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Original Articles

Evaluation of Hemodynamic and Regional Tissue Perfusion Effects of Minimized Extracorporeal Circulation (MECC®)

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Abstract: Minimized extracorporeal circulation (MECC®, Maquet, Cardiopulmonary AG, Hirrlingen, Germany) is an established procedure to perform coronary revascularization. Studies showed positive effects of MECC compared to conventional cardiopulmonary bypass (CCPB) procedures in terms of transfusion requirements, less inflammation reactions, and neurological impairments. Recent retrospective studies showed higher mean arterial pressure (MAP) and a lower frequency of vasoactive drug use. We addressed this issue in this study. The hypothesis was to find a higher MAP during coronary bypass grafting surgery in patients treated with MECC systems. We performed a prospective, controlled, randomized trial with 40 patients either assigned to MECC ($n = 18$) or CCPB ($n = 22$) undergoing coronary bypass grafting. Primary endpoints were the perioperative course of mean arterial pressure, and the consumption of norepinephrine. Secondary endpoints were the regional cerebral and renal oxygen saturation (rSO_2) as an indicator of area perfusion and the course of hematocrit. Clinical and demographic characteristics did not significantly differ between both groups. Thirty-day mortality was 0%. At four of five time points during extracorporeal circulation (ECC) MAP values were significantly higher in the MECC group compared to CCPB patients (after starting the ECC 60 ± 11 mmHg vs. 49 ± 10 mmHg, $p = .002$). MECC patients received significantly less norepinephrine (MECC 22.5 ± 35 µg vs. CCPB 60.5 ± 75 µg, $p = .045$). The rSO_2 measured at right and left forehead and the renal area was similar for both groups during ECC and significantly higher at CCPB group 1 and 4 hours after termination of CPB. Minimized extracorporeal circulation provides a higher mean arterial pressure during ECC and we found a lower consumption of vasoactive drugs in the MECC group. There was a decrease in regional tissue saturation at 1 and 4 hours post bypass in the MECC group possibly due to increased systemic inflammation and extravascular fluid shift in the CCPB group. **Keywords:** minimized extracorporeal circulation, MECC, mini circuits, mean arterial pressure, regional tissue oxygenation, organ protection, system vascular resistance, hemodilution. *JECT. 2010;42:30–39*

The introduction of extracorporeal circulation has facilitated open-heart surgery. The development of modern techniques in extracorporeal circulation (ECC) is the result of the combined efforts of physiologists, physicians, and engineers. During the second half of the 20th century, scientists refined their methods in the development of extracorporeal circulation (new oxygenators [membrane], pumps [centrifugal], and modified surfaces [coatings] were introduced) so that it could be used in humans (1). All these improvements and new developments had only one aim: to reduce the observed deleterious effects of extracorporeal circulation (2). At the end of the 1990s many practitioners and scientists devised a new kind of ECC system in which the surface area and priming amount of the tubes was reduced to reduce the deleterious and hemodilutional

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effects of extracorporeal circulation. These circuits are better known as minimal extracorporeal circulation. The idea was to have one system with all observed advantages. The first commercial mini-system was the CorX® System from Cardiovention®, (Santa Clara, CA). This system included an integrated centrifugal pump-polypropylene oxygenator, a complete heparin-coated surface, and a low priming volume (3). The minimized extracorporeal circulation system (MECC®, Maquet) was introduced almost at the same time (1999). MECC® has been conducted to evaluate its effectiveness for extracorporeal support during coronary bypass grafting (CABG) and valve replacement surgery. Findings include a reduction in the use of blood products and a reduction in serum markers of inflammation in comparison to conventional cardiopulmonary bypass (4–7). The literature shows a lot of injuries and side effects from extracorporeal circulation on the major organ systems, especially to the cerebrum and abdominal organs like the kidneys. Efforts to find clear correlations between organ impairment and ECC or the superiority of off pump coronary aortic bypass surgery over conventional cardiopulmonary bypass (CCPB) surgery was not significant in terms of neurological declines and renal injury (8–11). The main factors in terms of impairment to renal and cerebral function in correlation regarding the ECC systems are embolism (cerebral) followed by hypoperfusion (renal + cerebral) (12). Regarding the ECC systems per se left heart venting (13) (cerebral injury) and the duration of CPB (13–15) seems to be more relevant. But also a higher consumption of vasopressor was referred with an increased organ injury (16,17). Wiesenack et al. recently showed in a retrospective analysis of 970 patients (485 MECC vs. 485 CCPB) that, despite a reduced preoperative cardiac index, the mean arterial pressure (MAP) among MECC patients was significantly higher compared to CCPB. Patients in the MECC group received less frequent neosynephrine (318 (65%) vs. 429 (88%)) (4). In our experience over the last 3 years, the maintaining of ECC with MECC is linked to a higher mean arterial pressure and lower consumption of norepinephrine (mean µg norepinephrine per MECC and CCPB: 16.2 ± 27.1 vs. 91.4 ± 174.9 (patient database, Heart Center Coswig). In this study we want to examine this observation and whether it has any influence on regional tissue perfusion in patients who received a coronary arterial bypass surgery treated with MECC compared to those treated with CCPB. Secondary endpoints were the transfusion rate and the course of hematocrit and intracorporeal volume status perioperatively.

MATERIAL AND METHODS

The completion of a pilot study on 10 consecutive patients was followed by a sample size calculation to detect a mean difference of 10 mmHg with 80% power ($\beta = .8$) at a significance level of 5% ($\alpha = .05$). The two-sided test revealed a sample size of 18 patients in each group.

