Transmyocardial laser revascularization (TMLR) in patients with unstable angina and low ejection fraction

Georg Lutter a,*, Bernward Saurbier b, Egbert Nitzsche c, Frank Kletzin a, Jürgen Martin a, Christian Schlensak a, Christoph Lutz a, Friedhelm Beyersdorf a

a Department of Cardiovascular Surgery, Albert-Ludwigs-University, Freiburg, Germany
b Department of Cardiology, Albert-Ludwigs-University, Freiburg, Germany
c Department of Nuclear Medicine, Albert-Ludwigs-University, Freiburg, Germany

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Abstract

Objective: Does perioperative use of the intraaortic balloon pump (IABP) improve the postsurgical outcome of patients presenting with endstage coronary artery disease, unstable angina and low ejection fraction transferred for transmyocardial laser revascularization (TMLR)?

Methods: TMLR, as sole therapy combined with the perioperative use of an intraaortic balloon pump has been assessed in seven patients with endstage coronary artery disease, unstable angina and low ejection fraction (EF ≤ 35%). Six out of seven patients had signs of congestive heart failure. These patients are compared with 23 patients with endstage coronary artery disease, stable angina and EF > 35%, who were treated with TMLR as sole therapy without the use of IABP. The creation of transmural channels was performed by a CO2-laser. All patients were evaluated by hybrid positron emission tomography (perfusion SPECT and viability PET) and ventriculography preoperatively. Echocardiography, clinical status and hemodynamic assessment by Swan Ganz catheter were performed perioperatively.

Results: The perioperative mortality of this combined procedure (TMLR and IABP) was zero. Three out of seven patients had pneumonia with complete recovery. Swan Ganz catheter examinations showed deterioration of LV-function after TMLR intraoperatively and improvement after 2 h and further after 6 h on ICU (P ≤ 0.05). In contrast, a decrease of LV-function in sole TMLR patients with an EF > 35% has not been observed. Patients with EF < 35% needed the IABP for 2.3 days and moderate dose catecholamines for a mean of 3.0 days. The postoperative EF and resting wall motion score index (WMSI) of all analysed LV segments (evaluated by echocardiography) did not change compared to baseline (EF 31.3 ± 2.6 preop. to 32.8 ± 3.2 postop.; WMSI: 1.75 ± 0.14 at baseline to 1.71 ± 0.17 postop.). The average Canadian Angina Class at the time of discharge decreased from 4.0 ± 0 (baseline) to 2.3 ± 0.5 (P < 0.05) and the NYHA-Index from 3.9 ± 0.3 to 2.7 ± 0.5. No patient had signs of angina pectoris, whereas two patients still had signs of congestive heart failure.

Conclusions: The reported data support our concept to start IABP preoperatively in patients with reduced LV contractile reserve in order to provide cardiac support during the postoperative phase of reversible decline of LV-function induced by TMLR.

Keywords: Lasers; Revascularization; Coronary disease; Intraaortic balloon pump

1. Introduction

Transmyocardial laser revascularization (TMLR) is a new surgical technique of indirect revascularization for patients with symptomatic end stage coronary artery disease refractory to medical therapy, percutaneous transluminal coronary angioplasty (PTCA) or coronary
artery bypass grafting (CABG). TMLR creates transmural channels in ischemic viable myocardium via laser ablation [1]. Multicenter, as well as single center [2,3], reports have documented significant symptomatic improvement in these patients. Results of measurements of regional myocardial perfusion have indicated a significant improved perfusion of the TMLR treated ischemic areas [2,4].

However, the exact mechanism by which TMLR is facilitating these subjective and objective improvements still remains unknown.

Patients with unstable angina and reduced LV-function represent a high risk group for TMLR with significantly higher mortality and morbidity, as compared to stable patients with normal ejection fraction [5,6].

Therefore, this high risk group is considered to be a contraindication for TMLR by some groups. However, patients with reduced LV function and unstable angina are at high risk for fatal acute heart failure and routinely require i.v. medication (heparin, nitroglycerin). This study tested the hypothesis, that the use of an IABP in patients presenting with endstage heart failure and EF < 35% for TMLR may improve the outcome.

