Transmyocardial laser revascularization using the Holium-YAG laser for treatment of end stage coronary artery disease

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Abstract

Objective: Transmyocardial Laserrevascularization (TMLR) is a treatment for end-stage coronary artery disease, that is not eligible for surgery or PTCA. The experience with TMLR using the Holium YAG laser is presented. Methods: Transmyocardial Laserrevascularization (TMLR) was performed in 28 patients with end stage coronary artery disease, using a new Holium YAG Laser. All patients were refractory to a maximum of medical treatment. In 16 patients TMLR was used as the sole therapy with a mean of 28 ± 4 laser created channels (group A). In 12 patients TMLR was combined with coronary artery bypass graft surgery with a mean of 17 ± 2 channels and 1.3 ± 0.2 grafts (group B). Preoperative and postoperative examination included angina classification, exercise test and thallium scan. Results: Postoperative demographics were as follows: (a) age 55–71 years (mean 63.9 ± 6.5 years); (b) Canadian Cardiovascular Society Angina Scale (CCS) mean 3.3 ± 0.5; (c) ejection fraction 35–71% (mean 54 ± 13.7%). All patients had an peri- and postoperative course without major complications and a duration of hospitalization of 8.2 ± 1.9 days. Minor complications were a clinically silent myocardial infarction n = 1, atrial arrhythmia n = 2 and pneumothorax n = 2. A follow-up at 3–12 months was completed in 23 patients (82%). Only one patient died 5 months after surgery (cardiac related death). In all remaining patients CCS had improved with a mean of 1.6 ± 0.3, P < 0.01. The exercise tolerance test (bicycle) improved in 17 patients with a mean 26.5 ± 6.5 watt, P < 0.01. The ejection fraction did not significantly improve. The repeated thallium scan did not show an improvement of perfusion in the lasered area to a significant level. Subjective benefit from the treatment was confirmed by 21 patients. Conclusion: Based on these results it is concluded that TMLR with the Holium-YAG laser is a safe therapy for the treatment of end stage coronary artery disease. The postoperative clinical results are comparable to that achieved with the CO2-laser in terms of reducing angina symptoms and improving exercise tolerance and quality of life. However, relief of symptoms is not correlated to objective findings of cardiac function. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

Transmyocardial revascularization using different laser energy sources has recently gained interest for the treatment of medically refractory angina pectoris in patients who are not eligible for coronary bypass surgery or PTCA. Similar to the blood supply of the snake heart [1], transmyocardial channels were thought to increase the perfusion of the endocardial layer of the myocardium by a direct connection between the left ventricular cavity and intramyocardial sinusoids. Sen and colleagues first brought this concept to clinical use when they reported a new technique of direct myocardial perfusion by the creation of transmyocardial channels by needle acupuncture [2]. Mirhoseini and Cayton [3] introduced laser energy to drill channels through the myocardium to the left ventricular cavity to achieve
direct perfusion of the myocardium with oxygenated blood from the left ventricle. Recently a new Holium YAG (Yttrium Argon Garnet) laser has been introduced for transmyocardial revascularization (TMLR). As opposed to CO₂ lasers the Holium YAG laser emits its energy at a wave length of 2100 nm, which can be conducted through a flexible fiber. A prospective clinical study was started in March 1996, which included a follow up period of 1 year. Patients were either treated with TMLR alone (group A) or in combination with a coronary artery bypass graft to a different myocardial area (group B). Results of the first 28 patients were reported.

2. Materials and methods

From March 1996 to April 1997, 28 patients had transmyocardial revascularization (TMLR) using the Holium YAG Laser (CardioGenesis, Santa Clara, CA). Inclusion criteria for TMLR as the sole therapy were severe angina pectoris class III or IV according to the Canadian Cardiovascular Society (CCS), refractory to medical therapy of at least two antianginal medications on a maximal tolerable dose, ineligible for PTCA or coronary artery bypass grafting (CABG).

Inclusion criteria for TMLR in combination with CABG were demonstrable ischemic reaction in an area of vital myocardium under stress proved by thallium scan. The area had to be ineligible for CABG.