This was a prospective, controlled, randomized trial on 40 patients undergoing coronary artery bypass grafting. The perioperative course of mean arterial pressure, system vascular resistance, and the consumption frequency of norepinephrine were major study end points. After written, informed consent, 40 patients were enrolled into the study and underwent isolated elective coronary revascularization for double, triple, or four vessel diseases. Patients were randomized into two groups minimized extracorporeal circulation (MECC study group) and conventional cardiopulmonary Bypass (CCPB control group) by using computer-generated random allocations the previous day. The authors decided to compare the "gold standard set" (roller-pump, uncoated surface, and open hardshell reservoir) with the minimized system. To ensure matching groups in our study, we included only patients between 18 and 80 years, body weight between 60 and 100 kg, and an ejection fraction >40%. Excluding criteria were as follows: hematocrit <30% or preoperative transfusion, less than two vessel disease, redo operation, renal disease and serum creatinine >120 µmol/L, hepatic disease or prothrombin time >70 seconds, any coagulation disorders, serious peripheral vascular disease, carotid stenosis >50%, hemodynamic instability, acute myocardial infarction, mechanical assist device and/or preoperative intra-aortic balloon pump. The evaluation of potential study patients was performed by a medical doctor in-house and double-checked by a scientist at the biomedical institute.

Extracorporeal Circulation with MECC (Group 1)

The MECC system was a customer modified standard configuration, including the membrane oxygenator Quadrox® (Maquet), the venous bubble trap VBT®, the centrifugal pump Rotaflow®, and the arterial filter Quart® (Maquet) from Maquet. The differences of a standard MECC system are a quick bypass line between Cell-Saver Reservoir and the venous line and a low flow line including a level sensor between aortic vent and venous line (Figures 1 and 2). The system was connected with 3/8″ lines. The whole system was coated with Bioline® (Maquet; Polypeptid - Heparin Coating). We used a 28 French venous return catheter, Tristage® (Maquet), specially designed for MECC and optimized for venous drainage under active suction.

Extracorporeal Circulation with CCPB (Group 2)

Clinical CCPB routine practice at the MediClin Heart Center Coswig includes the use of a membrane oxygenator Quadrox®, (Safeline), roller pump (standard drive for coronary revascularization), an open perfusion system containing a venous Hardshell Cardiotomy Reservoir (4.2 l, cardiotomy filtration 40 µm), and an arterial filter Quart® (40 µm). As standard, an arterial cannula with 7 mm Softflow® (Terumo, Ann Arbor, MI) and a two stage

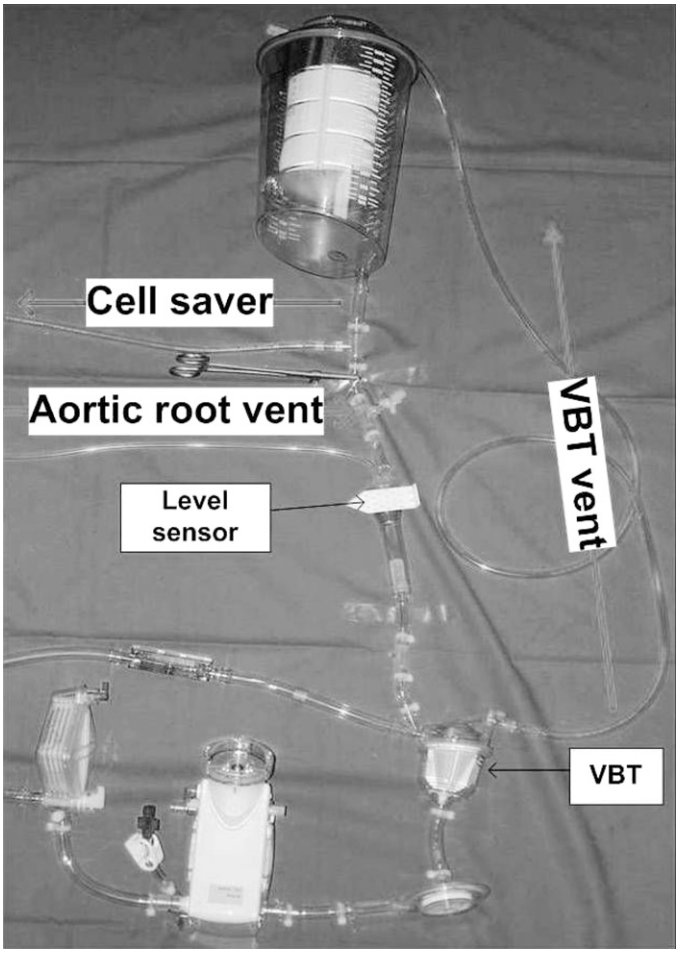

Figure 1. MECC Set, Maquet – customized for MediClin Heart Center Coswig, including out – clamped Cell-saver Reservoir and VBT (venous bubble trap).

cannula (Medos, Stolberg, Germany) for the right atrium were used. The system includes 3/8″ arterial and 1/2″ venous lines.

Data Analysis and Statistical Considerations: The statistical analyses were performed with the software program SPSS 14. All continuous data were expressed as mean ± SD. The clinical profiles of two groups were compared with analysis of variance for continuous data and by the Fisher exact test for categorical data. Analysis of data with non-normal distribution were performed with the Mann-Whitney U-Test. Statistical significance was assumed for $p < .05$.