2. Materials and methods

The study was approved by the Human Subject Protection Committee. All patients signed informed consent, after the investigative nature of the study, its risks and merits had been explained (Votum No. 21/96).

Between September 1995 and May 1997 TMLR, as sole therapy combined with a peri-operative support of an IABP, was performed in seven patients (mean age 68 ± 4 years, no females) presenting with severe three-vessel coronary artery disease, unstable angina and EF < 35%. In the same time period, TMLR was utilized as sole therapy for 23 patients with endstage coronary artery disease (mean age 67 ± 8 years, 3 females, 20 males), EF > 35%, stable angina, which were not treated with IABP.

Patients were selected for TMLR based on the following criteria:

- severe angina refractory to maximal medical therapy
- viable myocardium (demonstrated by hybrid positron emission tomography, [7])
- coronary arterial diameter < 1 mm (small vessel disease)
- no candidates for PTCA or CABG

In the past medical history of the low EF group (EF < 35%) 7/7 patients had a myocardial infarction, 7/7 underwent previous CABG, 1/7 had PTCA. Their average left ventricular function was 31.5 ± 2.7% (ventriculography). The mean Canadian Cardiovascular Society (CCS) angina class was 4 ± 0, the mean NYHA-index was 3.9 ± 0.3. Seven patients had unstable angina and six out of seven patients had signs of congestive heart failure. They still had angina under iv.-nitrate and heparin-therapy. However, no inotropic support was required preoperatively.

In the EF > 35%-group, 21/23 patients (91%) had a previous myocardial infarction, 20/23 patients (87%) underwent previous CABG, 7/23 patients had PTCA (30%). Their average EF was 44.7 ± 10.9%. The mean CCS angina class was 3.6 ± 0.6, the mean NYHA-index was 3.2 ± 0.5. Fifteen patients (65%) had angina at rest, no patient had signs of congestive heart failure.

2.1. Perioperative evaluation

All patients were evaluated by hybrid positron emission tomography (perfusion SPECT, single photon emission computed tomography and viability PET, fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography, [7]) and ventriculography (to determine EF) preoperatively. Clinical evaluation (preoperatively, preop., and 1 week postop.), hemodynamic assessment using the Swan Ganz catheter (analysis of cardiac output, CO; cardiac index, CI; pulmonary capillary wedge pressure, PCWP; pulmonary artery pressure, PAP; central venous pressure, CVP; mean arterial pressure, MAP; heart rate, HR; preop.; after skin closure, intraop.; 2 h after TMLR, 2 h; 6 h after TMLR, 6 h) and transesophageal (TEE; introperatively) and transthoracal echocardiography (preop. and 1 week postop.; LVEF and resting wall motion analysis) were performed. Regional myocardial wall motion observed during echo-cardiography as assigned by scores of 1 (normokinetic), 2 (hypokinetic), 3 (akinet) or 4 (dysk- inetic). The wall motion score index (WMSI) was calculated by averaging the scores of lased and nonlased segments.

Preoperatively, an i.v.-digital subtraction angiography of the distal aorta and the iliac arteries was performed in the EF < 35% group, to exclude peripheral vascular disease in the area of IABP implantation.

2.2. Operative technique

Preoperatively, an IABP was surgically inserted only in the EF < 35% group. The patients underwent a left anterolateral thoracotomy through the 4th or 5th intercostal space. The pericardium was incised anteriorly or posteriorly (or both) to the phrenic nerve and the pericardial adhesions were dissected (previous CABG). A focusing end-piece coupled to the articulating arm of the 800 W carbon dioxide Heart Laser (PLC Medical Systems, Milford, MA) was brought next to the surgical field. TEE was used to detect the intraventricular microbubbles as a sign of transmural penetration of each pulse. The radiation of the carbon dioxide laser
Table 1
Intraoperative data

