Minimised versus conventional cardiopulmonary bypass: outcome of high-risk patients

Assad Haneya a,*, Alois Philipp a, Christof Schmid a, Claudius Diez a, Reinhard Kobuch a, Stephan Hirt a, Wolfgang Zink b, Thomas Puehler a

a Department of Cardiothoracic Surgery, University Medical Center Regensburg, Franz-Josef-Strauss-Allee 11, D-93053 Regensburg, Germany
b Department of Anesthesiology, University Medical Center Regensburg, Franz-Josef-Strauss-Allee 11, D-93053 Regensburg, Germany

Received 13 November 2008; received in revised form 15 April 2009; accepted 25 May 2009; Available online 19 August 2009

Abstract

Background: Coronary artery bypass grafting (CABG) with extracorporeal circulation (ECC) is the gold standard for surgical coronary revascularisation. Recently, minimised extracorporeal circulation system (MECC) has been postulated a safe and advantageous alternative for multi-vessel CABG. Method: Between January 2004 and December 2007, 244 high-risk patients (logistic Euroscore (ES) > 10%) underwent CABG in our institution. ECC was used in 139 (57%) and MECC in 105 (43%) patients. Demographic data including age (MECC: 73.4 ± 6.4 years), ES (MECC: 19.2 ± 9.8%; ECC: 21.4 ± 11.9%), left-ventricular ejection fraction (MECC: 45.6 ± 16.1%; ECC: 43.1 ± 15.3%), diabetes mellitus (MECC: 14.3%; ECC: 15.1%) and COPD (MECC: 6.7%; ECC: 7.9%) did not differ between the two groups. Preoperative end-stage renal failure was an exclusion criterion. The clinical course and serological/haematological parameters in the ECC and MECC patients were compared in a retrospective manner. Results: Although the numbers of distal anastomoses did not differ between the two groups (MECC: 3.0 ± 0.9; ECC: 2.9 ± 0.9), ECC time was significantly shorter in the MECC group (MECC: 96 ± 33 min; ECC: 120 ± 50 min, p < 0.01). Creatinine kinase (CK) levels were significantly lower 6 h after surgery in the MECC group (MECC: 681 ± 1505 U l−1; ECC: 1086 ± 1338 U l−1, p < 0.05) and the need of red blood cell transfusion was significantly less after MECC surgery (MECC: 3 [range: 1–6]; ECC: 5 [range: 2–9] p < 0.05). Moreover, 30-day mortality was significantly lower in the MECC group compared to the ECC group (MECC: 12.4%; ECC: 26.6, p < 0.01). Discussion: MECC is a safe alternative for CABG surgery. A lower 30-day mortality, lower transfusion requirements and less renal and myocardial damage encourage the use of MECC systems, especially in high-risk patients.

Keywords: Extracorporeal circulation (ECC); Minimised extracorporeal circulation system (MECC); Coronary artery bypass grafting (CABG); EuroScore; High-risk patients

1. Introduction

Coronary artery bypass grafting (CABG) using cardiopulmonary bypass (CPB) is still the most accepted method to treat coronary artery disease surgically. It is a safe and established technique with a mortality rate as low as 3% [1–3]. A systemic inflammatory response syndrome (SIRS) is still associated with CPB, which can result in bleeding, arrhythmias, thrombo-embolism, neurological disorders or organ dysfunction [4,5].

The minimised extracorporeal circulation system (MECC system) is a closed, fully heparin-coated and pre-connected ECC system, consisting of a diffusion membrane oxygenator and a centrifugal pump. The MECC system is able to reduce the negative effects associated with conventional ECC, such as systemic inflammatory reaction, haemolysis, haemodilution, disturbances of blood clotting disorders and postoperative complications [6].