According to these criteria TMLR was performed as the sole therapy in 16 patients (group A) and combined with coronary artery bypass surgery in 12 patients (group B).

2.1. Laser source

The Holium YAG Laser delivers a beam with a wave length of 2100 nm. The R-wave triggered energy delivery is pulsed as a triple burst with 350 μs/pulse of duration. At the tip of the flexible probe the laser beam is focused and delivered with an energy of 2 J/pulse. Tissue ablation is performed by a direct contact of the lens at the tip of the probe with the surrounding tissue.

2.2. Operative technique

Patients of group A were operated using a left anterior lateral or left posterior lateral thoracotomy. TMLR was performed without using cardiopulmonary bypass (CPB). Single lung ventilation was performed in some but not all patients. After lateral thoracotomy through the 4th intercostal space, the pericardium was opened and the target area was identified on the basis of the preoperative angiography and area which has been determined as being ischemic by thallium scan. Laser channels were drilled by direct contact of the lens of the probe with the myocardium but without manual force. To avoid injury laser channels were created in a distance of at least 5 mm to a major coronary artery and in a distance of 1–1.5 cm² to each other.

Patients of group B were operated using a conventional sternotomy and using Cardiopulmonary bypass (CPB). After median sternotomy, opening of the pericardium and cannulation for CPB, coronary artery bypass grafting was performed on the arrested heart using cold antegrade crystalloid cardioplegia. The laser channels were drilled in the same way as described for group A, during reperfusion on CPB.

Postoperative ECG was documented after 6, 12, 18 and 24 h together with CK/CK-MB enzymes. A defined diagnosis of myocardial infarction was made when both criteria were positive. (1) Development of a new abnormal Q-wave not present on the preoperative ECG (Minnesota Code for pathologic Q-waves). (2) Enzymatic changes defined as more than 10% of the ratio of peak CK-MB/peak total CK on three consecutive samples.

According to the protocol, the preoperative and postoperative examination during follow-up included: (a) physical examination; (b) medical history; (c) functional status of angina (classification according to CCS); (d) angina questionnaire (according to The Seattle Angina Questionnaire); (e) ECG: (f) stress ECG (bicycle, 25 watt steps for 2 min each); and (g) stress thallium scan. For stress scintigraphy 90 MBq Ti-201-Cl was administered 4 min after completion of dipyridamole infusion (0.54 mg/kg). Patients had abstained from cardiac related medication and from caffeine and aminophylline. The next day 90 MBq Ti-201-Cl was injected under resting conditions and under full medication. SPET acquisition was performed 10 min and 4 h p.i. by use of a dual-head camera (ADAC, Vertex, USA). Data were reconstructed iteratively with attenuation correction. For semiquantitative evaluation relative count densities were determined in 12 wall segments (anterior, lateral, inferior and septal wall segments in an apical, a middle and a basal short axis slice). For follow-up studies count rates were related to that of a initially well perfused septal wall segment which was not immediately influenced by the surgical treatment. Follow-up examination were performed after 3, 6, 9 and 12 months, respectively.

3. Results

Demographics of all 28 patients, which were comparable between both groups, are depicted in Table 1. The mean preoperative angina class according to CCS was 3.3 ± 0.5 for both groups, 3.5 for group A and 3.2 for group B, respectively. The ejection fraction was
more than 35% in both groups according to the study protocol.
Operative procedures and perioperative results are listed in Table 1.

3.1. Complications

The onset of a pneumothorax in each group was due to a technical failure in one and an incorrect removal of a chest tube in another patient. There was one intraoperative myocardial infarction with a typical increase in cardiac enzymes and changes in ECG but without impaired hemodynamics. There was no hospital death. All 28 patients were discharged home and followed-up for a period of 3 months (n = 23), 6 months (n = 13), 9 months (n = 7) and 12 months (n = 4). A total of 5 patients, who had surgery less than 3 months ago were contacted by telephone. All of them were alive and well.