<table>
<thead>
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<th>EF &lt;35% group</th>
<th>EF &gt;35% group</th>
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<tbody>
<tr>
<td>Number of channels</td>
<td>28.0 ± 7.8 (15–40)</td>
<td>26.4 ± 10.5 (6–43)</td>
</tr>
<tr>
<td>Number unconfirmed channels</td>
<td>1.7 ± 0.4 (1–2)</td>
<td>0.9 ± 0.20–2</td>
</tr>
<tr>
<td>Pulse energy (J)</td>
<td>42.3 ± 2.8 (35–50)</td>
<td>41.3 ± 4.8 (30–60)</td>
</tr>
<tr>
<td>Pulse width (ms)</td>
<td>46.0 ± 2.9 (40–62)</td>
<td>45.2 ± 3.9 (38–59)</td>
</tr>
<tr>
<td>Regional distribution:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior wall</td>
<td>11.2 ± 3.7 (6–17)</td>
<td>7.7 ± 2.7 (4–20)</td>
</tr>
<tr>
<td>Apical wall</td>
<td>4.2 ± 1.8 (3–8)</td>
<td>1.6 ± 0.4 (2–6)</td>
</tr>
<tr>
<td>Lateral wall</td>
<td>7.2 ± 2.3 (4–12)</td>
<td>9.2 ± 3.1 (5–23)</td>
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<tr>
<td>Inferior wall</td>
<td>3.7 ± 1.2 (2–8)</td>
<td>6.1 ± 1.7 (3–22)</td>
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All values expressed as mean ± S.D. and range in brackets.

was highly absorbed by fatty tissue as well as by water. Hemostasis was ensured with external gaze pressing onto the epicardium. No epicardial suture was necessary.

2.3. Statistics

Comparison of the results was made using an unpaired Student’s t-test. Differences were considered significant at $P < 0.05$. Results are expressed as mean ± S.D.

3. Results

3.1. Intraoperative data

An average of 28.0 ± 7.8 (EF <35% group) and 26.4 ± 10.5 (EF >35% group) impulses were delivered per patient, with 94–95% confirmation by TEE. The intraoperative data are listed in Table 1.

3.2. Mortality

The perioperative mortality in the EF <35% group (TMLR and IABP) was zero. However one patient died on the 33rd post-operative day in a different hospital after he developed a left hemothorax. Anti-coagulation had been stopped and pulmonary embolism occurred 3 days later. The complications are listed in Table 2.

In the EF >35% group, 1/23 patients (4%) died of septicemia on the 23rd post-operative day caused by pneumonia. Another patient of this group died on the 280th post-operative day (late mortality 4%) caused by left heart failure.

3.3. Morbidity

A total of 57% of all patients (of the EF <35% group) were free of complications and three out of seven patients developed pneumonia. The mean duration of ventilation was 91 h (range 15–220 h). After food-aspiration on the normal ward, one patient, with preoperative chronic obstructive pulmonary disease, had to be reintubated after developing pneumonia. No laser-induced arrhythmias occurred. Neither complications related to IABP insertion were observed, nor reinsertion because of hemodynamic instability, was required.

In the EF <35% group, the average stay in the ICU was 6 ± 6 days, the average hospital stay was 16.5 ± 7.0 days.

In the EF >35% group, 5/21 patients (24%) had complications (Table 2). The mean duration of ventilation was 32 h (range 8–422 h). The average stay in the ICU was 3 ± 9 days. The average hospital stay was 12.8 ± 8.7 days.

3.4. Hemodynamic data

Perioperative hemodynamic analyses of the seven patients with EF <35% (Fig. 1 and Table 3.) showed a significant decrease of CI ($P < 0.05$) shortly after TMLR (compared to preoperative value), although an increase of CI after 2 h and significantly after 6 h ($P < 0.05$) could be assessed (preop.: 1.9 ± 0.3, intraop.: 1.5 ± 0.3, 2 h postop.: 2.2 ± 0.6, 6 h postop.: 2.7 ± 0.5 l/min per m²). In this period of time, catecholamines were not further increased. Inotropic support was needed on average for 3.0 ± 2.6 days (operative day: 0.05 ± 0.07, 1.postop. day: 0.05 ± 0.04, 2.postop. day: 0.05 ± 0.06 μg/kg per min nor- or epinephrine).

