Beta-blockade versus Buckberg blood-cardioplegia in coronary bypass operation

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Abstract

Objective: Continuous perfusion of the coronary arteries with β-blocker (esmolol)-enriched normothermic blood during cardiac surgery has been suggested as an alternative technique for myocardial protection. The aim of the present study was to compare the β-blocker technique to Buckberg’s blood cardioplegia during coronary artery bypass grafting (CABG).

Methods: Sixty patients with coronary artery disease were randomly assigned to either the esmolol group (ES, n = 30) or the blood cardioplegia group (BC, n = 30). During aortic cross-clamp ES patients received continuous normothermic coronary perfusion with esmolol-enriched blood. Hearts of the BC group were protected by antegrade cold blood cardioplegia according to Buckberg. We measured left ventricular (LV) contractility using TEE (fractional area of contraction, FAC) and hemodynamic parameters prior to cannulation for cardiopulmonary bypass (CPB), after declamping, and 4 h postoperatively. Myocardial lactate release was measured prior to aortic cross-clamp, during cross-clamp, and after declamping. LV biopsies for determination of heat-shock protein (HSP-70), actin pattern and intercellular adhesion-molecule (ICAM-I) as indicators for structural changes were collected prior CPB, at the end of the aortic cross-clamp period, and prior to weaning off CPB.

Results: There was no significant difference between both groups with respect to grafts and cross-clamp time. ES hearts did not release lactate during cross-clamp. In contrast, BC hearts released significant amounts of lactate. Post CPB FAC and hemodynamics under similar inotropic stimulation showed no difference between groups, whereas at 4 h postoperatively Myocardial lactate release was measured prior to aortic cross-clamp, during cross-clamp, and after declamping. LV biopsies for determination of heat-shock protein (HSP-70), actin pattern and intercellular adhesion-molecule (ICAM-I) as indicators for structural changes were collected prior CPB, at the end of the aortic cross-clamp period, and prior to weaning off CPB.

Conclusion: Our data demonstrate that application of the β-blocker technique during routine CABG was associated with slightly better functional recovery and less structural myocardial alteration as compared with intermittent cold blood cardioplegia, however, both techniques provided equivalent myocardial protection in terms of patient outcome. Future studies are required to investigate if myocardial ischemia minimization by use of the β-blocker technique may be beneficial in compromised hearts.

Keywords: Beta-blocker; Esmolol; Myocardial protection; Blood cardioplegia; Coronary surgery; Intercellular adhesion molecule; Cardiopulmonary bypass

1. Introduction

Cardioplegic arrest is the current standard approach for myocardial protection in coronary artery bypass grafting (CABG). The underlying principle consists of reduction of myocardial energy demand by cardiopulmonary bypass (CPB)-induced cardiac work load reduction, cardiac arrest and hypothermia. However, in severely compromised hearts and in procedures requiring prolonged cross-clamp time protection by cardioplegia may be inadequate. As a result reversible and/or irreversible ischemic myocardial damage may occur [1].

Crystallloid cardioplegia has been shown to be associated
with anaerobic myocardial metabolism and edema formation which leads to impaired cardiac function and prolonged myocardial recovery after cardiac surgery [2–7]. Even blood cardioplegia has been shown to result in impaired left ventricular (LV) function [8–12].

Considering the changing profile of CABG patients with an increased perioperative risk [13–15] the major goal of myocardial protection during CABG should be a further reduction of ischemic periods.

The insight that both above mentioned broadly applied protection techniques show important disadvantages brought us to the technique of continuous perfusion of the coronary arteries with normothermic \(\beta\)-blocker-enriched blood, herewith inducing a hypocontractile, slow beating heart and avoiding ischemia.

This technique was first described by Sweeney and Frazier who applied the ultrashort acting \(\beta\)-blocker esmolol (half-life: 7–9 min) systemically to create surgical conditions on a continuously oxygenated and substrate provided beating heart [16]. The \(\beta\)-blocker technique combines avoidance of ischemia by continuous perfusion with the application of a cardioprotective agent, herewith reducing oxygen demand [17]. In addition, experimental work demonstrated that the persistence of minimal cardiac contraction supports myocardial lymphatic function resulting in reduced myocardial edema formation [18].

