Minimized extracorporeal circulation system in coronary artery bypass surgery: a 10-year single-center experience with 2243 patients

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Abstract

Objective: Coronary artery bypass grafting (CABG) is the gold standard for the surgical therapy of multivessel coronary artery disease. To reduce the side effects, associated with standard extracorporeal circulation (ECC), a concept of minimal extracorporeal circulation (MECC) was devised in our center. We report on our 10-year experience with the MECC for coronary revascularization. Methods: From January 1998 to August 2009, 2243 patients underwent CABG with MECC in our center. In a retrospective observational study, we analyzed indication, preoperative patient co-morbidity, postoperative clinical course, and perioperative outcome of all patients operated on with MECC. Furthermore, the risk factors for mortality in the MECC group were assessed. Results: Patients showed a mean logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) of 4.5 ± 0.1%. The mean age of the patients was 66.8 ± 9.1 years. The overall 30-day mortality after CABG with MECC was 2.3%, ranging from 1.1% for elective to 13.0% for emergent patients and was significantly better than standard ECC. Only 15.3% (n = 344) of patients with MECC required intraoperative blood transfusion. Postoperative catecholamine support, red blood cell transfusion, need for hemodialysis, release of creatinine kinase, incidence of stroke, and postoperative delirium were low after MECC revascularization. Ejection fraction below 30% (odds ratio (OR): 5.1), emergent operation (OR: 9.4), and high-dose catecholamine therapy (OR: 2.6) were associated predictors for mortality. Conclusion: MECC until now is an established concept and has become an alternative for ECC in routine CABG in our center. The use of the MECC system is associated with low mortality and conversion rate. Excellent survival rates and low transfusion requirements in the perioperative course were achieved.

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1. Introduction

In modern surgical practice, several techniques are suitable to perform risk-adjusted coronary artery bypass grafting (CABG). Conventional extracorporeal circulation (ECC) is sometimes associated with deleterious side effects, such as systemic inflammatory response syndrome and coagulation disorders that lead to end-organ failure and a certain postoperative mortality and morbidity [1]. Although the outcome improved with changes in pump, oxygenator, and cardioplegia techniques, off-pump surgery gained wide acceptance as an alternative for ECC revascularization [2]. However, recent studies assumed incomplete revascularization and less satisfactory results in the long-term course after off-pump revascularization [3].

Over the past 10 years, a concept of minimized ECC (MECC) was devised in our institution with the aim of reducing the side effects and strengthening the advantages of standard ECC [4]. MECC is a fully Bioline® (Maquet Cardiopulmonary, Hirrlingen, Germany)-coated, preconnected closed-tube system completely avoiding blood–air contact. Biocompatible MECC components consist of a diffusion membrane oxygenator and a centrifugal pump. Previous studies demonstrated a decreased inflammatory response and reduced myocardial damage after CABG, as well as lower transfusion requirements [5]. Moreover, it was shown that MECC may well serve as an alternative to ECC and off-pump CABG [6].

We report our single-center 10-year experience with the MECC system in CABG surgery.

2. Methods

2.1. Patients and study design

From January 1998 to August 2009, a total of 2243 patients underwent CABG with MECC in our institution. Beating-heart surgery with MECC was performed in 225 (10.1%) patients. No restriction toward patient selection and data collection was
done. All relevant patient data were extracted from the hospital database after approval by the local ethics committee. Predicted perioperative mortality was calculated with the European System for Cardiac Operative Risk Evaluation (EuroSCORE) [7]. Indication for CABG was established on the basis of current published guidelines [8]. Emergent patients were operated upon immediately, and urgent patients were operated within 24 h after admission.

All serological parameters were obtained at three different time points: preoperative (T0), 30 min after arrival to the intensive care unit (ICU) (T1), and 6 h after surgery (T2). Hemodynamic parameters were retrieved from the anesthesiologists’ and perfusionists’ protocols.