The European system for cardiac operative risk evaluation score (EuroSCORE) was introduced for stratification of operative risk mortality for cardiac surgery [7]. The EuroSCORE has been shown to provide a relevant estimate for short and late outcome after CABG, prolonged length of stay and specific postoperative complications such as renal failure and respiratory failure, as well as the cost of cardiac surgery [8].

In this retrospective study, we analysed the assumed benefits of using the MECC in high-risk patients.

2. Patients and methods

After approval by the local ethics committee, data of 244 patients who underwent isolated CABG with a logistic EuroSCORE >10% from January 2004 to December 2007 were analysed in a retrospective manner. Combined valvular and...
Heparin was administrated (375 IE kg\(^{-1}\)) to initiate cardiac arrest. Blood was saved and collected in an open system with a non-heparin-coated tube system. A two-stage cannula (39–50 F) (Stöckert, Germany) to drain the venous blood from the right atrium, and a 22 F aortic cannula (Maquet, Germany) for the distal ascending aorta were used. The system was primed with 500 ml Gelafundin 4%* (Gelatinepolysuccinat, B. Braun, Melsungen AG, Germany), 500 ml Jonosteril® (Fresenius, Germany) and 200 ml Mannit 20%* (Serag-Wiessner, Germany). Heparin (5000 IE kg\(^{-1}\)) was added to the prime volume. A non-pulsatile HL 30 roller pump (Maquet, Germany) established a blood flow of 2.4–2.6 l min\(^{-1}\) m\(^{-2}\). Minimal rectal temperature was 33.8 °C. During cross-clamping, a single-shot crystalloid of HKT 2.6 l min\(^{-1}\) (Maquet, Germany) established a blood flow of 2.4–2.5 l min\(^{-1}\) m\(^{-2}\). The ACT was accurately controlled every 30 min in all groups. In the standard ECC group, a Quadrox 2000 (Maquet, Germany) or a Hilite 7000 (Medos, Germany) oxygenator was used.

### Table 1
Demographic data and preoperative risk factors.

<table>
<thead>
<tr>
<th></th>
<th>ECC</th>
<th>MECC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>139 (57%)</td>
<td>105 (43%)</td>
<td>0.26</td>
</tr>
<tr>
<td>Age (mean ± SD) (years)</td>
<td>73.3 ± 6.4</td>
<td>73.4 ± 7.4</td>
<td>0.12</td>
</tr>
<tr>
<td>Gender male (%)</td>
<td>92 (66.2)</td>
<td>59 (56.2)</td>
<td>0.12</td>
</tr>
<tr>
<td>BMI (kg m(^{-2}) ± SD)</td>
<td>27.1 ± 3.8</td>
<td>26.3 ± 3.6</td>
<td>0.47</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>21 (15.1%)</td>
<td>15 (14.3%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Hypertension</td>
<td>60 (43.2%)</td>
<td>47 (44.8%)</td>
<td>0.36</td>
</tr>
<tr>
<td>COPD</td>
<td>11 (7.9%)</td>
<td>7 (6.7%)</td>
<td>0.39</td>
</tr>
<tr>
<td>EuroSCORE ± SD (%)</td>
<td>21.4 ± 11.9</td>
<td>19.2 ± 9.8</td>
<td>0.61</td>
</tr>
<tr>
<td>Ejection fraction ± SD (%)</td>
<td>43.1 ± 15.3</td>
<td>45.6 ± 16.1</td>
<td>0.18</td>
</tr>
</tbody>
</table>

BMI: body mass index; COPD: chronic obstructive pulmonary disease; ns: not statistically significant.