In a recent prospective randomized clinical study we demonstrated the superiority of the \(\beta\)-blocker technique in CABG patients compared to Bretschneider’s crystalloid cardioplegia [18]. The purpose of our present study was to compare the impact of the \(\beta\)-blocker technique versus Buckberg’s blood cardioplegia on myocardial protection and postoperative LV function in routine CABG patients.

2. Materials and methods

2.1. Patients

The study design was approved by the University of Cologne Ethics Committee and written informed consent was obtained from each patient during the preoperative interview. Sixty patients, male and female with coronary artery disease were randomly assigned to either the \(\beta\)-blocker, esmolol group (ES, \(n = 30\)) or the blood cardioplegia group (BC, \(n = 30\)). Preoperative values showed no significant difference between groups. Left ventricular (LV) ejection fraction (EF) was measured by preoperative single-plane ventriculography during left heart catheterization (Table 1).

2.2. Anesthesia

Following premedication with flunitrazepam 2 mg per os 1 h prior to transport to the operating area general anesthesia was induced by intravenous sufentanil 1–3 \(\mu\)g/kg body weight, midazolam 5 mg, and pancuronium 0.1 \(\mu\)g/kg body weight and maintained by continuous infusions of propofol: 1.5–2 \(\mu\)g/kg body weight per h and sufentanil: 1.5–2 \(\mu\)g/kg body weight per h. Pancuronium was applied as required.

2.3. Hemodynamic monitoring

Catheters were placed into the radial artery, the central and at least one peripheral vein as well as into the pulmonary artery (Swan–Ganz thermodilution catheter) after endotracheal intubation. Patients were ventilated (Servo 900 C, Siemens) with 50% oxygen in room air in a volume controlled modus: 10–12 respirations/min, 100–150 ml/kg body weight per min. Ventilation was modified in accordance to arterial blood gas analyses. Thereafter, a 5 MHz transesophageal echocardiography (TEE) probe (Vingmed CFM 800 \(^\text{TM}\), Sonotron, Horten, Norway) was positioned into the esophagus. For coronary sinus blood sampling a 5F catheter was introduced into the coronary sinus via the right atrium. To ease coronary sinus blood withdrawal, we cut several holes at the tip of this catheter prior to placement in the coronary sinus.

2.4. Operative procedures

All 60 patients were operated by the same surgeon. Following standard surgical preparation a median sternotomy, preparation of the internal mammary artery and the saphe-

Table 1

Preoperative patient data

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>ES group</th>
<th>BC group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male (n)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66 ± 1.2</td>
<td>64 ± 1.1</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>77.5 ± 1.8</td>
<td>79.6 ± 1.8</td>
</tr>
<tr>
<td>Body surface (m²)</td>
<td>1.9 ± 0.1</td>
<td>1.96 ± 0.1</td>
</tr>
<tr>
<td>Single-/double-/triple-vessel disease</td>
<td>1/5/24</td>
<td>1/27/2</td>
</tr>
<tr>
<td>History of MI (no. of patients)</td>
<td>11/30 (37%)</td>
<td>9/30 (30%)</td>
</tr>
<tr>
<td>Elective/urgent revascularization</td>
<td>26/4</td>
<td>23/7</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>66.3 ± 2.5</td>
<td>68.6 ± 2.6</td>
</tr>
<tr>
<td>LVEDP ≤ 10 mmHg</td>
<td>2/30 (7%)</td>
<td>1/30 (3%)</td>
</tr>
<tr>
<td>LVEDP ≥ 10 mmHg</td>
<td>13 ± 1.0</td>
<td>12.6 ± 1.1</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.9 ± 0.1</td>
<td>0.7 ± 0.1</td>
</tr>
<tr>
<td>(\beta)-Blockers preoperatively (n)</td>
<td>24/30 (80%)</td>
<td>22/30 (73%)</td>
</tr>
</tbody>
</table>

Data are mean ± SEM. MI, myocardial infarction; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end diastolic pressure.
nous vein was performed. Heparin (300 IU/kg body weight) was injected followed by cannulation of the ascending aorta (aortic cannula 6.5 mm, Stöckert Instruments, Munich, Germany) and venous cannulation by a 36/51F two stage cannula (Jostra Medizintechnik, Hirrlingen, Germany) into the right atrium and vena cava inferior. A vent was placed into the left ventricle via the right upper pulmonary vein and left atrium.

