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Minimized extracorporeal circulation is improving outcome of coronary artery bypass surgery in the elderly

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Abstract

Advanced age is a known risk factor for morbidity and mortality after coronary artery bypass grafting (CABG). Minimized extracorporeal circulation (MECC) has been shown to reduce the negative effects associated with conventional extracorporeal circulation (CECC). This trial assesses the impact of MECC on the outcome of elderly patients undergoing CABG. Eight hundred and seventy-five patients (mean age 78.35 years) underwent isolated CABG using CECC (n=345) or MECC (n=530). The MECC group had a significantly shorter extracorporeal circulation time (ECCT), cross-clamp time and reperfusion time and lower transfusion needs. Postoperatively, these patients required significantly less inotropic support, fewer blood transfusions, less postoperative hemodialysis and developed less delirium compared to CECC patients. In the MECC group, intensive care unit (ICU) stay was significantly shorter and 30-day mortality was significantly reduced [2.6% versus 7.8%; p<0.001]. In conclusion, MECC improves outcome in elderly patients undergoing CABG surgery.

Keywords

minimized extracorporeal circulation; coronary artery bypass surgery; postoperative outcome; elderly; conventional extracorporeal circulation

Introduction

Population aging is a global phenomenon and many first world countries will face a situation where, within the next twenty years, the largest population cohort will be those over 65.[1] Reportedly, in 2009, 50.8% of individuals undergoing cardiac surgery with cardiopulmonary bypass (CPB) were over 69 years of age and 11.8% were older than 80 years.[2] Age is an established independent risk factor for morbidity, mortality and adverse events following coronary artery bypass grafting (CABG) and a review of the Society of Thoracic Surgeons (STS) database showed increased mortality of nonagenarians undergoing cardiac surgery.[3]

Conventional CABG using CECC can be associated with severe complications, such as stroke, peripheral embolization, acute kidney injury and systemic inflammatory response syndrome (SIRS).[4] In open-heart surgery, the main etiology for SIRS is blood cell contact with the artificial bypass surfaces, such as the oxygenator membranes and CPB tubing.[5,6] SIRS is characterized by complement activation and the release of cytokines and vasoactive peptides, which can, subsequently, lead to complications, including cardiac arrhythmias, coagulopathy or thromboembolism.[4] The MECC system was engineered in 2000; details have been previously published by our group.[7] The system was designed to provide adequate tissue perfusion with much shorter tubing and a more biocompatible pump-oxygenator circuit than conventional CECC. Previous studies indicate that there is a significant reduction in CPB-associated side effects, including SIRS, hemolysis, hemodilution and coagulopathy.[8,9] Data also indicate a reduced need for postoperative transfusions, less renal and myocardial damage, shorter length of stay and a lower incidence of sternal wound infections, with an explicit benefit in high-risk

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Table 1. Demographic data and preoperative risk factors.

	CECC	MECC	p-value
No. of patients	345 (39.4%)	530 (60.6%)	
Mean age, (range) years	78.2 ± 2.9 (75 – 91)	78.5 ± 3.0 (75 – 89)	0.14
Gender, male	243 (70.4%)	365 (68.9%)	0.65
Body mass index, kg/m²	28.2 ± 4.2	27.8 ± 3.8	0.15
EuroScore, %	10.8 ± 8.3	10.2 ± 7.8	0.28
Ejection fraction, %	57 ± 15	58 ± 14	0.32
Three vessel disease	287 (83.2%)	423 (79.8%)	0.22
Urgency of surgery			
Elective	168 (48.7%)	245 (46.2%)	0.49
Urgent/Emergent	177 (51.3%)	285 (52.8%)	0.49
Acute myocardial infarction	53 (15.4%)	86 (16.2%)	0.78
Previous cardiac surgery	25 (7.2%)	42 (7.9%)	0.79
Diabetes mellitus	114 (33.0%)	154 (29.1%)	0.23
Peripheral vascular disease	71 (20.6%)	93 (17.5)	0.29
Arterial hypertension	259 (75.1%)	416 (78.5%)	0.25
Atrial fibrillation	34 (9.9%)	36 (6.8%)	0.13
Chronic obstructive pulmonary disease	41 (11.9%)	44 (8.3%)	0.10

patients, like those suffering diabetes mellitus (DM) and individuals with reduced ejection fraction or chronic kidney disease (CKD).[10–13] However, limited data are currently available regarding elderly patients undergoing CABG on MECC. Therefore, the purpose of this retrospective study was to evaluate the impact of MECC on the early outcome of elderly patients undergoing CABG.

