained after discharge. Anticoagulants are usually not given and all patients receive antiplatelet drugs.

2.5. Data collection and statistical analysis

Patients are reevaluated at our center at 3, 6 and 12 months after the procedure. Data on angina class, functional class and number of hospitalizations following TMLR are collected. Repeat 2D-echocardiographic evaluation, stress test by cycle-ergometer and 201 Tl-SPECT are also scheduled. Pre- and post-operative scans are reviewed to assess the changes in the distribution of fixed and reversible ischemia; the viability scores of lased and non lased (septum) segments are also calculated. The results are compared using a paired Student’s t-test, considering significant a P value of <0.05.

3. Results

3.1. Operative results

Twenty patients were operated through a limited left antero-lateral thoracotomy, while in two a thoracoscopic approach was employed. The laser procedure lasted from 11 to 58 min (mean, 27 ± 13 min), while mean duration of the entire procedure was 130 ± 28 min (range 63–187 min). The mean duration of TMLR and of operation in the two patients with the thoracoscopic approach was 43 min and 163 min, respectively. The mean number of transmynocardial channels performed per patient was 33 ± 8 (range 22–55 channels). Mean post-operative ventilation time was 10 ± 7 h (range 1–24 h), with a mean intensive care unit.
stay of 27 ± 23 h (range 9–126 h). The two patients with thoracoscopic approach were extubated after 2 and 4 h, respectively, and both discharged to the ward after 12 h.

There were no operative deaths and no major post-operative complications. Mean blood loss was 359 ± 216 ml and reoperation for bleeding was never required. Mild inotropic support (dobutamine 3–5 μg/kg per min) was necessary in ten patients. Two patients experienced runs of ventricular tachycardia, and four transient ST-segment depression with negative T waves. Mean peak creatine kinase-MB isoenzyme (CK/MB) was 42 ± 28 IU/l (range 5–113 IU/l); enzyme elevation was not correlated with number of channels, electrocardiographic changes and need for inotropic support. Patients were discharged with a mean hospital stay of 7 ± 3 days. The two patients undergoing a thoracoscopic approach were discharged after 4 and 5 days.

3.2. Follow-up

Two patients died during follow-up: one because of stroke 40 days after TMLR and the other because of myocardial infarction 4 months following the operation. In both necropsy was not performed. Follow-up of current survivors ranges from 2–15 months (mean 10 ± 6 months), with 19 patients followed for 3 months, 14 for 6 months and seven for 1 year; cumulative follow-up is 213 patient-months. At last follow-up, mean CCS angina class is 19 ± 0.6 (P < 0.001), with five patients (25%) in class I, 13 (65%) in class II and two (10%) in class III (Table 2). Fig. 4 shows the comparison between pre-operative and post-operative angina class, with an improvement of at least two CCS classes in 60% of the patients. Mean left ventricular EF increased from 46 ± 8% to 49 ± 7% (P, n.s.), while exercise tolerance increased from 3.5 ± 1.4 min to 5.1 ± 1.7 min (P = 0.01). The mean number of hospitalizations due to angina decreased from 4.9 ± 1.5 in the 6 months before to 1.5 ± 1.0 in the 6 months after TMLR (P < 0.001).

A control 201Tl-SPECT was performed in 14 patients at 3 months and in eight at 6 months. The distribution of segmental perfusion defects did not vary significantly; the percentage of myocardial segments that showed an improved perfusion was 9.5 ± 2.4% and 11.1 ± 3.2% at 3 and 6 months, respectively, while 3.2 ± 2.1% of the segments

<table>
<thead>
<tr>
<th>Table 2 Post-operative results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Mean CCS angina class</td>
</tr>
<tr>
<td>Exercise tolerance (min)</td>
</tr>
<tr>
<td>No. of hospitalizations</td>
</tr>
<tr>
<td>Mean viability score at 201Tl-SPECT</td>
</tr>
</tbody>
</table>

*On the cycle-ergometer. †During the 6 months before and after TMLR.

4. Discussion

The concept of transmyocardial revascularization derives from comparative anatomy studies which demonstrated that the reptilian heart is perfused through vascular channels from the endocardium into the left ventricular wall. Similar sinusoidal communications have been described by Wearns and colleagues [6] in humans, suggesting the presence of a microcirculation directly connecting the ventricle to the myocardium. In the 1970s, Mirhoseini began to use a CO2 laser in an effort to reproduce such channels in animals and then in humans [1,2,4,5]. The encouraging preliminary results prompted clinical trials aimed to verify the efficacy of TMLR in patients with severe angina who are not candidates for other interventional therapies. The major findings of these studies are that TMLR achieves an improvement both in anginal status and exercise tolerance [3,7–9]. However, randomized studies comparing TMLR surgery with medical treatment are needed, to determine the real advantages and limits of this new technique [10]. Despite its clin-
hospitalizations reported by others for TMLR with a CO₂ laser are consistent with the increase in exercise tolerance and the significant reduction of mean angina class and number of hospitalizations reported by others for TMLR with a CO₂ laser. Frazier et al. [3] observed also an improvement in subendocardial perfusion with positron emission tomography (PET) but not with ⁹⁹ᵐTc-sestamibi scan. However, Horvath et al. [9] demonstrated an increased myocardial perfusion at ⁹⁹ᵐTc-sestamibi scan in the lased segments, in 20 patients treated with CO₂ laser and followed-up for 12 months. In contrast, we could not find a significant improvement of myocardial perfusion in the lased segments at 3 and 6 months after the operation. Possibly, a technique with higher sensitivity, such as PET, is needed to appreciate small changes in the amount and transmural distribution of myocardial flow.

In conclusion, TMLR with a holmium laser is a safe procedure, yielding clinical improvement in the majority of patients with severe angina unsuitable for conventional surgical treatment. Despite the gratifying results in terms of anginal status and exercise tolerance, no significant changes in myocardial perfusion could be detected at early follow-up. However, demonstration that TMLR through a thoracoscopic approach is feasible and safe can contribute to a more widespread application of this procedure.

Acknowledgements

We wish to thank Sorin Biomedica, Saluggia, Italy, official distributor of the Eclipse TMLR holmium laser, for providing technological support and in particular Enrico Pasquino and Gioacchino De Giorgi for their continuous help during the study and data collection. This investigation was made possible also by the skillful technical assistance of Rocco Colangelo and Stefano Niccoli.

References


---

Fig. 6. Mean viability score of left ventricular segments treated with TMLR. No significant difference between pre-operative and post-operative values is evident.