Cardiopulmonary bypass (CPB) circuit (HLM-CAPS®, Stöckert Instruments, Munich, Germany) and the membrane oxygenator (Maxima®, Medtronic, Düsseldorf, Germany) were primed with 1500 ml Ringer’s solution, 500 ml oxy-polygelatine (Gelifudol®, Biotest Pharma, Dreieich, Germany), 100 mEquiv. sodium bicarbonate, and 2000 IU heparin. During CPB we maintained a systemic flow of 2.2–2.6 l/min per m². Mean arterial pressure was kept between 50 and 70 mmHg and norfenerfine (Novadral®, Güdecke, Berlin, Germany) was administered as required. Normothermia was kept in both groups.

The aorta was then cross-clamped. After institution of surgical conditions i.e.: hypothermia, bradycardia in the ES group and cardiac arrest in the BC group (for details see below) distal coronary artery anastomoses were performed. Proximal bypass anastomoses were completed after aortic cross-clamp removal. For weaning off CPB in all patients dopamine at 3 μg/kg per min was started and titrated as required to maintain stable hemodynamics. Following decannulation and sternal closure the intubated patients were transferred to the intensive care unit (ICU).

2.5. Myocardial protection in the β-blocker, esmolol-group (ES)

After aortic cross-clamp in 30 patients the coronary arteries were perfused with oxygenated normothermic CPB blood via an aortic root cannula (Medtronic DLP, Grand Rapids, MI) with a pressure monitoring line. Perfusion pressure was kept at 50–70 mmHg. Initially, a bolus of 100 mg esmolol (Brevibloc®, Gensia Europe, UK) was added to the blood followed by continuous esmolol infusion at 10–15 mg/min dependent on the degree of contractility and heart rate. By this method a flaccid and hypocontractile heart, beating at a rate of about 40/min was obtained. Different methods were applied to remove blood from the operating field.

Dependent on the diameter of the coronary arteries which must be greater than 1.5 mm, intravascular shunts (Intravascular arteriotomy cannula®, Medtronic, Grand Rapids, MI) were inserted into the incised coronary arteries to prevent bleeding out of the vessel and to maintain blood flow through the shunt to the peripheral myocardium.

In case of smaller coronary arteries and sufficient retrograde blood flow through the coronary arteries vessel occluders were applied.

In addition, tip suckers, saline rinse, or filtered room air blowers were used to remove blood out of the operating field. After accomplishment of the peripheral anastomoses the aortic cross-clamp was released and the aortic root perfusion discontinued. Hearts returned rapidly to normal heart rate. Patients were then weaned off CPB.

2.6. Myocardial protection in the blood-cardioplegia group (BC)

In accordance with the propositions of Buckberg [19–21] hearts of the other 30 patients were protected by an antegrade cold blood cardioplegia. After aortic cross-clamp we started with an antegrade high potassium cold induction (Dr. F. Köhler Chemie, Alsbach-Hähnlein, Germany), continued with antegrade cold low potassium reperfusion every 20 min, and gave an antegrade warm low potassium reperfusion (hot-shot) prior to reopening of the aortic cross-clamp. Except three hearts which went into ventricular fibrillation, all remaining hearts resumed spontaneous sinus rhythm. Patients were then weaned off CPB.