Methods

We reviewed our database of 3909 cases for elderly patients who had undergone elective, emergent or urgent isolated CABG surgery between January 2005 and December 2012 in our institution. Eight hundred and seventy-five patients (aged ⩾75 years, mean age 78.35 ± 2.95 years) underwent CECC (n = 345; 39.4%) or MECC (n = 530; 60.6%) and were included. Exclusion criteria were heparin-induced thrombocytopenia and combined procedure (CABG plus valve or aortic surgery). Baseline characteristics of the population are shown in Table 1. MECC was not implemented in patients with significant aortic insufficiency or a body mass index (BMI) >30 kg/m². Data analysis was performed retrospectively from anonymized data, routinely collected for the German Federal Office of Quality Assurance in Cardiac Surgery. According to the guidelines in our institution, ethics committee approval was not needed for retrospective analysis of anonymized data.

Perfusion procedure with CECC

We used an extracorporeal circuit consisting of a diffusion membrane oxygenator (Quadrox 2000, Maquet Cardiopulmonary®, Rastatt, Germany) and a non-pulsatile roller pump, established for a blood flow of 2.5 L/min/m² (HL 30, Maquet Cardiopulmonary®), a two-stage cannula (39-50 Fr) (Stöckert®, Munich, Germany), draining venous blood from the right atrium, and a 22 Fr aortic cannula (Maquet Cardiopulmonary®) for the distal ascending aorta. Lost blood was collected in an open cardiotomy reservoir and transfused back to the patient. The total surface area was >12 m² and the system requires a priming volume of 1200 ml, including 5000 IU heparin. In addition, 350 IU/kg heparin were given as a bolus after harvesting the bypass grafts, with a goal activated clotting time (ACT) of >450 seconds. We used a single shot of crystalloid cardioplegia (Bretschneider HKT, Franz-Koehler-Chemie®, Alsbach-Haenlein, Germany) or Calafiore blood cardioplegia to initiate cardiac arrest, depending on the surgeon's preference.

Perfusion procedure with MECC

We used a closed-loop MECC circuit without air-blood contact. It consisted of a diffusion membrane oxygenator (Quadrox D, Maquet Cardiopulmonary®), a centrifugal pump (RotaFlow, Maquet Cardiopulmonary®), a table line (3/8", 2 x 90 cm), a venous two-stage cannula (32-40 Fr), an aortic cannula (21 Fr) and a 1000-ml infusion bag with sodium chloride. The total surface area was <3 m² and less than 600 ml of priming volume were required without the addition of heparin. The tubing was prepared before surgery, pre-connected and comes completely coated with heparin. Therefore, an intraoperative ACT of 250-300 sec was sufficient and only 150 IU/kg of heparin were administered before cross-clamping. In all cases, warm Calafiore blood cardioplegia was used. A cell-saving device (Cell Saver®, Hemonetics GmbH, Munich, Germany) was used to salvage intraoperative blood loss.

Surgical Procedure

The same group of experienced senior surgeons, trained and capable to use both MECC and CECC, performed all cases. The decision for MECC or CECC was based on the discretion of the operating surgeon. In all elective cases, platelet inhibitors or anticoagulation were stopped seven days prior to surgery, if possible. Heparin was stopped six hours preoperatively. All patients underwent generalized anesthesia with propofol, fentanyl and pancuronium per standardized institutional protocol. In all cases, a median sternotomy was performed. The internal mammary artery (IMA) and either the radial artery or the saphenous vein were harvested prior to the institution of CPB. In both groups, a brief period of hypothermia (34°C) was established. Distal anastomoses were sutured in cardiac arrest. Reperfusion was performed per protocol and CPB was weaned. The chest was closed with common sternotomy wires. The patients remained sedated and intubated and were transferred to the ICU for standardized postoperative weaning and care. Extracorporeal circulation time (ECCT), cross-clamp time and reperfusion time and the number of transfused red blood cell (RBC) units were recorded.