Table 1
Demographics and perioperative results

Demographics

| Patients | 28 |
| Female | 10 |
| Male | 18 |
| Age range (mean ± S.D.) | 37–78 years (64.5 ± 10.3) |
| CCS (mean) | 3.3 |
| EF range (mean ± S.D.) | 35–71% (52 ± 13.1) |
| Previous CABG | 18 |
| MI | 19 |
| PTCA | 12 |

Perioperative results

Group A (TMLR alone)

- Laser channels: 26 ± 6
- Mortality: 0 (0%)
- Myocardial infarction: 0 (0%)
- Atrial arrhythmia: 1 (6.2%)
- Ventricular arrhythmia: 1 (6.2%)
- Bleeding: 0 (0%)
- Pneumothorax: 1 (6.2%)

Group B (TMLR + CABG): n = 12

- Graft-anastomoses: 1.4 ± 0.2
- LAD: 8 (ITA)
- RCA: 3
- RIM: 2
- RCX: 3
- Laser channels: 17 ± 5
- Mortality: 0 (0%)
- Myocardial infarction: 1 (8.3%) uncertain
- Atrial arrhythmia: 0 (0%)
- Ventricular arrhythmia: 0 (0%)
- Bleeding: 0 (0%)
- Pneumothorax: 1 (8.3%)

Table 2
Follow-up results

Group A (TMLR alone):

| CCS-classification | 1.9 ± 0.3 (pre-Op: 3.2 ± 0.1) |
| EF | 62 ± 11% (no change to pre-Op) |
| Exercise test | 64.4 ± 14.7 W (pre-Op: 37.9 ± 10.3) |
| Thallium scan | no significant change |
| Reduction of angina | 12/14 (85.7%) |
| Reduction of nitrate usage | 12/14 (85.7%) |
| Increase of exercise | 10/14 (71.4%) |
| Subjective benefit | 12/14 (85.7%) |
| Mortality | 2/14 = 14.2% (after 5 and 10 months) |

Group B (TMLR + CABG):

| CCS-classification | 1.2 ± 0.2 (pre-Op: 3.4 ± 0.5) |
| EF | 44 ± 12% (no change to pre-Op) |
| Exercise test | 92.4 ± 14.7 watt (pre-Op: 42.9 ± 10.3) |
| Thallium scan | all improved |
| Reduction of angina | 9/9 (100%) |
| Reduction of nitrate usage | 9/9 (100%) |
| Increase of exercise | 9/9 (100%) |
| Subjective benefit | 9/9 (100%) |

CABG, coronary artery bypass graft; TMLR, transmyocardial laser revascularization; EF, ejection fraction; CCS, Canadian Cardiovascular Society; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; TMLR, transmyocardial laser revascularization.

During follow-up two male patients (group A) died 5 months after surgery with signs of a cardiac related death, which could not be confirmed by autopsy since permission was refused.

The results of follow-up examination are listed in Table 2 and Figs. 1 and 2, respectively. The mean CCS class was 1.9 ± 0.3 for group A. The improvement compared to preoperative (3.5 ± 0.4) was statistically significant P ≤ 0.01. For group B CCS class during the

CABG, coronary artery bypass graft; TMLR, transmyocardial laser revascularization; CCS, Canadian Cardiovascular Society; ITA, internal thoracic artery; LAD, left anterior descendens; RCA, right coronary artery; RIM, intermedious branch; RCX, circumflex artery.

* Area: anterior: n = 9; lateral: n = 8; posterior: n = 5.

* Area: anterior: n = 4; lateral: n = 6; posterior: n = 5.