2.7. Measurements

After median sternotomy and pericardiotomy and prior to aortic cannulation baseline measurements of hemodynamics and left ventricular (LV) contractility as well as metabolic parameters were recorded. Five milliliters of arterial and coronary sinus blood were taken for blood gas analysis and determination of the arterio-coronary sinus lactate difference. A transmural biopsy from a fat free region of the LV anterior wall was collected using a 14G biopsy needle (Tru-Cut®, Baxter Healthcare Corp., Deerfield, IL). Thereafter, CPB and myocardial protection were established as described above. In the β-blocker group, simultaneous arterial and coronary sinus blood collections were performed after each distal anastomosis except the last one. In the blood cardioplegia group simultaneous arterial and coronary sinus blood samples were drawn during each reperfusion period. Following the last distal anastomosis, a second LV needle biopsy was taken. The aortic cross-clamp was removed, and arterial and coronary sinus blood samples were simultaneously drawn at 2 and 5 min, respectively. Prior to weaning off CPB and prior to application of catecholamines a third LV needle biopsy was taken. After separation from CPB and 10–15 min following decannulation hemodynamic and functional parameters as described above were measured, and the last simultaneous arterial and coronary sinus blood samples were collected. The coronary sinus catheter was then removed. Four hours postoperatively the last hemodynamic and functional measurements were performed in the ICU.

2.8. Hemodynamic and left ventricular (LV) contractility parameters

Beside standard hemodynamics including arterial, pulmonary artery, and central venous pressures as well as car-
diac output, we determined LV contractility using transesophageal echocardiography (TEE). LV short-axis images at the mid-papillary level were then recorded for 1 min. The fractional area of contraction (FAC, in %) was derived as average of ten consecutive beats using the following equation [22,23]:

\[
\text{FAC} = \left( \frac{\text{end} - \text{diastolic area} - \text{end} - \text{systolic area}}{100} \right) \times \text{end} - \text{diastolic area}
\]

End-diastolic area was defined as the endocardial area corresponding to the ECG R wave peak, end-systolic area as the smallest systolic endocardial area [22,23].

2.9. LV biopsies

LV biopsies were used to quantify structural myocardial alterations by determination of inducible heat shock protein-70 (HSP-70), intercellular adhesion molecule-I (ICAM-I) expression, and myocardial actin pattern using immuno-histochemical methods.

After cryopreservation with liquid nitrogen, the biopsies were cut into 5 μm slices at –20°C, air-dried, and immunostained [24]. Specimens were then fixed in methanol at –20°C followed by incubation with 0.1% Triton X-100 and 0.01 mol phosphate buffered saline (PBS; pH 7.4) +1 mg/ml bovine serum albumin (BSA). Sections were then incubated with the primary antibody against the inducible HSP-70 (anti-HSP 70 i; dilution 1:200; monoclonal mouse antibody against ICAM-I (CD 54; dilution: 1:200; monoclonal mouse antibody C 92 F 3 A-5, Stress Gen, Victoria, Canada) and anti-mouse IgG antibody; dilution 1:1000; Fc specific, Sigma, St. Louis, MO) was applied and rinsed off using 0.01 mol/l PBS. Finally, the specimens were incubated in 0.01 mol/l PBS.

Actin-pattern was visualized using a FITC-labelled Phalloidin technique [25]. Specimens were cut at 5 μm in a cryostat, mounted, fixed in 3.7% formaldehyde at room temperature, and incubated in 0.01 mol/l PBS (pH: 7.4). Subsequently, 5 × 10⁻¹⁵ FITC-labelled Phalloidin (Sigma, St. Louis, MO) was applied and rinsed off using 0.01 mol/l PBS. Finally, the specimens were incubated in 0.01 mol/l PBS.

Table 2

<table>
<thead>
<tr>
<th>Perioperative patient data</th>
<th>ES Group</th>
<th>BC-Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distal anastomoses</td>
<td>3.1 ± 0.1</td>
<td>3.3 ± 0.1</td>
</tr>
<tr>
<td>IMA use (no. of patients)</td>
<td>28/30 (93%)</td>
<td>26/30 (87%)</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>91.2 ± 5.1</td>
<td>88.8 ± 3.5</td>
</tr>
<tr>
<td>Aortic cross-clamp time (min)</td>
<td>56.3 ± 3.8</td>
<td>52.7 ± 2.1</td>
</tr>
<tr>
<td>Reperfusion time (min)</td>
<td>31.4 ± 3.4</td>
<td>28.4 ± 1.0</td>
</tr>
<tr>
<td>Shunt used (no. of patients)</td>
<td>24/30 (80%)</td>
<td>–</td>
</tr>
<tr>
<td>Esmolol dose (mg)</td>
<td>885 ± 40</td>
<td>–</td>
</tr>
<tr>
<td>IABP (no. of patients)</td>
<td>1/30 (3%)</td>
<td>1/30 (3%)</td>
</tr>
<tr>
<td>Dopamine dose (µg/kg per min)</td>
<td>4.1 ± 0.3</td>
<td>3.9 ± 0.2</td>
</tr>
</tbody>
</table>