Postoperative course

Immediately after arrival in the ICU, labs were collected, including complete blood count (CBC), basic metabolic panel (BMP) and lactate and cardiac enzymes (T1), which were repeated 6 hours postoperatively (T2) and on the morning of postoperative day (POD) 1 (T3). After the achievement of hemodynamic stability and normothermia, sedation and ventilator settings were weaned and early extubation was attempted. The patients were then transferred to the step-down unit for mobilization and later to the regular floor for standard postoperative care. All patients were enrolled into cardiac rehab after discharge. The need for inotropic support, re-exploration due to bleeding, hemodialysis (HD) and RBC transfusion, 48-hr postoperative blood loss, duration of mechanical ventilation, ICU and hospital stay in days, occurrence of atrial fibrillation (AF), delirium, stroke and infection rates (pulmonary and deep sternal wound infections) were monitored. Death of any cause within 30 days postoperatively was recorded and defined as mortality.

Statistical analysis

We used SPSS 18.0 (SPSS, Chicago, IL) and Stata 10 SE (Stata Corp, College Station, TX). Continuous data are presented as mean ± SD or as median with interquartile range when appropriate. Categorical variables are reported as frequency distributions (n) and simple percentages (%). Multivariate logistic regression analysis for risk factors associated with 30-day mortality was performed. P-values of <0.05 were considered statistical significant.

Results

Baseline characteristics

Table 1 shows the baseline characteristics and preoperative risk factors of both groups. The MECC group (n=530; 60.6%) was larger than the CECC group (n=345; 39.4%), but no statistically significant differences occurred regarding risk factors, including age, gender, BMI, EuroScore, left ventricular ejection fraction (LVEF), urgency status of surgery, acute infarction, previous surgery, DM, AF, hypertension, chronic obstructive pulmonary disease or peripheral vascular disease.

Intraoperative data

There were no statistically significant differences in the use of distal anastomoses between the groups. However, in the MECC group, we found a statistically significant shorter ECCT (78 ± 27 min versus 95 ± 35 min; p<0.001), cross-clamp time (46 ± 16 min versus 53 ± 18 min; p<0.001) and reperfusion time (26 ± 14 min versus 34 ± 19 min; p<0.001), as well as lower RBC transfusion needs [n = 177 (33.4%) versus 225 (65.2%); p<0.001](Table 2).

Laboratory data

No significant difference was seen in the baseline labs (T0) between the groups. Postoperatively, the only statistically significant variable was lactate (mg/dL), which we found significantly lower in the MECC group (T1: 13 ± 12 versus 23 ± 21; p<0.001, T2: 15 ± 17 versus 28 ± 32; p< 0.001, T3: 10 ± 9 versus 13 ± 8; p<0.001). No differences were observed in CBC and creatinine (Table 3).

Postoperative course and data

Table 4 reports the postoperative differences of both groups. Patients in the MECC group required significantly less inotropic support [47 (8.9% versus 56 (16.2%); p<0.001], fewer blood transfusions (1 [0 – 2] units versus 2 [0 – 3] units; p<0.001), less postoperative hemodialysis [n = 12 (2.3%) versus n = 20 (5.8%); p=0.009] and developed less delirium [n = 17 (3.2%) versus n = 22 (6.4%); p=0.03] compared to patients in the CECC group. In addition, in the MECC group, ICU stay was significantly shorter (2 [2 – 4] days versus 3 [2 – 5] days; p<0.01) and 30-day mortality was significantly reduced [n = 14

Table 2. Intraoperative course.

	CECC (n = 345)	MECC (n = 530)	p-value
Use of internal thoracic artery (%)	321 (93.0%)	498 (93.9%)	0.58
Number of distal anastomoses	2.9 ± 0.7	3.0 ± 0.8	0.45
Extracorporeal circulation time, minutes	95 ± 35	78 ± 27	***<0.001***
Cross-clamp time, minutes	53 ± 18	46 ± 16	***<0.001***
Reperfusion time, minutes	34 ± 19	26 ± 14	***<0.001***
Transfusion of red blood cells (%)	225 (65.2%)	177 (33.4%)	***<0.001***
Number of packed red blood cells, unit	1 [0 – 2]	0 [0 – 1]	***<0.001***

Table 3. Biochemical/serological data.