Preparations and Priming: The cardiopulmonary perfusion system for each patient was set 1 hour before the operation started. The priming for CCPB included three solutions: 500 mL Jonosteril, (Fresenius KABI, Germany), 500 mL Mannitol (Serag-Wiessner, Germany, theoretical osmolarity 550 mosm/L) and 500 mL Voluven (Fresenius Kabi, Germany, theoretical osmolarity 308 mosm/L). For the minimized system we used ~430 mL Voluven and ~430 mL

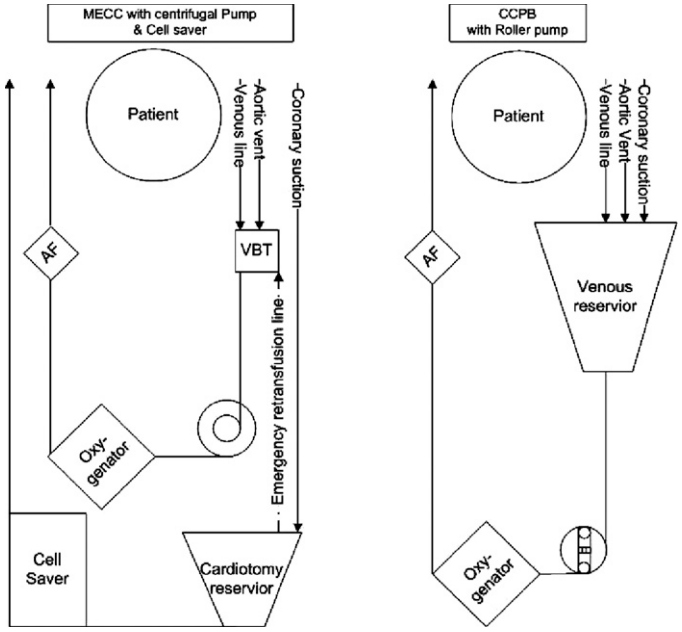

Figure 2. Comparison of both ECC systems, MECC (minimized extracorporeal system) and CCPB (conventional cardiopulmonary bypass).

Mannitol for priming. Each perfusion set was flushed with carbon dioxide for 3 minutes before priming procedure was initiated. The patient's body surface area was determined and individual ECC flow was calculated on the basis of 2.5/L/min/m^2. Anticoagulation strategy was performed with heparin concentrate-based anticoagulation management (Hepcon HMS; Medtronic, Minneapolis, MN). The heparin dose–response was performed before skin incision. However, as calculation of the volume of a patient according to body surface area is an approximation, particularly in cardiac surgery, the "pump" heparin was added to the patient as a bolus to create a safety window. Both circuits were primed with 10,000 international units heparin (Table 1).

Maintaining ECC: Hemodynamic Strategy and Measurements: To ensure the same conditions for both study groups we followed a strict hemodynamic strategy. Arterial flow was maintained at 2.5/L/min/m^2 and the mean arterial pressure between 45 mmHg and 75 mmHg. If the mean arterial pressure decreased, the arterial flow was increased up to a maximum of 120% of the calculated flow. If mean arterial pressure further decreased, a 5 µg norepinephrine bolus was given to raise the MAP on CCPB between 45 and 75 mmHg.

The measurements start after induction of anesthesia with Time point T1 and continue until 4 hours after termination of CPB (T1: pre-CPB; T2: after start CPB; T3: after cardioplegia; T4: 15 minutes after cardioplegia; T5: after X-clamp opening; T6: before termination of CPB; T7: 15 minutes after CPB; T8: 1 hour after CPB; T9: 4 hours after CPB). The mean arterial pressure (mmHg) was

Table 1. Comparison of MECC system and CCPB system for surface and priming.

Components	CCPB	Surface cm^2	Priming mL	MECC	Surface cm^2	Priming mL
Coating	No			Bioline®		
Venous tubing	1/2 inch	618	~500	3/8 inch	614	~100
Arterial tubing	3/8 inch	659	~250	3/8 inch	494	~150
Reservoir including 40 µm filter	VHK2000®	~8000	~400	No		
Oxygenator	Quadrox®	1800	~250	Quadrox®	1800	~250
Arterial filter 40 µm	Quart®	570	180	Quart®	570	180
Drive unit	1/2 inch Silicon Tube	390	150	Centrifugal Pump: Rotaflow®	190	32
VBT® (venous bubble trap)	No			Yes	36	160
Total	CCPB	12037	1630	MECC	3704	872

invasively measured direct from anesthesia monitoring; data was recorded at 5 minute intervals and averaged into the time point's epochs. Cardiac output (CO, L/min) was measured pre-ECC and post-ECC with partial carbon dioxide rebreathing noninvasive cardiac output (NICO®) and during ECC direct from the pump flow of the heart lung machine. The systemic vascular resistance ($dyn \cdot sec \cdot cm^{-5}$) were calculated (MAP – central venous pressure × 80/CO). And the consumption of norepinephrine was summarized between all time points' epochs. The hematocrit was maintained between 25 and 40%. Patients up to 70 years received red blood cell transfusion if hematocrit felt below 25%, whereas the cut-off value for patients >70 years was set at 28%. The temperature strategy for each patient was set as normotherm perfusion at 36.5°C–37°C.

Cardiac Arrest and Unloading of Heart: We used a modified warm Calafiore's blood cardioplegia (perfusate: 1.6 mmol potassium chloride and 0.22 mmol magnesium sulphate/mL) initially with 300 mL pump flow/min with oxygenated blood containing a potassium chloride concentration of 13.33 mmol/L + 2 mmol bolus for 2 minutes and at 3 minutes again with 300 mL pump flow/min with 10 mmol/L potassium chloride. At least every 20 minutes during cardiac arrest we repeated the procedure with 10 mmol/L potassium chloride and, if necessary (not complete cardiac arrest), with an additional bolus of 1 mL per minute perfusate for an additional 2 minutes (18,19).

If the unloading of the heart during cardiac arrest was poor, and/or the surgical conditions were not optimal (heart not fully unloaded, bleeding anastomosis) and therefore required an additional emptying of the heart, in the conventional systems (CCPB) the venous clamp was opened completely and if necessary the pump flow was decreased to a minimum of 80 percent of the calculated flow. In contrast to conventional perfusion, in closed minimized systems without reservoir, we increased arterial flow to drain more volume out of the right heart and to shift it into the venous system of the body. To reach this, we used three consecutive actions. First, we increased the arterial pump flow. Second we changed the patient position (head up, feet down). And third, patients received nitroglycerin boli to open the venous vascular system.