Data are mean ± standard error of mean (SEM).
In both groups, myocardial HSP-70 expression increased from baseline (ES: 4.0 \pm 0.3 vs. BC: 3.9 \pm 0.5 spots/174 \mu m^2) to the end of the cross-clamp period baseline (ES: 6.7 \pm 0.5 vs. BC: 5.8 \pm 0.7 spots/174 \mu m^2), and remained elevated at the end of CPB (ES: 5.6 \pm 0.4 vs. BC: 6.3 \pm 0.6 spots/174 \mu m^2). Similarly, myocardial actin band length increased from baseline (ES: 1.07 \pm 0.04 vs. BC: 1.12 \pm 0.05 \mu m) to the end of the cross-clamp period baseline (ES: 1.21 \pm 0.05 vs. BC: 1.39 \pm 0.05 \mu m), and remained elevated at the end of CPB (ES: 1.24 \pm 0.05 vs. BC: 1.31 \pm 0.04 \mu m). There was no difference between both groups for either HSP-70 or actin band length.

Postoperatively, patients of both groups needed inotropic drugs but no difference between groups was noticed. Duration of ventilation, frequency of arrhythmias, time of ICU stay, and mortality did not differ (Table 4).

The maximum postoperative CK values were elevated compared with preoperative values but showed no significant difference between both groups. CK-MB values did not exceed 10% of CK in either group (Table 4).

4. Discussion

These data demonstrate the efficacy of the \(\beta\)-blocker technique with continuous perfusion of the coronary arteries with warm, oxygenated and esmolol enriched blood during routine CABG. Although both myocardial protection techniques resulted in equivalent patient outcome, continuous coronary perfusion resulted in myocardial ischemia minimization, less ICAM-I expression, and was associated with slightly better LV function at 4 h post CPB as compared with intermittent cold antegrade blood cardioplegia.

The \(\beta\)-blocker technique combines continuous coronary perfusion with the application of a cardioprotective agent. In...
comparison to intermittent blood cardioplegia avoidance of ischemia might be a significant advantage of the β-blocker technique. Continuous oxygen supply is demonstrated by markedly reduced lactate concentration differences. High oxygen saturation values in the ES group can be explained by markedly reduced oxygen demand of the myocardium owing to β-blockade, and thus, oxygen supply exceeding demand [17].

Despite hypothermia and complete mechanical inactivity blood cardioplegia did not prevent significant lactate production during aortic cross-clamp time. Although a rapid decrease of lactate production after aortic cross-clamp release was noticed myocardial ischemia and subsequent reperfusion resulting in myocardial stunning is likely. This is supported by the fact that during reperfusion the number of ICAM-I positive myocytes increased in the BC-group, whereas in the ES group ICAM-I expression did not further increase between cross-clamp removal and weaning off CPB. This suggests that ischemia miminization in the ES group minimizes reperfusion injury and subsequent myocardial stunning. In contrast, myocardial ischemia during intermittent blood cardioplegia and subsequent reperfusion results in myocardial stunning which corresponds to the LV functional data measured at 4 h post CPB. These data suggest that aerobic myocardial metabolism during continuous coronary perfusion with warm blood is the major advantage of the β-blocker technique as compared to intermittent cold blood cardioplegia which is in agreement to other studies demonstrating slightly better myocardial protection by use of continuous warm blood cardioplegia in comparison to intermittent cold cardioplegia techniques [7–9,12,17–19].