In this retrospective observational study, in-hospital mortality and 30-day mortality rates were calculated. To compare the primary outcome of mortality to standard ECC, a EuroSCORE-matched collective of the latter \((n = 1685)\) was compared with MECC patients. Intra-operative data (number of distal anastomoses, extracorporeal clamp- and reperfusion time, and hemodynamic parameters), serological parameters (creatinine kinase (CK), lactate, hemoglobin, and serum creatinine), and data from the ICU (ventilation time, use of blood components, catecholamine dosage, drainage loss, and ICU stay), as well as patient’s in-hospital course (postoperative dialysis, and in-hospital stay) were analyzed.

### 2.2. Patient selection for MECC revascularization

In general, there were no restrictions toward MECC. According to our center’s policy, every patient is operated with MECC, if service capacity is not exhausted. Because of the fact that the MECC is a closed perfusion system, which makes it unable to unload the heart, the only contradiction for the MECC system was severe aortic insufficiency. However, there are some restrictions to MECC, such as high body mass index (BMI) \((>35 \text{ kg m}^{-2})\), terminal renal insufficiency, and redo cases where the decision whether to use the MECC system or not was up to the surgeons’ and perfusionists’ preference.

### 2.3. Extracorporeal techniques

The MECC is a closed miniaturized bypass system without blood-air contact. The components include a membrane oxygenator (Quadrox D, Maquet, Germany), a centrifugal pump (Rotaflo, Maquet, Germany), a preconnected Bioline® (Maquet, Germany)-coated tubing system as well as an arterial and venous cannula. Priming was achieved with up to 500 ml of crystalloid solutions \((20\% \text{ Mannitol/Serag-Wiesner, Germany; Perfluflac® solution, B. Braun, Germany)}\). Because of the reduced artificial surface of less than 3 m², heparinization was lowered to 125 U kg⁻¹ aiming at an activated clotting time of 250–300 s. All patients received Calafiore’s blood cardioplegia for cardiac arrest. A total of 225 (10.1%) patients were operated with the beating-heart technique assisted by MECC.

### 2.4. Surgical and anesthesiologic technique

A median sternotomy approach was performed in all patients. Patients were handled with the same anesthesiologic and hemodynamic protocol before and during MECC. The target mean arterial pressure at cardiopulmonary bypass (CPB) ranged between 50 and 60 mm Hg with a cardiac index of about 2–3 l min⁻¹ m⁻². In case of beating-heart surgery with MECC, stabilization and rotation of the beating heart was then achieved by the Acrobat V® and Xpose 4® system (Maquet Cardiopulmonary, Hirrlingen, Germany). Coronary anastomoses with beating-heart technique were performed with different-sized Axius® intracoronary shunts (Guidant Corporation, Indianapolis, IN, USA). All CABG procedures were performed under normothermia.

### 2.5. Statistical analysis

Statistical analysis was performed using the SPSS 16.0 software (SPSS, Chicago, IL, USA). After an overall analysis of the entire MECC patient cohort, normal distribution was assessed by Lilliefors’ modification of the Kolmogorov—Smirnov test. Continuous data are presented as a mean ± standard deviation, or as a median (range), where appropriate. Categorical variables are displayed as frequency distributions (n) and simple percentages (%).

Univariate analysis of variance (ANOVA) with a post-hoc Sheffé test was performed for specific differences between the groups for normally distributed continuous variables and with the Kruskal–Wallis test, followed by the Mann–Whitney U-test for not normally distributed continuous variables. Univariate comparison between the groups for categorical variables was made using the \(\chi^2\) and Fisher’s exact test when appropriate. Statistical significance was considered when \(p \leq 0.05\).

To analyze several preoperative risk factors, odds ratios (ORs) plus 95% confidence intervals (CIs) were calculated. The ORs were defined as the probability that an event will occur divided by the probability that the event will not occur. CIs that cross 1.0 have not been considered statistically significant.

### 3. Results

#### 3.1. Demographic data (Table 1)

From January 1998 to August 2009, a total number of 2243 patients underwent CABG with MECC in cases of coronary artery disease with elective (55.5%), urgent (35.9%), and emergent (8.6%) indications. The main reason for emergent CABG was acute myocardial infarction (7.6%), troponin-t (TNT) positive coronary syndromes (11.6%), and unstable angina pectoris (17.7%). There were 1668 (74.3%) male and 575 (25.7%) female patients with a mean age of 66.8 ± 9.1 years.