Regional Tissue Oxygenation: The regional oxygen saturation (rSO_2) was measured by using noninvasive transcranial near-infrared spectroscopy, the INVOS™ system (Somanetics®, Troy, MI). We measured the regional oxygen saturation at the forehead and over the kidney area to evaluate the impact of a changed mean arterial pressure on forehead and renal perfusion. The regional cerebral oxygen saturation ($rCSO_2$) tends to remain remarkably stable over a wide range of temperatures, perfusion pressures, and anesthetic state (20).

Cerebral: The brain has the highest blood flow and metabolic demand of all organs, thus representing the ideal and most logical place in monitoring the adequacy of body perfusion (21).

Thirty minutes before start of ECC, a photoconductive detector containing a near-infrared light transmitting optode and a light detector was placed in the right and left frontotemporal region below the hairline. Resting baseline rSO_2 values were obtained after waiting at least 1 minute after placement of sensors once values had stabilized. Monitoring starts before sternotomy and continuous until 4 hours after ECC conclusion at the intensive care unit. Data were recorded at 15 second intervals and averaged into 60 second periods The use of near-infrared reflectance spectroscopy (NIRS) for assessment of bifrontal regional oxygen saturation (rSO_2) has demonstrated in CABG patients a correlation between low $rCSO_2$ values and cognitive dysfunction, prolonged hospital length of stay, and most recently, perioperative cerebral vascular event (CVA) (22–24).

Renal: The third and fourth channel measures the regional oxygenation over the dorsal lateral flank-renal area. The approach of measurement for adults in this area has, so far as the authors know, not been described yet. Despite this knowledge, the authors decided to measure in this area to have an approximate trend of the perfusion deviation between cerebral vascular and posterior abdominal perfusion. We wanted to clarify the impact of

the arterial pump flow, systemic vascular resistance, and the norepinephrine consumption on the oxygen tissue saturation in this region.

RESULTS

Patient Characteristics

Forty-three patients were enrolled for randomization; one patient was excluded preoperatively due to an indication for aortic root replacement. One patient developed preoperatively acute myocardial infarction and was treated in an emergency operation. The third patient was excluded because of the intraoperative indication for aortic valve replacement as diagnosed by echocardiography. Eighteen patients were randomized to group 1 (MECC) and 22 to group 2 (CCPB). Clinical and preoperative data of both groups have been summarized in Table 2. Demographic data did no differ significantly between the groups with respect to age, body surface area, and left ventricular function. The majority of the patients were male (67%). Associated diseases are typical for patients suffering coronary disease (Table 2). Differences between perioperative data MECC (group 1) and CCPB (group 2) are presented in Table 3. In particular, the number of grafts, the duration of ECC (perfusion time), and the aortic cross clamping time (X-clamp time) were similar in both groups (Table 3).

Hemodynamics and Vasopressor Use

In the MECC group the mean arterial pressure values were significantly higher during ECC at T2, T3, T5, and T6 compared to the control group (CCPB). The presented norepinephrine values at Figure 3 present the sums of norepinephrine doses between each time point (T1-T2; T2-T3….). The majority of patients received norepinephrine (32/40 = 80%) during the study. The portion of patients with norepinephrine administration was in the MECC group 66% (12/18) and in the CCPB group 91% (20/22) $p = .109$. CCPB patients received norepinephrine significantly more frequently and in higher dosage compared to the MECC group (Figures 3 and 4).

Regional Cerebral and Renal Oxygen Saturation $rCSO_2$; rSO_2

Regional cerebral oxygen saturation did no differ before ECC was established. Baseline was set between induction of anesthesia and starting arteria thoracica interna preparation. The cerebral saturation values were similar in both groups from T1 to T6. Significant differences were found at T7 and T8 in the CCPB group (T7: 71 ± 7.3% rSO_2 vs. 66 ± 7.9% rSO_2; $p = .044$; T8: 68 ± 8.4% rSO_2 vs. 62 ± 8.4% rSO_2; $p = .037$) (Figure 5). Regional renal oxygen saturation were almost identical for both groups during ECC (T2–T6) and significantly higher after ECC (T7–T8) in the CCPB group (Figure 6).

Table 2. Preoperative characteristics of the study groups.

Variable	MECC ($n = 18$)	CCPB ($n = 22$)	Difference (Mean or Median)	95% Interval of Confidence Difference	p value
Age (years)	68 ± 8.9	65 ± 11.7	–3	–3.7–9.9	.36
Sex					
Male	13	16			1.0*
Female	5	6			
Body surface area (m^2)	1.89 ± .13	1.97 ± .23	.09	–.21–.04	.172†
Calculated flow (L/min)	4.72 ± .36	4.78 ± .43	.06	–.33–.19	.23†
EuroSCORE (%)	3.6 ± 2.1	2.9 ± 2.1	–.7	–.67–2.09	.30†
EF (%)	57 ± 11	60 ± 8	–3	–8.4–4.1	.48†
Diabetes mellitus (%)	6 (33)	7 (41)	1		.75*
Systemic Hypertension (%)					
Prehypertension (syst. 120–139 to diast. 80–89 mmHg)	12 (67)	18 (82)			.30*
Stage 1 (syst. 140–159 to diast. 90–99 mmHg)	2 (11)	0			
Stage 2 (syst. >160 to diast. >100 mmHg)	0	0			
Previous AMI (%)	6 (33)	6 (27)	0		.74*
Angina pectoris (%)	13 (72)	12 (55)	1		.33*
Previous PTCA (%)	5 (28)	4 (18)	1		.71*
Previous atrial fibrillation (%)	0	2 (9)	–2		.49*
Arteria carotis stenosis (%)	0	1 (5)	1		1*
Renal insufficiency (%)					
Stage 2 (GFR: 60–89)	3 (17)	1 (5)	3		.31*
Stage 3 (GFR: 30–59)	1 (6)	1 (5)	0		1*
COPD (%)	2 (11)	3 (14)	1		1*
PAVK (%)	2 (11)	2 (9)			1*

*Fisher's exact test
†Student t test
Syst., systolic arterial pressure in mmHg; diast., diastolic arterial pressure in mmHg; GFR, glomerular filtration rate; EF, ejection fraction; AMI, acute myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; COPD, chronic obstructive pulmonary disease; PAVK, peripheral artery occlusive disease.