However, even in the ES-group structural changes demonstrated by elevated postoperative HSP-70 ex-pression and actin band length indicate some degree of myocardial injury. Manipulation of the heart, especially for circumflex artery grafting with even short ischemic periods could explain these data. This is supported by studies showing that brief ischemia periods result in increased HSP-70, ICAM-I and actin-pattern values [26–28]. However, myocardial CK release was similar for both techniques suggesting that structural changes in the BC group were only temporary, and thus reversible, because myocardial stunning is known to recover with time [1].

Continuous β-blocker application for myocardial contractility reduction without arresting the heart is particularly dependent on an ultra-short acting agent such as esmolol with a half-life of 7–9 min [29]. The rapid onset of β-blockade following cross-clamping and esmolol administration allows the surgeon to immediately start anastomoses construction. In addition, the fast elimination of negative ino-

### Table 3

**Hemodynamic data**

<table>
<thead>
<tr>
<th></th>
<th>ES group</th>
<th>p CPB</th>
<th>4 h p CPB</th>
<th>BC group</th>
<th>pCPB</th>
<th>4 h p CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (1/min)</td>
<td>77.7 ± 2.8</td>
<td>98.5 ± 2.6*</td>
<td>66.7 ± 2.0</td>
<td>76.6 ± 1.8*</td>
<td>71.8 ± 1.5*</td>
<td></td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>17 ± 1.0</td>
<td>21.8 ± 1.3*</td>
<td>16.7 ± 0.9</td>
<td>16.6 ± 0.6</td>
<td>17.6 ± 1.0*</td>
<td></td>
</tr>
<tr>
<td>PAP (mmHg)</td>
<td>11.2 ± 0.6</td>
<td>14.4 ± 1.3*</td>
<td>7.5 ± 2.6</td>
<td>92.6 ± 2.8*</td>
<td>94.6 ± 3.0*</td>
<td></td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>7.9 ± 2.4</td>
<td>7.6 ± 1.8</td>
<td>19.6 ± 2.8</td>
<td>19.6 ± 2.8</td>
<td>19.6 ± 2.8</td>
<td></td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>4.8 ± 0.6</td>
<td>6.2 ± 0.5</td>
<td>7.9 ± 0.5*</td>
<td>11.3 ± 0.7</td>
<td>11.7 ± 0.8</td>
<td></td>
</tr>
</tbody>
</table>

Data are mean ± SEM. HR, heart rate; MAP, mean arterial pressure; PAP, mean pulmonary artery pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; BL, baseline; p CPB; post cardiopulmonary bypass; 4 h p CPB; 4 h post cardiopulmonary bypass. *P < 0.05 versus baseline.

### Table 4

**Postoperative patient data**

<table>
<thead>
<tr>
<th></th>
<th>ES group</th>
<th>BC group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-op. mechanical ventilation (h)</td>
<td>18.2 ± 4.2</td>
<td>12.3 ± 0.7</td>
</tr>
<tr>
<td>ICU stay (h)</td>
<td>39.7 ± 5.9</td>
<td>30 ± 2.17</td>
</tr>
<tr>
<td>Hospital mortality</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CK$_{max}$ (IU/l)</td>
<td>371 ± 46</td>
<td>272 ± 29</td>
</tr>
<tr>
<td>CK-MB$_{max}$ (IU/l)</td>
<td>27 ± 4</td>
<td>15 ± 1</td>
</tr>
<tr>
<td>Perioperative MI</td>
<td>2/30 (7%)</td>
<td>1/30 (3%)</td>
</tr>
<tr>
<td>Creatinine$_{max}$ (mg/dl)</td>
<td>1.2 ± 0.1</td>
<td>1.2 ± 0.1</td>
</tr>
</tbody>
</table>

ICU, intensive care unit; CK, creatine kinase; MI, myocardial infarction; criteria: new Q-wave or R-reduction on electrocardiogram, CK-MB > 30, and new LV regional dysfunction [31].

![Graph](https://academic.oup.com/ejcts/article-abstract/15/1/67/450061/20)
tropy and chronotropy following esmolol cessation and cross-clamp removal allows rapid weaning off CPB.