Table 2
Mortality and morbidity

<table>
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<th>EF &lt;35% group</th>
<th>EF &gt;35% group</th>
</tr>
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<tbody>
<tr>
<td>Mortality: Perioperative (0–30th day postop.)</td>
<td>0/7 (0%)</td>
<td>1/23 (4.3%) (Died of septicemia on the 23rd post-operative day caused by pneumonia)</td>
</tr>
<tr>
<td>Late</td>
<td>1/7 (16.7%) (Died of pulmonary embolism, 33rd postop. day)</td>
<td>1/23 (4.3%) (Died of left heart failure 280th postop. day)</td>
</tr>
<tr>
<td>Morbidity</td>
<td>3/7 (43%): 3 × Pneumonia</td>
<td>5/21 (24%): 2 × Pneumonia, 1 × pleural effusion, 1 × re-thoracotomy for bleeding, 1 × wound infection</td>
</tr>
</tbody>
</table>
In comparison to this low EF group, 23 patients with an EF > 35% treated with sole TMLR showed no decrease of CI shortly after operation (Fig. 1 and Table 3) and needed no inotropic support (preop.: 1.8 ± 0.3, intraop.: 1.8 ± 0.3, 2 h: 2.0 ± 0.6, 6 h: 2.7 ± 0.7 min/m²).

PCWP in the EF < 35% group (preop.: 12.3 ± 4.2 mmHg, intraop.: 15.3 ± 4.9 mmHg) and in the EF > 35% group (preop.: 10.3 ± 3.0 and intraop.: 13.2 ± 6.5 mmHg) did not change. Also, PAP, MAP and CVP did not show any difference in both groups.

The postoperative EF (checked by echocardiography) did not change compared to baseline either in the EF < 35% group (EF 31.3 ± 2.6% preop. to 32.8 ± 3.2% postop., n.s.) or in the EF > 35% group (EF 44.7 ± 10.9% preop. to 43.8 ± 9.8% postop., n.s.). Shortly after TMLR, neither deterioration nor improvement of the EF has been observed in both groups.

3.5. IABP support

The IABP in the EF < 35% group was needed on average for 2.3 ± 2.4 days (range 1–7). In contrast, for patients with EF > 35%, no IABP insertion was necessary.

3.6. Medications

The patients preoperative antianginal medication was continued and adjusted as needed during the postoperative course. Despite the inotropic support, no patient has required increased dosages or types of medications from preoperative levels or regimens.

3.7. Clinical evaluation

The average CCS angina class at the end of their hospital stage decreased from 4.0 ± 0 (baseline) to 2.3 ± 0.5 (P < 0.05) and the NYHA-index from 3.9 ± 0.3 to 2.7 ± 0.5 in the EF < 35% group. The CCS angina class in the EF > 35% group declined from 3.6 ± 0.6 (preop.) to 2.1 ± 0.4 (P < 0.01) and the NYHA-index from 3.2 ± 0.5 to 2.1 ± 0.4 (P < 0.01).

No patient had signs of angina pectoris, whereas two patients still had signs of congestive heart failure in the EF < 35% group (preop.: 6/7 patients).

3.8. Regional wall motion

The resting wall motion score index showed no difference 1 week after TMLR compared to baseline in the lasered and non-lasered LV segments as well as in the low EF group (WMSI: 1.75 ± 0.14 at baseline to 1.71 ± 0.17 postop.) and in the EF > 35% group (WMSI: preop.: 1.39 ± 0.15; postop.: 1.40 ± 0.25). During TMLR, neither deterioration nor improvement of the WMSI has been observed in either group. A significant difference between the two groups in their WMSI could be seen pre- and postoperatively (P < 0.01).