Table 3. Perioperative data.

Variable	MECC (n = 18)	CCPB (n = 22)	Difference (Mean or Median)	95% Interval of Confidence Difference	p value
Perfusion time (min)	72 ± 17	76 ± 20	4	–15–8	.51‡
X-clamp time (min)	40 ± 11	41 ± 15	1	–9–8	.9‡
Reperfusion time (min)	27 ± 6	31 ± 9	4	–8.4–1.3	.15‡
Grafts per patient (n)	3.0 ± .6	2.9 ± .5	–.1	–.67–.45	.61‡
Inotropic dependence postoperatively, n (%)					
Norepinephrine	1 (6)	1 (5)	0		1*
Suprarenine	0	5	–5		.053*
Dobutamine	2 (11)	3 (14)	–1		1*
Intensive care unit stay time					
<30 hours	16 (89)	17 (77)	–1		.43*
30–90 hours	1 (6)	3 (14)	–2		.61*
>90 hours	1 (6)	1 (9)	0		1*
Ventilation time (hours)	12.8 ± 2.7	12.6 ± 3.2	.2	–1.76–2.14	.84‡
CPAP time	2.8 ± 3.1	1.8 ± 2.3	–1	–.79–2.78	.27‡
Bleeding (mL)					
4 hours postoperative	271 ± 248	227 ± 123	44.3	–77–165	.46‡
24 hours postoperative	678 ± 274	830 ± 419	–152	–385–80	.19‡
Weight: pre to postoperative (Δ kg)	–.78 ± 2.1	–1.64 ± 2.9	.86	–.78–2.5	.30‡
CVVH n (%)	0	0	0		1
Neurocognitive disorders, n (%)	1 (6)	1 (5)	0		1*
TIA, n (%)	1 (6)	0	1		.45*
Sepsis	0	0	0		1
Atrial fibrillation new postoperative, n (%)	3 (18)	6 (28)	3		.47*
Revision for bleeding, n (%)	1 (6)	1 (5)	0		1*
Revision for graft failure, n (%)	0	0	0		1
Pleural effusion (%)	2 (11)	2 (9)	0		1*
Hospital stay (days)	10 (10; 12.5)	11 (10; 13.25)	1	–1.45–3.45	.42†
Thirty-day mortality, n (%)	0	0	0		1

*Fisher Exact Test
†Whitney U test for non parametric variables
‡Student t test
CPAP, continuous positive airway pressure; CVVH, continuous veno-venous hemofiltration; TIA, transischemic attack.

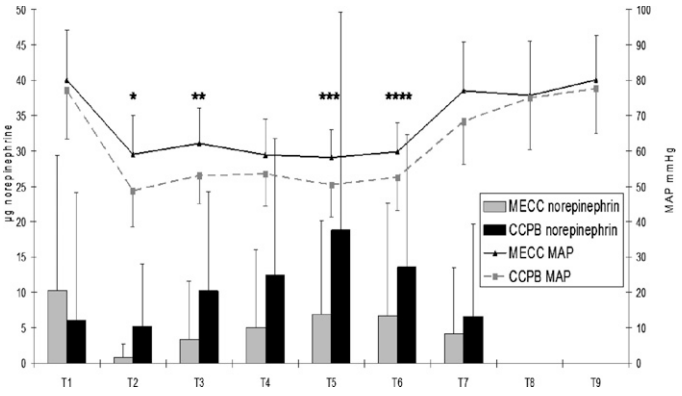

Figure 3. MAP and norepinephrine consumption. Data are shown as mean ± SD (*p = .002; **p = .01; ***p = .015; ****p = .021). T1: preCPB; T2: after start of CPB; T3: after cardioplegia; T4: 15 minutes after cardioplegia; T5: after X-clamp opening; T6: before termination of CPB; T7: 15 minutes after CPB; T8: 1 hour after CPB; T9: 4 hours after CPB.

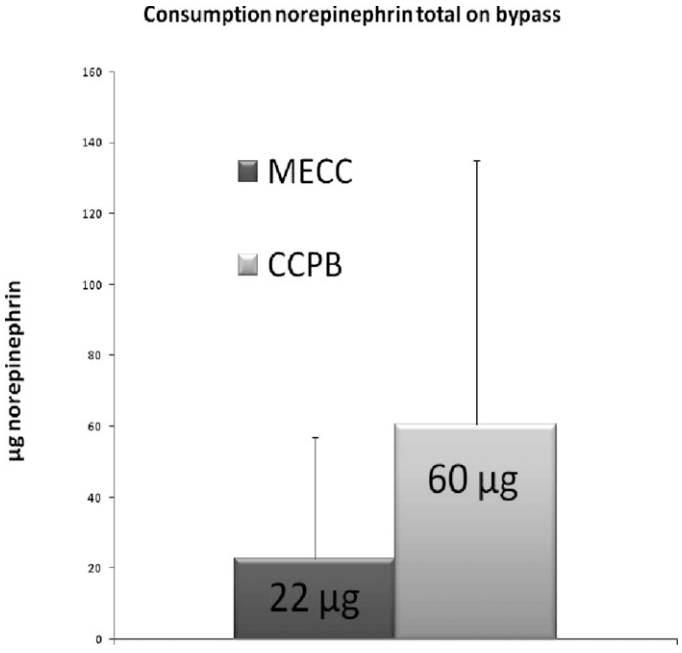

Figure 4. Norepinephrine consumption total on bypass MECC 22.5 µg vs. CCPB 60.5 µg, p = .033. Data are shown as mean ±SD.