The patients were divided into two groups according to the operative technique employed:

**CABG with standard ECC and cardioplegia (group I) [n = 139 (57%)]:**

The extracorporeal circuit of the standard ECC consisted of an open system with a non-heparin-coated tube system. A two-stage cannula (39–50 F) (Stöckert, Germany) to drain the venous blood from the right atrium, and a 22 F aortic cannula (Maquet, Germany) for the distal ascending aorta were used. The system was primed with 500 ml Gelafundin 4%* (Gelatinepolysuccinat, B. Braun, Melsungen AG, Germany), 500 ml Jonosteril® (Fresenius, Germany) and 200 ml Mannit 20%* (Serag-Wiessner, Germany). Heparin (5000 IE kg\(^{-1}\)) was added to the prime volume. A non-pulsatile HL 30 roller pump (Maquet, Germany) established a blood flow of 2.4–2.6 l min\(^{-1}\) m\(^{-2}\). Minimal rectal temperature was 33.8 °C. During cross-clamping, a single-shot crystalloid of HKT 2.6 l min\(^{-1}\) (Maquet, Germany) established a blood flow of 2.4–2.5 l min\(^{-1}\) m\(^{-2}\). The ACT was accurately controlled every 30 min in all groups. In the standard ECC group, a Quadrox 2000 (Maquet, Germany) or a Hilite 7000 (Medos, Germany) oxygenator was used.

**CABG with MECC and cardioplegia (group II) [n = 105 (43%)]:**

The MECC is a closed system without contact of blood with air. The components of the system included a membrane oxygenator (Quadrox D, Maquet, Germany), a centrifugal pump, a table line (3/8 in., 180 cm), a venous two-stage cannula (32–40 F), an aortic cannula (21 F) as well as a 1.000-ml bag with sodium chloride. The bag was used to fill the system and to substitute the volume during perfusion. A left-ventricular vent was implanted into the ascending aorta. A \(p_O_2\) sensor was integrated into the arterial line. The tube set was pre-connected and completely coated with heparin. Therefore, the dose of heparin was reduced to 125 IE kg\(^{-1}\) and an ACT of 250–300 s was deemed sufficient. The MECC system was primed with 300 ml Gelafundin 4%*, 200 ml Jonosteril® and 100 ml Mannit 20%*. No heparin was added to the prime volume. Minimal rectal temperature was 33.8 °C. Apart from Calafiore’s blood cardioplegia, MECC patients received nearly normotherm conditions during the procedure. Blood was saved only with Cell Saver.

During CPB grafting, both systems were routinely controlled for pump flow, mean arterial pressure (MAP) and systemic vascular resistance (SVR). Measuring dates were recorded at three different time points: M1 refers to the start of CPB, M2 to 20 min after aortic cross-clamping (ACC) and M3 to a time point immediately after the release of ACC. In both groups, serial blood samples were taken preoperatively (T0), as well as 30 min (T1) and 6 h (T2) postoperatively.

### 2.1. Statistical data analysis

Statistical analysis was performed using the SPSS 15.0 software (SPSS, Chicago, IL, USA) and Statas 10 SE (Stata, College Station, TX, USA). Normal distribution was assessed by Lilliefors Modification of the Kolmogorow-Smirnow test. Values of continuous data are presented as mean ± SD or as median (range) when appropriate. Categorical variables are displayed as frequency distributions (n) and simple percentages (%). Univariate comparison between the groups for categorical variables was made using the chi-square and the Fisher’s exact tests when appropriate. Logistic regression helped to examine the relationship between the outcome variable mortality and potential risk factors. Statistical significance was considered when \(p < 0.05\).

### 3. Results

#### 3.1. Demographic data

Patients’ characteristics were similar in both the groups. As shown in Table 1, demographic data did not differ significantly between the two patient groups, particularly for age (ECC 73.3 ± 6.4 years, MECC 73.4 ± 7.4 years; \(p = ns\)), EuroSCORE (ECC 21.4 ± 11.9%, MECC 19.2 ± 9.8%, \(p = ns\)) and preoperative left-ventricular ejection fraction (ECC 43.1 ± 15.3%, MECC 45.6 ± 16.1%, \(p = ns\)). In addition, there was no difference between the two groups regarding preoperative risk factors (e.g., diabetes mellitus, hypertension, COPD and obesity) (Table 1).