The mean logistic EuroSCORE for all MECC and ECC patients did not differ significantly \((\text{MECC: } 4.5 \pm 0.1\%; \text{ ECC: } 4.1 \pm 0.2\%; p = 0.13)\). Mean ejection fraction (EF) was 60.3 ± 15.1%. Only 38 (1.7%) patients had prior open-heart surgery and six (0.3%) patients were dependent on dialysis.

During the observation period, the number of cases with coronary revascularization with MECC increased continuously from 121 in the beginning of 1999 to a maximum of 551 cases in 2007 (Fig. 1). Although nearly twice as many patients were operated upon with the MECC system in 2009 in comparison...
with conventional ECC, numbers did not increase further due to the saturation of service capacity.

### 3.2. Intra-operative course

Patients received 3.0 ± 0.9 bypass grafts, and in 2028 (90.4%) patients, the left internal thoracic artery was used for the left anterior descending artery. In 44 (2.0%) patients, the right internal thoracic artery and in 78 (3.5%) patients the radial artery was used for bypass grafts. Extracorporeal circulation time was 82.4 ± 28.3 min with a cross-clamping time of 49.3 ± 17.5 min. The median total dosage of epinephrine during CPB was 0.2 mg (0.0; 1.0) per patient to reach the mean target arterial pressure. A median total amount of 300 ml (300; 600) of red blood cells (RBCs) was administered in only 344 (15.3%) patients during CABG. From January 1998 to August 2009, the perioperative inotrope therapy did not change in quality and quantity. Postoperative stabilization of blood pressure was possible with dobutamine at a low-dose regime below 20 mg h\(^{-1}\). High dobutamine dosages above 20 mg h\(^{-1}\) were mandatory in 10 (0.5%) patients. Left-ventricular support by intra-aortic balloon pump counterpulsation (IABP) was mandatory in 38 (1.7%) patients with a median support time of 3.9 ± 5.8 days.

### 3.3. Outcome and perioperative course (Table 2)

During the observation period, the overall 30-day mortality rate was 2.3% for the MECC group. This was significantly better in comparison to the standard ECC. In the elective group, 14/1245 (1.1%) patients and in the urgent group, only 13/807 (1.6%) patients died within 30 days. In contrast, patients of the emergent group showed a considerably higher 30-day mortality rate of 13% (25/191) \(p < 0.001\) and did not differ from the standard ECC outcome (Table 3). During the observation period, the mortality rate remained stable \(p = 1.0\), despite a significant increase of the median logistic EuroSCORE of the patients up to 5% \(p < 0.05\) (Fig. 2).
Postoperative bronchopulmonary infection occurred in 80 (3.6%) patients. The median stay in the ICU was 1.0 (1.0; 2.0) days. The incidence of postoperative myocardial infarction after coronary surgery was 1.8%. Postoperative cerebrovascular accidents appeared in 52 (2.2%) patients. A total of 45 (2.0%) patients suffered from postoperative neurocognitive disorders. Temporary dialysis due to postoperative renal failure was required in 10 (0.5%) patients. As a result of the uncomplicated course, patients could be discharged from hospital after a median stay of 10.0 (8.0; 13.0) days.

### 3.4. Risk factors for in-hospital mortality (Table 4)

Several risk factors associated with mortality could be identified, especially emergent operation (OR: 11.3; 95% CI (6.41—19.9)), revision and re-operation (OR: 9.4; 95% CI (3.44—25.8)) and an EF below 30% (OR: 2.6; 95% CI 2.6—9.93). In the group with an EF below 30% 12/122 (9%) patients died, whereas only 22/431 (4.9%) patients died in the group of an EF of 40—60%. Critical ill patients with a EuroSCORE above 10% died in 10.4% (20/192 patients) of the cases, whereas only 0.6% (7/1181 patients) with a EuroSCORE from 0% to 3% died.