Intraoperative Volume Status, Blood Counts, and Transfusion

The accurate volume status calculated as intracorporeal volumes was determined pre-operatively and at each time point during ECC and 4 hours post ECC (pre ECC, T1–T7;

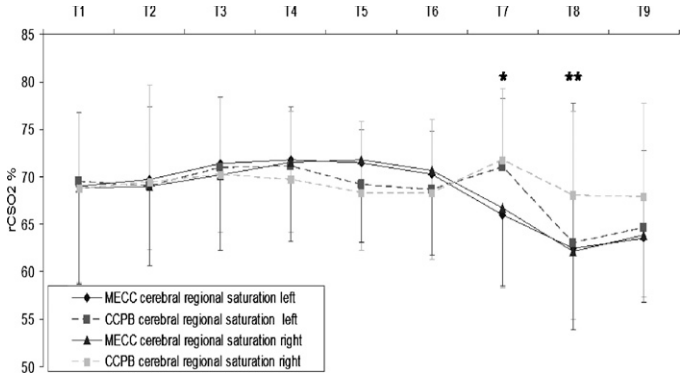

Figure 5. $rCSO_2$ during ECC (Regional cerebral oxygen saturation). Data are shown as mean ± SD (*p = .044, **p = .037). T1: preCPB; T2: after start CPB; T3: after cardioplegia; T4: 15 minutes after cardioplegia; T5: after X-Clamp opening; T6: before termination of CPB; T7: 15 minutes after CPB; T8: 1 hour after CPB; T9: 4 hours after CPB.

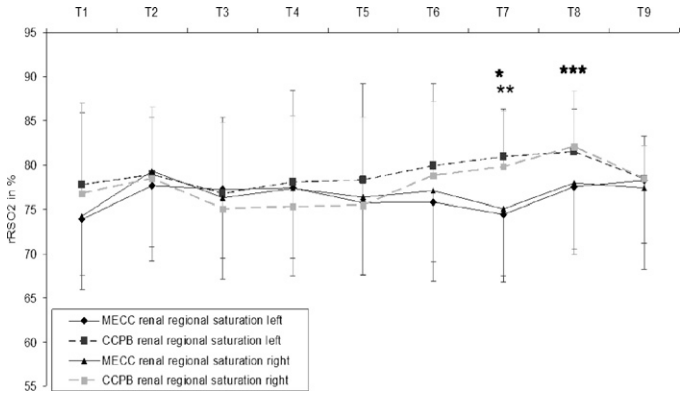

Figure 6. $rRSO_2$ during ECC (Regional renal oxygen saturation). Data are shown as mean ± SD (*p = .004, **p = .044, ***p = .043). T1: preCPB; T2: after start CPB; T3: after cardioplegia; T4: 15 minutes after cardioplegia; T5: after X-Clamp opening; T6: before termination of CPB; T7: 15 minutes after CPB; T8: 1 hour after CPB; T9: 4 hours after CPB.

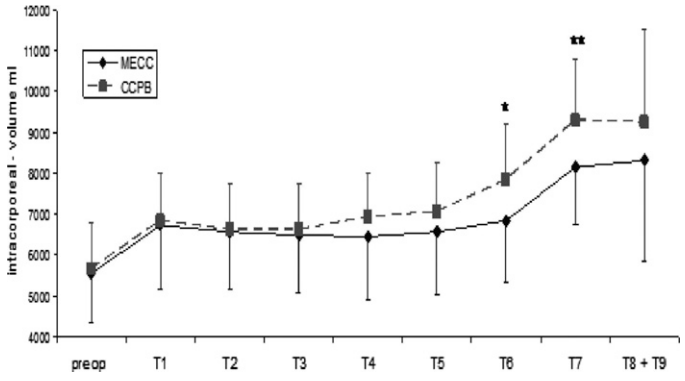

Figure 7. Intracorporeal volumes. Data are shown as mean ± SD (*p = .043; **p = .019). T1: preCPB; T2: after start CPB; T3: after cardioplegia; T4: 15 minutes after cardioplegia; T5: after X-Clamp opening; T6: before termination of CPB; T7: 15 minutes after CPB; T8: 1 hour after CPB; T9: 4 hours after CPB.

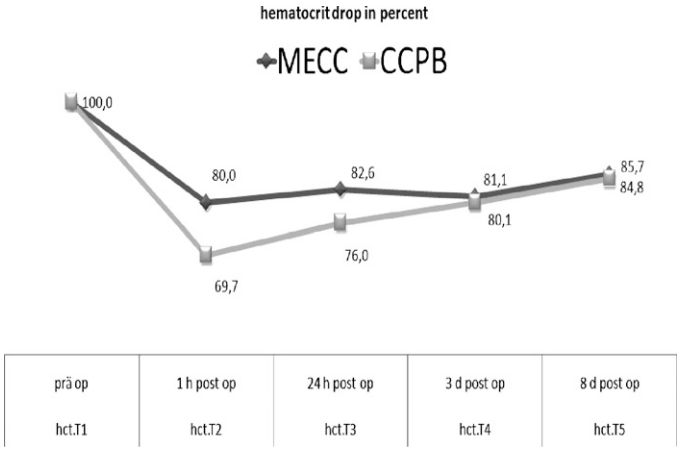

Figure 8. Drop of hematocrit perioperatively: Data are shown in percent from baseline to postoperative day 8. T1: preoperative; T2: 1 hour postoperative; T3: 24 hours postoperative; T4: 3. days postoperative; T5: 8. days postoperative.