Fig. 1. Pre- and post-operative angina classification.
follow-up was 1.2 ± 0.3 versus 3.2 ± 0.3 preoperatively 
$P \leq 0.01$. Patients of group A showed an increase of 
exercise tolerance to 64.4 ± 14.7 W after 6 months 
versus 37.9 ± 10.3 watt preoperatively ($P < 0.05$). In 
group B the increase was up to 92.4 ± 14.7 versus 
42.9 ± 10.3 preoperatively ($P < 0.05$). For the postoperative 
thalium scan results, the signal density was compa-
red as percentage of the density of the septal area, 
which was valued as 100%. For group A, during phar-
macological stress there was a decrease of density 67 ± 
17% after 3 and 68 ± 15% after 6 months. Compared 
with the preoperative value of 73 ± 17% this was statis-
tically significant ($P < 0.05$). After 12 months the den-
sity turned to the preoperative value 71 ± 17%. 
However, under resting conditions, density diminished 
irreversibly to 76 ± 16 versus 89 ± 15% preoperatively. 
In group B, the myocardial perfusion increased in the 
bypassed area up to 90 ± 13 versus 80 ± 21% preopera-
tively ($P < 0.05$). In the lasered area there was no 
increase or decrease during stress, 74 ± 18 versus 73 ± 
16% but a diminished density under resting conditions, 
80 ± 16 versus 87 ± 19% ($P < 0.05$), 3 months after 
TMLR. This decrease recovered to the initial values 
after 6 months. Left ventricular function did not change 
significantly in both groups (Table 2).

4. Discussion

In the history of surgical treatment for coronary 
artery disease many attempts have been made to achieve 
direct myocardial perfusion through channels between 
the left ventricular cavity and the intramyocardial sinus-
oids or by a direct implantation of the internal thoracic 
artery into the left ventricular free wall [2,4–10].

Since Kolessov and Favaloro introduced coronary 
bypass surgery and Grünzig introduced coronary angioplasty, 
these two techniques became the golden stan-
dard for the treatment of coronary artery disease. Most 
alternative techniques, which were performed before 
this milestones in medicine were abandoned. With an 
increasing number of patients with diffuse coronary 
artery disease, not amenable to interventional treat-
ments and refractory to medical treatment, there is 
renewed interest in alternative treatment modalities.

Most patients, included in this study, had a long 
history of several treatments including coronary bypass 
surgery and PTCA. Quality of life was limited by the 
recurrence of severe angina and severely impaired exer-
cise capacity. The use of laser energy to create transmyo-
cardial channels has been introduced by Mirhoseini 
and Cayton in 1981 [11]. This concept was based on 
studies done by Sen in the sixties, when he used a 
transmyocardial puncture for immediate myocardial 
revascularization [2]. These channels were thought to 
create a direct connection between the left ventricular 
cavity and the intramyocardial sinusoids mimicking 
direct myocardial perfusion as it is known from snakes 
and some reptiles. The laser energy was thought to 
create transmyocardial channels in an atraumatic way, 
so that long term patency could be expected [12,13]. The 
theory of direct myocardial perfusion through laser 
created channels as the underlying mechanism for the 
clinical improvement after TMLR is still not revok-

Despite the fact that the underlying mechanisms are 
not clarified yet [16], the clinical improvement after 
TMLR has been demonstrated in several clinical trials 
using CO2 lasers [3,12,17–23]. As compared to the CO2 
laser, the Holium YAG laser has some advantages in 
terms of handling. Firstly, the probe is flexible and any 
target area of the myocardium is easily attainable. 
Secondly, the energy is delivered as a pulsed triple burst 
of 350 μs. Usually three to four bursts are needed for 
transmyocardial perforation. This gives more control 
than a high energy one-shot perforation applied with 
the CO2 laser. Thirdly, the energy release is triggered by 
ECG, thus no severe ventricular arrhythmia was ob-
served during the procedure performed without car-
diopulmonary bypass.