### 3.5. MECC as a beating-heart procedure

A total of 225 (10.0%) patients underwent CABG as beating-heart procedure on MECC (bhMECC). EuroSCORE for these patients was 4.7 / 0.2%. Special indications for bhMECC procedure were re-operations and revisions (7.1%), acute myocardial infarction (9.8%), reanimation and cardiogenic shock (9.8%), severe calcified aorta (2.7%), heparin-induced thrombocytopenia type II (0.9%), and Jehovah’s Witness (0.9%). This group includes 180 (80.0%) elective and 45 (20.0%) emergent patients (Table 5). Patients received 2.6 / 0.8 bypass grafts with an ECC time of 88.9 / 35.9 min. Mean EF of the patients was 59.9 / 19.2%. Total mortality rate for those patients was 8.0%, whereas 2 (0.9%) patients died in the elective and 16 (7.1%) patients died in the emergent group (Table 5). The incidence of postoperative stroke in the bhMECC group was 1.8% and the incidence of postoperative neurocognitive disorders was 3.1%. Four patients (1.7%) of the bhMECC group suffered from postoperative renal insufficiency and dialysis. The emergent patients, in particular, had a significantly better outcome in the bhMECC (7.1%) group compared with the MECC (13%) group (p = 0.0008). In the elective group, there was no difference between the mortality rate of bhMECC (0.9%) and MECC (1.1%) (p = 1.0).

### 3.6. Conversion from the MECC system

In only eight (0.4%) patients, conversion from the MECC to standard ECC was necessary. In two patients, MECC with an arrested heart was converted to bhMECC due to technical
problems. In one case, the oxygenator occluded and, in another case, the driving unit failed several times during the revascularization. In six patients (one aortic dissection during cannulation, three ruptures of the right atrium, one severe bleeding during re-operation, and one necessity of aortic-valve replacement), surgical problems led to conversion from MECC to standard ECC procedure. No patient (0/8) died after conversion to standard ECC.

### 3.7. Biochemical/serological parameters

In the MECC patients, the preoperative hemoglobin value was 12.7 ± 1.6 g dl⁻¹ on average. During surgery, the hemoglobin values remained stable (minimum 10.1 ± 1.6 g dl⁻¹ and maximum 11.1 ± 1.4 g dl⁻¹), only 15.3% of patients received packed red blood cells (PBRC). In the ICU, only 48.6% of the patients’ received PBRC to maintain stable hemoglobin values (T0: 10.5 ± 4.9 g dl⁻¹; T1: 10.6 ± 5.9 g dl⁻¹). The median maximum perioperative lactate level (12.0 (10.0; 15.0) g dl⁻¹) was in the same range as the preoperative lactate level (10.0 (8.0; 12.0) g dl⁻¹), that is, lactate levels were stable throughout the perioperative time (T0: 10.0 (7.3; 14.0) g dl⁻¹) and T1 (11.0 (8.0; 17.2) g dl⁻¹). CK increased at T1 (121.0 (79.0; 177.0) U l⁻¹) and T2 (203.0 (131.0; 307.0) U l⁻¹). The rate of creatinine kinase—MB (CK—MB) fraction at T1 (24.7 (18.0; 38.0) U l⁻¹) and T2 (18.0 (13.0; 27.0) U l⁻¹) did not change in the postoperative course. Postoperative creatinine levels remained in the same range at T1 and T2 prior to the surgery too (Table 6).

### 4. Comment

The development of modern and risk-adjusted concepts for complete and safe revascularization for patients suffering coronary artery disease should be the main goal in CABG surgery. Therefore, minimizing the surgical trauma and the side effects related to ECC are a desirable future approach. In our current analysis of 2243 MECC patients, we demonstrated again that MECC is a valuable tool to facilitate coronary revascularization.

Our present observational study demonstrated low 30-day mortality for the elective MECC surgery group of about 1.1%. Nevertheless, a learning curve for the MECC procedure is necessary for perfusionists, anesthesiologists, and heart surgeons. With time, the number of MECC procedures increased and the 30-day mortality rate improved during a 10-year period, even though the EuroSCORE of the patients increased significantly.