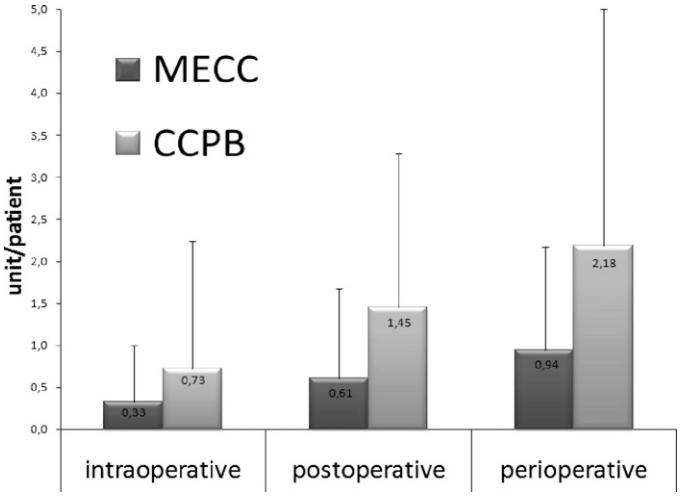

Figure 9. Transfusion, red blood cell units per patient, perioperative includes all red blood cell –transfusions. Data are shown as mean ± SD.

T8 + T9). Intracorporeal volumes were significantly lower in group 1 (MECC) before weaning the extracorporeal circulation (T5: 6852 ± 1390 vs. 7830 ± 1535, p = .043) and 15 minutes after ECC (T6: 8144 ± 1535 vs. 9307 ± 1453, p = .019) (Figure 7).

The drop of hematocrit-value was 30 percent from preoperative baseline to 1 hour after ECC in the CCPB group and 20 percent in the MECC group (Figure 8). The mean intraoperative transfusion per patient was .33 ± .67 in the MECC group and .73 ± 1.5 in the CCPB group (p = .32) (Figure 9). During the hospital stay, the frequency of patients without transfusions in the MECC group was 56% compared to 36% in the CCPB group.

DISCUSSION

Hemodynamic

CABG with cardiopulmonary bypass still remains the method of choice for the treatment of coronary disease (25,26). Gold et al. showed in their randomized clinical trial that a higher mean arterial pressure during conventional cardiopulmonary bypass can improve outcomes after coronary bypass surgery (17). The interpretation of MAP and ECC is complicated because the interaction of mean arterial pressure, vasotonia, and volume balance in a patient forms a complex process under physiological and pathophysiological conditions. In this study the central venous pressure as an indicator of cardiac preload was indifferent between both groups and the volume balance between both groups were comparable, although the calculated intracorporeal blood volumes differed significantly during weaning of CPB (MECC vs. CCPB: 6852 ± 1390 vs. 7830 ± 1535, $p = .043$).

Limitations

A critical issue still remains with the dosage and frequencies of vasoactive drug (norepinephrine) administration in both groups at the defined time points. Immediately after CPB start, the mean norepinephrine dose was significantly lower in the MECC group (.56 ± 1.6 vs. 5.35 ± 8.85; $p = .038$). More frequently, patients in the MECC group remained free of norepinephrine administration at T2 (94% vs. 52%, $p = .027$), T3 (88% vs. 33%, $p = .004$), T4 (81% vs. 44%, $p = .047$), and T5 (75% vs. 33%, $p = .048$). Therefore the interpretation of arterial pressure in this study proved to be difficult because of varying inter- and intraindividual vasoactive drug applications in both groups. The hypothesis of a higher MAP during CPB with a MECC system could not be unequivocally confirmed.

Organ Supply: Regional Tissue Oxygenation

$rCSO_2$ Regional Cerebral Tissue Oxygenation: Changes in rSO_2 values reflect changes in the critical balance between arterial oxygen delivery and cerebral consumption. The value of rSO_2 reflects a proportional mix of arterial and venous blood, which is approximately 70% venous and 30% arterial during most physiological conditions in humans. The measurement of regional tissue saturation as a useful indicator of cerebral oxygen supply is a standard non-invasive and safe method for neurological monitoring during cardiac surgery and helps to decrease postoperative complications (27).

Liebold et al. compared the regional cerebral oxygen tissue oxygenation in minimized and conventional cardiopulmonary bypasses by near-infrared spectroscopy. During extracorporeal circulation, there was a significant decrease in the cerebral tissue saturation index, whereas this effect was only moderate in the MECC group (MECC vs. CCPB; $p = .01$) (28). The authors argue that the reduced hemodilution, the loss of pulsatile flow, an impaired cerebral autoregulation, isovolumetric perfusion, or a decrease in MAP may be possible reasons. Another explanation may be the more frequent application of norepinephrine and a more accentuated systemic inflammatory response among patients undergoing CCPB. The different cerebral blood supply as a function of the MAP has been controversially discussed during the recent years. Sungurtekin et al. examined the relation between pump flow and MAP on cerebral blood flow (CBF) in seven dogs. A normal pump flow proved not to be sufficient for an effective cerebral blood perfusion if MAP was simultaneously decreased. If MAP was kept normal and pump flow was reduced, the CBF did not change significantly. Only MAPs below 50 mmHg resulted in a linear relationship between pump flow, MAP, and CBF (29). Thus, MAP seemed to be the major determinant for cerebral blood flow. A clinical study in 1989 did not confirm the evident relation between MAP and cerebral blood flow. In this study with 18 patients the middle cerebral artery blood flow velocity (MCAv) was measured by transcranial Doppler ultrasonography during coronary revascularization. Additionally, the relation between MCAv, MAP base excess, and nasal/rectal temperature was also examined. In this study, MCAv was most dependent on the patient's temperature: nasal temperature ⇩ = MCAv ⇩, (median $r_s = .84$, range .61–.99, $p = .0001$) (30). The study design of Liebold et al. and this study is comparable. Both studies used Maquet's MECC system and an open roller pump system from the same manufacturer as the control system. Differences were found in the temperature management. Whereas Liebold et al. preferred mild hypothermia; patients in this study were kept at normothermia. The major endpoint in the current study was the MAP, which was elevated during CBP. Despite higher MAPs in the MECC group at T2 (start ECC) and T3 (15 minutes after ECC), the regional cerebral tissue saturation ($rCSO_2$) at the forehead did not differ significantly between MECC and CCPB. Thus, the results found in this study could not link MAP and $rCSO_2$ irrespective the sort of extracorporeal circulation system used. One possible explanation might be the different temperature management strategies. Interestingly, cerebral $rCSO_2$ in the present study were decreased at T6 and T7 in the MECC group. We discuss this finding later.