Despite technical refinements such as intracoronary shunt insertion, room air blower, suction, or saline rinse we still observed some limitations of the esmolol technique. First, revascularization of the circumflex artery and their branches usually requires luxation of the heart which sometimes results in aortic insufficiency. As a consequence, myocardial perfusion is impaired which may cause ischemia and subsequent myocardial damage. This is easily detected by a pressure drop in the aortic root and has to be corrected by repositioning the heart [18].

5. Conclusions

The data of the present study show that continuous coronary perfusion with warm esmolol-enriched blood resulted in slightly better functional and structural myocardial protection at 4 h post CABG as compared with intermittent cold blood cardioplegia with terminal hot-shot. However, patient outcome in terms of catecholamine requirement, ICU stay, ventilation time, and hospital mortality were similar for both groups, and thus, both techniques provided equivalent myocardial protection in the present study. As our patients had relatively normal cardiac function, it is possible that myocardial protection with esmolol-enriched warm blood may have a more dramatic impact on clinical outcome in compromised hearts such as those with low ejection fractions as suggested by Sweeney and Frazier’s work [16]. Future studies are required to determine if myocardial ischemia mini-

mization by use of the β-blocker technique may have advantages in patients with poor LV function or in those undergoing surgical revascularization in acute myocardial ischemia as suggested by recent work [16,30].

Acknowledgements

This study was supported by the ‘Köln Fortune’ research fund of the University of Cologne.

References

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Appendix A. Conference discussion

Dr L. von Segesser (Lausanne, Switzerland): If I understood correctly, first, you have a clamp on the aorta in both groups?

Dr Kuhn-Régnier: Yes.

Dr von Segesser: What are the blood flows you use for the esmolol group for the coronaries?

Dr Kuhn-Régnier: Well, the coronary blood flow rates varied between 150 and 300 milliliters, at a pressure of about 60 mmHg.

Dr A. Royse (Melbourne, Australia): I put it to you that your study has shown no more than that continuous blood cardioplegia, compared to intermittent blood cardioplegia has less ischemia. Now, most of us use intermittent cardioplegia because we like to see during the anastomosis unobscured by blood. Can you tell us if your technique can be adjusted for an intermittent cardioplegic technique rather than a continuous one?

Dr Kuhn-Régnier: You mean, if I understand it correctly, why didn’t we use continuous blood cardioplegia?

Dr Royse: Well, your conclusion is that the beta blocker group has less myocardial ischemia. That has got nothing to do with the beta blocker. That has got to do with the fact that you gave continuous blood. Now, we would like to have an intermittent technique so that we could have no blood coming out of the coronary artery whilst doing the anastomosis; but instead of using potassium, are you able to use a beta blocker instead to achieve the same thing?

Dr Kuhn-Régnier: Well, we know from publications in the past that continuous blood cardioplegia, for example, is associated with edema formation and reduced cardiac function postoperatively. This was published in Circulation in 1995. And to induce cardiac arrest is, in our opinion, not ideal because we know that by the contraction of the heart, lymphatic function, and thus, lymphatic flow in the heart is present. So by this way, by slow contracting hearts, we could reduce edema formation.

Dr Royse: If I may, Mr. Chairman, a cross-clamp on the lymphatics would probably stop them working?

Dr Kuhn-Régnier: I did not understand. Sorry.

Dr Royse: Your lymphatics go up the aorta. If you put a cross-clamp on there, you have effectively stopped your lymphatics, surely.

Dr Kuhn-Régnier: The myocardial lymphatics do not go to the aorta; they run through the connective tissue between aorta and superior vena cava. So, if you clamp the aorta, you don’t stop myocardial lymph flow, as we have previously demonstrated. In addition, myocardial lymphatics have connections to the pulmonary lymph system.

Mr H. Gama (Glasgow, UK): I just want to know if you looked into the incidence of atrial fibrillation post-op in your esmolol hearts, if it was lower?

Dr Kuhn-Régnier: No, there was no difference of atrial fibrillation between the groups.

Dr A. Royse: Well, my conclusion is that the beta blocker group has less myocardial ischemia. That has got nothing to do with the beta blocker.