In 2004, Wiesenack and colleagues reported on our first series and thus introduced the new concept of MECC into clinical practice. They demonstrated that CABG surgery with MECC for elective multivessel disease is possible with a mortality rate similar to standard ECC [9].

Recently, we and others could demonstrate that MECC offers the same benefit as off-pump CABG with the same clinical benefits, in terms of postoperative ventilation time, release of postoperative CK, and catecholamine therapy [10–12].

Meanwhile, further randomized studies confirmed that MECC patients need less blood during coronary bypass surgery [13]. One reason is the reduced priming volume of the MECC system and the possibility to maintain a normal hematocrit during the surgical procedure because of the absent venous reservoir and the absent cardiomyocrit suction.

This leads to the advantage that only 15% of the patients had intra-operative RBC transfusion in our current analysis. In several studies, the transfusion rate for different MECC systems could be reduced to 30–50% in comparison to standard CPB [14,15]. Several studies demonstrated that blood transfusion is an independent predictor of postoperative morbidity and mortality and, especially after CABG, every unit of RBC transfused is associated with an incrementally increased risk for adverse outcome [16,17]. Low transfusion rates of RBC in our patients might be one reason for an advanced outcome in the current analysis.

We speculated that the intra-operative isovolumetric perfusion with MECC is a great advantage and is reflected by the low incidence of postoperative cardiac failure, low postoperative CK and CK-MB fraction at ICU admission and 6 h, postoperatively.

A better liver function in MECC patients, especially in patients with liver diseases, was found by Prasser and colleagues [20].

Some studies observed a better renal function in the early postoperative period and a lower incidence of acute kidney injury after coronary revascularization with MECC in contrast to standard ECC [21,22]. Considering these results, the preserved kidney function and the incidence of postoperative dialysis of only 0.5% was remarkably low in our patients. In addition, Haneya and colleagues demonstrated that end-organ protection, especially in high-risk patients with remarkably high EuroSCORE, is important. The latter benefit from the use of MECC by a lower 30-day mortality rate, and less renal and myocardial damage [23].

We also could confirm good neurological outcome, with a low incidence of postoperative stroke and cognitive disorders in the MECC patients that Liebold and colleagues described. As the underlying pathophysiology for these advantages, a better cerebral tissue oxygenation and a significant decrease of cerebral microembolization in the MECC group is assumed [24].

Beating-heart MECC procedures may also serve as an alternative for MECC CABG surgery at the arrested heart. Patient outcome is equal to that of the MECC group with
cardioplegic arrest. It is especially useful for urgent and emergent cases with impaired left-ventricular function and thus progressively increased up to 20% in our institution. Accordingly, the results for beating-heart MECC were significantly better than in the normal MECC group with the arrested heart in high-risk cases. Although emergent CABG is a risk factor for mortality, the mortality rate in the beating-heart MECC group was significantly lower than in the MECC group with the arrested heart. In a small series, Stassano and colleagues reported a reduction of the inflammatory response with the same mortality rate during left-ventricular assisted-beating-heart CABG [25]. This underlines our clinical finding for a significant better outcome for those patients operated as bhMECC revascularization. Except for special permissions, bhMECC procedure gained acceptance in clinical routine in our institution.

In conclusion, our data on the application of the MECC system in routine CABG surgery in our center may strengthen previous reports with regard to the advantages of that system including low mortality, excellent end-organ protection, and easy application in clinical practice. Beating-heart revascularization with the MECC system is an alternative for high-risk cases with quite acceptable results. In our opinion, MECC should be considered more often as an alternative to standard ECC procedures in modern CABG surgery. Some postulated benefits and effects of the MECC related to the better intra-operative perfusion are still a matter of debate and unclear. Prospected studies and further experiments should prove the causal relationship in the near future.

5. Limitations of our study

Our data analysis is done in a retrospective matter. Though defining indications and contraindications, various factors, including surgical bias and patient selection, may influence the positive outcome of our patients. Therefore, conclusions are limited in their application and causality.

References