$rRSO_2$ Regional Renal Tissue Oxygenation: To comparably measure the perfusion distribution between head and body, we examined not only cerebral tissue saturation ($rCSO_2$) but also the tissue saturation on the renal region (dorsal lateral flank). As far as the authors know, the assessment of renal saturation in adults by near-infrared spectroscopy has been not yet described. Using the musculus abductor digiti minimi manus for the measurement, Soller et al. compared in a prospective randomized trial

with 22 patients during extracorporeal circulation for cardiac surgery both methods near-infrared spectroscopy and invasive measurement of muscle pH and pO_2. Both methods recognized subtle changes in tissue perfusion during CPB. NIRS correlated positively with the invasive measurement (31). Kaufman and co-workers examined in a prospective trial with 20 children the association between gastric acid pH (gastric tonometer), mixed venous oxygen saturation, regional abdominal tissue saturation, and renal regional saturation. This study suggested that the NIRS abdominal site oximeter can be used as a valid, continuous, noninvasive monitor of splanchnic tissue oxygenation in the postoperative neonate and infant with congenital heart disease (32). In this study there was a significant decrease in renal regional tissue saturation at T7 and T8 in the MECC group.

Discussion about Postoperative Regional Saturations

One possible explanation for this finding might be the volume balance. The intracorporeal volume in the CCPB group steadily increased from T4 and proved to be significant at T6/T7 compared to the MECC group. Patients in the CCPB group received not only significantly more volume during CPB weaning compared to the MECC group (CCPB: 1043 mL ± 438 vs. MECC: 564 mL ± 161, $p < .0001$), but also during the total procedure (CCPB: 4104 mL ± 1210 vs. MECC: 3158 mL ± 1262 mean difference 945 mL, $p = .024$). Other groups also reported a reduced total volume in MECC patients. Schöttler et al. found a significantly reduced intrathoracic volume index 2 hours postoperatively in the MECC group ($p < .005$). However, MECC patients ($n = 30$) required temporarily more vasoactive support ($p < .01$) compared to CCPB patients ($n = 30$) (33). Although we could not find an increased frequency of postoperative catecholamine use (norepinephrine: MECC 1/18 vs. CCPB 1/22, $p = 1.0$; Suprarenine MECC 0/18 vs. 5/22, $p = .053$), there might be relative lack of volume in the MECC group. Thus, to compensate for this shortcoming of MECC patients, an amended volume strategy should be initiated. In contrast, some inflammatory markers in the CCPB group were increased after arrival at the intensive care unit (TNF-alpha: MECC 11.6 ± 6 vs. CCPB 40.9 ± 57, $p = .029$) (Figure 4). Since the regional tissue saturation has been measured in the peripheral regions of the human body and near-infrared spectroscopy has only been able to capture saturation data 3 cm below skin surface, an increased peripheral perfusion may have led to an increased regional tissue saturation.

Transfusion

Our priming strategy resulted in an increased hemodilution (~250 mL). However, the small additional amount of fluid does not explain the 2.4 fold increase in transfusion requirement. One explanation might be differences in the indication for transfusions. During this study, the indication for transfusion was not homogenous. Older patients with increased comorbidities received red blood cell counts with a hematocrit below 28%, whereas younger patients did only receive transfusions if hematocrit fell below 25%. This critical issue will be considered in future studies.

Despite the use of this very safe kind of MECC system, including arterial filter, venous bubble trap, MECC patients in this study received less transfusion and have higher hematocrit values during coronary surgery compared to the control group.

CONCLUSIONS

The hypothesis of increased MAP with MECC systems compared to conventional CPB systems can be supposed when interpreting the results of this study. Patients supported with the MECC system had a statistically significant higher MAP and systemic vascular resistance than patients supported with CCPB. Furthermore, there was a significant higher use of vasopressors in the CCPB groups suggesting a heighten inflammatory response in the CCPB group. There was a significant decrease in regional tissue saturation at 1 and 4 hours post bypass in the MECC group possibly due to increased systemic inflammation and extravascular fluid shift in the CCPB group. Further studies are needed to examine the differences in regional oxygen delivery.

More than 500 myocardial revascularizations with MECC have been performed in our hospital. The MECC system proved to be a safe and useful extracorporeal circulation system. We would like to emphasize the fact that this study was performed in team work and the team has gained experiences during the recent 3 years. Systemic surgeon bias could be avoided. We think a controlled randomized multicenter trial with sufficient statistical power seems to be required to unambiguously confirm the hypothesis of elevated MAP with MECC.

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