4. Discussion

In our early experience of patients treated with sole TMLR, two patients died 2 h after operation of low
cardiac output, which has been reported elsewhere [8]. These two patients had unstable angina and a very low ejection fraction (EF = 20–25%) preoperatively and showed a significant decline of LV-function postoperatively after TMLR. The high risk of TMLR in patients with reduced EF and unstable angina is also reported by other groups [5,6].

However, this subgroup of patients very often cannot be discharged from the hospital without invasive treatment. We used the surgical strategy of inserting an IABP pre-operatively, since our hemodynamic data in this patient cohort have shown significant decrease in CI for the first hour after TMLR. Seven patients (with unstable angina and 6/7 patients with signs of congestive heart failure, EF ranged from 25 to 35%) were treated in this manner. These patients, with endstage coronary artery disease, had long been inactive due to debilitating angina and congestive heart failure, hence their cardiovascular, musculoskeletal and pulmonary conditions in the perioperative period were severely limited [9]. This may be the reason for these patients being more susceptible to pulmonary infections (3/7 patients with postoperative pneumonia). Two of these three patients (with preoperative chronic obstructive pulmonary disease), who had a pneumonia postoperatively, developed temperature and signs of infection on the day of operation.

Swan Ganz catheter examinations (in sole therapy TMLR with IABP, Fig. 1, Table 3) showed deterioration of LV-function after TMLR intraoperatively and improvement after 2 h and further after 6 h on ICU (P < 0.05). These patients were depended on the IABP for 2.3 days and received moderate dose catecholamines for 3.0 days. They all recovered after TMLR (and their postoperative pneumonia) very well. A decrease CI in sole TMLR patients with an EF > 35% has not been observed.

The reason for this decline in CI, only in cases with low EF immediately after TMLR, remains unclear. An inflammatory reaction and/or edema of the myocardium are possible explanations. Our post-mortem microscopic examinations in human myocardium 2 h postoperatively showed, in addition to a patent channel (diameter 1 mm) and a 1–2 mm rim of carbonization and necrosis, a 1–3 mm zone of myofibrillar degeneration and edema [10]. This additional potentially reversible injury [11] immediately after TMLR could serve as an explanation for the deterioration of LV-contracility shortly after operation. However, other authors did not find this additional MFD-zone in their post-mortem studies in patients treated with the same CO2-laser regimen on the third postoperative day [12] or described this zone to a much lesser extent on the second postoperative day [13]. There might be a reversibility of this MFD and edema zone within 24 h [11–13]. The TMLR-cases with EF > 35% seem to compensate the laser reaction with this reversible injury of MFD and edema because they do not show any reduction of cardiac index shortly after TMLR.

The angina relief occurred immediately after operation, although the functional status in the echocardiographic status did not change [14] and two patients still had signs of congestive heart failure in the low EF group. The average CCS angina class and NYHA-index declined significantly in both groups after TMLR. Almost all clinical studies of TMLR demonstrate this immediate onset of angina relief which cannot yet be explained [2,3,5,6,8,14,15]. Frazier et al. [6] suggested that patients in frank congestive heart failure are less likely to benefit from laser procedure.

Use of the IABP prophylactically prior to cardiac operations for the treatment of unstable angina, stabilization of patients with low cardiac output due to myocardial infarction and of patients with poor left ventricular function is becoming more widespread [16]. The most important limitation of IABP use has been associated with vascular trauma. The incidence of complications ranges from 8.7 to 36% [17,18]. In the above described seven TMLR cases with IABP insertion, no vascular morbidity could be observed. To reduce IABP-related complications, an iv.-digital subtraction angiography is performed preoperatively in patients with EF < 35% (preparing for TMLR) to detect peripheral vascular disease. This is performed routinely in our institution [16,19]. Im- and explantation of the IABP is done surgically, as recommended by others [20].

In conclusion, these data support our concept to start preoperatively intraaortic balloon pump in patients with reduced LV contractile reserve (EF < 35%), in order to provide cardiac support during the phase of reversible myocardial damage induced by TMLR.

Acknowledgements

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References