#### 3.2. Clinical data

The number of distal anastomoses and the type of grafts were similar in both the groups (ECC 2.9 ± 0.9%, MECC 3.0 ± 0.9%, \(p = ns\)). The mean aortic cross-clamp (ACC) time was 55 ± 23 min in the ECC group, and 52 ± 18 min in the MECC group. Despite a nearly similar number of distal anastomoses, the extracorporeal circulation time was significantly shorter for MECC patients (96 ± 33 min) in contrast to ECC patients (120 ± 50 min; \(p < 0.001\)). During ECC, the monitoring of mean arterial pressure (MAP) and
systemic vascular resistance (SVR) revealed significantly higher values in MECC ($p < 0.001$). The pump flow as a determinant of SVR also proved to be significantly lower in minimised systems ($p < 0.001$) (Figs. 1—3). Thus, minimised systems allow improved perfusion with higher MAPs and SVRs during CPB with a significantly reduced pump flow compared to conventional systems.

After surgery, the need for mechanical ventilation was shorter in MECC patients as compared with patients who were operated upon with ECC ($p = ns$). Though there was no significant difference in postoperative pleural drainage among the groups, the transfusion of packed red blood cells was significantly lower in the MECC group (3; range: 1—6) as compared to ECC group (4; range: 2—9) ($p < 0.05$). The transusions of fresh frozen plasma (FFP) were also significantly lower in the MECC group (3; range: 0—7) as compared to ECC group (6; range: 0—12) ($p < 0.05$). The ICU and the hospital stay were similar in both the groups.

The 30-day mortality in the MECC group (12.4%) was significantly lower compared to the ECC group (26.6%) ($p < 0.01$) (Table 2). However, we could not demonstrate that ECC was an independent risk factor for mortality in our study (Table 3).

### 3.3. Serological data

Postoperatively, the concentration of creatinine kinase (CK) in the MECC group was significantly lower at T1 ($545 \pm 1203$ vs $849 \pm 1271$ U l$^{-1}$, $p < 0.01$) and at T2 ($681 \pm 1505$ vs $1086 \pm 1338$ U l$^{-1}$, $p < 0.01$) compared to the ECC group. In addition, the MECC group showed significantly lower concentrations of CK-MB $106 \pm 142$ vs $161 \pm 236$ U l$^{-1}$ ($p < 0.01$) in the ECC group at T1 and $134 \pm 309$ vs $192 \pm 183$ U l$^{-1}$ ($p < 0.01$) at T2 postoperatively. Patients in the ECC group had significantly higher postoperative levels of creatinine at T1 and T2. Furthermore, at discharge, the creatinine levels increased significantly.
Table 4 Serological data.

<table>
<thead>
<tr>
<th></th>
<th>ECC</th>
<th>MECC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK preoperative</td>
<td>330 ± 643</td>
<td>387 ± 1005</td>
<td>0.44</td>
</tr>
<tr>
<td>CK postoperative 30 min</td>
<td>849 ± 1271</td>
<td>545 ± 1203</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CK postoperative 6 h</td>
<td>1086 ± 1338</td>
<td>681 ± 1505</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CK-MB preoperative</td>
<td>65 ± 87</td>
<td>69 ± 78</td>
<td>0.97</td>
</tr>
<tr>
<td>CK-MB postoperative 30 min</td>
<td>161 ± 236</td>
<td>106 ± 142</td>
<td>0.008</td>
</tr>
<tr>
<td>CK-MB postoperative 6 h</td>
<td>162 ± 183</td>
<td>134 ± 209</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lactate (mg dl⁻¹) Preoperative</td>
<td>21 ± 21</td>
<td>19 ± 28</td>
<td>0.23</td>
</tr>
<tr>
<td>Postoperative 30 min</td>
<td>51 ± 44</td>
<td>32 ± 37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Postoperative 6 h</td>
<td>55 ± 42</td>
<td>39 ± 47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum</td>
<td>40 ± 37</td>
<td>26 ± 32</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Creatinine (mg dl⁻¹) Preoperative</td>
<td>1.5 ± 0.9</td>
<td>1.3 ± 0.5</td>
<td>0.39</td>
</tr>
<tr>
<td>Postoperative 30 min</td>
<td>1.4 ± 0.7</td>
<td>1.2 ± 0.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Postoperative 6 h</td>
<td>1.5 ± 0.7</td>
<td>1.2 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>At discharge</td>
<td>1.7 ± 0.9</td>
<td>1.4 ± 0.7</td>
<td>0.002</td>
</tr>
</tbody>
</table>