Compared to the results of different centers using the 
CO2 laser or the Eximer laser; the results demonstrate 
the same clinical outcome after TMLR. Thus, the clin-
ical benefit is not related to the kind of laser. The 
different depth of acute injury created by the different 
laser energies [24,25] may also be of minor importance, 
since it has to be considered that patency of the channel 
is probably not the underlying mechanism for the clini-

Fig. 2. Pre- and post-operative exercise tolerance test.
cal benefit. Burkhoff and colleges demonstrated angiogenesis not only in the channel remnants but also in the surrounding myocardium as a reaction to the injury [14]. Nevertheless, no significant data are currently available that demonstrate an improved myocardial perfusion by angiogenesis. In contrast to the results of Horvath and colleges, who demonstrated a decrease in the number of segments with reversible perfusion defects in the treated area by a technetium sestamibi scan [21] these improvements could not be demonstrated in the study by using a thallium scan. Moreover, in some patients the early scan after 3 months showed a depression of the signal density in the lasered area compared to the unlasered septum. This depression was normalized after 12 months in most of these patients but only to the level of preoperative signal density. Another interesting observation was, that this signal depression was minor in the patients of group B, in which TMLR was performed in combination with coronary bypass grafting to a different myocardial area. This phenomena may be attributed to better perfusion of existing collateral by the new graft. Although thallium scan may not be sophisticated enough to reflect minor changes in myocardial perfusion, at least in this limited study myocardial perfusion did not increase in the lasered area soon after TMLR but decreased in some patients. Furthermore, there was no correlation between the clinical outcome and the results of thallium scan in the patients. Other mechanisms such as cardiac microinfarction, neuronal ablation or a change of molecular pathways between ischemia and the onset of angina may be responsible for the clinical response in absence of increased perfusion. However, the clinical benefit of TMLR in the treatment of angina pectoris is still important facing otherwise therapy refractory coronary artery disease. As a positive response to therapy was defined by an improvement of two angina classes according to the CCS scale, the overall success rate was 75% (11/12) in patients treated with TMLR alone (group A) and 91.6% (11/12) in patients with a combined treatment of CABG and TMLR (group B). This is reflected by an improvement of exercise tolerance, which improved in both group and was slightly significant, \( P = 0.047 \) in group A and \( P = 0.037 \) in group B. This improvement was confirmed by the subjective benefit of quality of life not only during the time soon after surgery but during the entire duration of follow-up, usually with a slight additional improvement after 6 months.

Furthermore the result of the study demonstrates that transmyocardial laser revascularization is a safe therapy. Despite the severe underlying disease there was no intraoperative death in both groups. The intra- and postoperative course was uneventful apart from one uncertain myocardial infarction without clinical symptoms and two pneumothoraces which were not related to the laser procedure itself. TMLR should be used only in patients with stable chronic angina. The leading symptom of the disease should be angina pectoris rather than dyspnoe or other signs of myocardial insufficiency. In one patient major coronary artery, which supplies the myocardium may increase the safety of the procedure. Since no acute improvement of perfusion after the creation of transmyocardial channels is believed, patients with unstable angina might be at increased risk for the procedure. As such patients were excluded in the study, hospital mortality was low as compared to other reports.

Despite good peri- and postoperative results, two patients of group A, who were nearly symptom free after TMLR died of a cardiac related dead. Thus, some questions remain unanswered. The underlying mechanisms for the release of angina symptoms have been not investigated yet. Based on the results, the patients with end-stage coronary artery diseased are still facing myocardial ischemia after TMLR, even if they do not develop angina. The question is, does TMLR target the ischemic myocardial disease or only the angina symptoms. This leads to the next question, are patients at more risk during exercise if myocardial perfusion is not improved after TMLR but warning symptoms are not developed. If so, this would have an influence on the long term survival after TMLR. The opposite could be true as well. As a result of the improved exercise tolerance, patients may continue exercise if they develop no angina symptoms and repeated myocardial ischemia could be a stimulus for angiogenesis and new collateral vascularization. Thus, myocardial perfusion may improve secondary to TMLR as likewise collateralization is improved during exercise in some patients having peripheral occlusive vascular disease. Based on the results, the maximal tolerable medical treatment should not be reduced after TMLR, even if patients are without angina symptoms.

In summary, the study demonstrates that transmyocardial laser revascularization with the Holium YAG laser is a safe and effective therapy in patients with severe angina pectoris, which is therapy refractory by other means. The benefit is related to a decrease of angina symptoms and an increase of exercise tolerance rather than an improvement of myocardial perfusion or function.

References