CK: creatine kinase; CK-MB: creatine kinase isoenzyme MB.

(ECC group 13%, MECC group 7%). The levels of serum lactate at T1 (51 ± 44 vs 32 ± 37 mg dl⁻¹, p < 0.05) and at T2 (55 ± 42 vs 39 ± 47 mg dl⁻¹, p < 0.05) were significantly higher in the ECC group compared with the MECC group (Table 4).

4. Discussion

CABG with the help of cardiopulmonary bypass (CPB) is an established, safe and effective procedure for coronary revascularisation. The CPB is always associated with a systemic inflammatory response syndrome (SIRS) characterised by complement activation and the release of several cytokines and vasoactive substances, which consecutively promote bleeding, arrhythmias, thrombo-embolism and endothelial dysfunction [4,5]. The main reason for the development of SIRS is the contact between the blood and the non-endothelial cell-coated artificial surfaces of the oxygenator and the blood lines [9,10].

Successful CABG for multi-vessel disease with the aid of the MECC system, that is, with minimised CPB, was first described by our group in 2004. We could demonstrate that the MECC system can well serve as an alternative to the standard ECC [11]. In this system, the priming volume can be reduced, preventing haemodilution. The entire circuit is heparin-coated for maximum biocompatibility, the blood—air interaction is eliminated and blood is suctioned through a cell-saving device, and washed before re-transfusion into the patient. In the current study, use of MECC resulted in significantly lower need of transfusion of packed red blood cells and fresh frozen plasma (FFP).

While the number of distal anastomoses in the MECC and ECC group was similar, duration of CPB and aortic cross-clamping were significantly lower in the MECC group due to the lacking necessity of a regular reperfusion period. We found that serum lactate levels were significantly higher in the ECC group postoperatively at T1 and T2. Though the interpretation of elevated lactate concentrations is limited by several confounding variables, measurement of serum lactate levels is widely used to assess the adequacy of tissue perfusion. Based on regional blood flow and lactate exchange measurements, Takala et al. stated that hyperlactataemia after cardiac surgery is a sign of inadequate or marginal tissue perfusion of the hepatosplanchnic region, as well as other tissues [12].

Furthermore, CK levels after MECC procedure were lower as compared with ECC procedures, indicating less myocardial damage and better organ and tissue perfusion as described by Puehler et al. [13].

Finally, we found that CK and CK-MB levels were also significantly reduced at T1 and T2 in the MECC group. In the MECC, the heart is not completely unloaded during the procedure and persistent coronary flow is observed in the majority of patients. This minimal, residual perfusion of the arrested heart needs to be elucidated, but it could be an explanation for improved myocardial protection because it completely eliminates the presence of air in the coronary system.

In our study, we could demonstrate a significantly lower 30-day mortality rate for MECC patients when compared with the ECC group (26.6% vs 12.4% p < 0.01).

In conclusion, the MECC is a safe alternative for ECC for CABG surgery. A lower 30-day mortality, lower transfusion requirements and less renal and myocardial damage may further promote the use of MECC systems, especially in high-risk patients.

5. Limitations

Our study is a retrospective analysis of data from a single centre. The patient groups are not randomised or blinded for the used CABG technique because the surgeons determine the methodology based on their preferred technique.

References