	CECC (n = 345)	MECC (n = 530)	p-value
Hemoglobin (mg/dL)			
T0	12.1 ± 1.9	12.1 ± 1.6	0.74
T1	9.9 ± 1.0	9.9 ± 1.9	0.79
T2	10.4 ± 5.2	10.2 ± 5.2	0.82
T3	10.9 ± 1.8	11.1 ± 1.7	0.10
Platelets (x 10^3/µL)			
T0	240 ± 69	250 ± 87	0.07
T1	152 ± 52	194 ± 84	0.30
T2	161 ± 56	168 ± 69	0.13
T3	217 ± 67	226 ± 79	0.08
Leukocytes (x 10^3/µL)			
T0	8.7 ± 5.3	8.2 ± 2.6	0.06
T1	13.8 ± 14.7	11.8 ± 9.9	***0.02***
T2	10.9 ± 8.9	10.4 ± 6.6	0.32
T3	8.8 ± 3.6	8.5 ± 2.9	0.44
Lactate (mg/dL)			
T0	12 ± 10	11 ± 8	0.12
T1	23 ± 21	13 ± 12	***<0.001***
T2	28 ± 32	15 ± 17	***<0.001***
T3	13 ± 8	10 ± 9	***<0.001***
Creatinine (mg/dL)			
T0	1.3 ± 0.9	1.2 ± 0.9	0.21
T1	1.3 ± 1.1	1.3 ± 1.0	0.73
T2	1.3 ± 0.9	1.1 ± 0.5	***<0.001***
T3	1.4 ± 0.8	1.3 ± 0.7	0.10

Blood samples were collected preoperatively (T0), 30 min after arrival at the intensive care unit (T1), 6 hours after surgery (T2) and at discharge (T3).

(2.6%) versus n = 27 (7.8%); p<0.001]. No statistically significant difference was found between the groups in 48-hour postoperative drainage output, need for re-sternotomy due to bleeding, the occurrence of AF, post-operative infections (pulmonary and deep sternal wound infections), stroke and hospital stay (Table 4).

Independent risk factors for 30-day mortality

In addition, we found that duration of CPB (Odds ratio 1.03, CI 1.02 – 1.04, p<0.001), cross-clamp time (Odds ratio 0.97, CI 0.94 – 0.99, p=0.016) and postoperative HD (Odds ratio 13.72, CI 5.27 – 35.74, p<0.001) were independent risk factors for 30-day mortality. No significance was found for CECC, urgency of surgery or blood transfusion. The results are summarized in Table 5.

Discussion

In a prior study, patients over 75 years of age were found to have no difference in mortality, myocardial infarction or stroke if they undergo CABG compared to drug-eluting stent (DES) placement, but a significantly higher

Table 4. Postoperative data.

	CECC (n = 345)	MECC (n = 530)	p-value
Inotropic support	56 (16.2%)	47 (8.9%)	***<0.001***
48-hour drainage loss, mL	560 [350 – 850]	550 [350 – 840]	0.65
Re-exploration for bleeding	10 (2.9%)	19 (3.6%)	0.70
Number of packed red blood cells, unit	2 [0 – 3]	1 [0 – 2]	***<0.001***
Duration of ventilation, hours	12 [9 – 17]	11 [8 – 15]	***<0.01***
Postoperative temporary dialysis	20 (5.8%)	12 (2.3%)	***0.009***
Postoperative atrial fibrillation	28 (8.1%)	58 (5.5%)	0.13
Pulmonary infection	20 (5.8%)	17 (3.2%)	0.08
Deep sternal wound infection	23 (6.7%)	33 (6.2%)	0.78
Delirium	22 (6.4%)	17 (3.2%)	***0.03***
Stroke	8 (2.3%)	7 (1.3%)	0.29
Intensive care unit stay, days	3 [2 – 5]	2 [2 – 4]	***<0.01***
Hospital stay, days	10 [8 – 12]	9 [8 – 12]	0.45
30-day mortality	27 (7.8%)	14 (2.6%)	***<0.001***

Table 5. Multivariate logistic regression analysis* for risk factors associated with 30-day mortality.
** = Hosmer-Lemeshow-Test* x^2*: p=0.309.*

	Odds ratio	95% Confidence interval	p-value
Conventional extracorporeal circulation	1.75	0.78 – 3.95	0.18
Urgency of surgery	1.14	0.71 – 1.84	0.59
Extracorporeal circulation time	1.03	1.02 – 1.04	***0.001***
Cross-clamp time	0.97	0.94 – 0.99	***0.016***
Transfusion of red blood cell	1.45	0.63 – 3.36	0.39
Postoperative temporary dialysis	13.72	5.27 – 35.74	***0.001***

incidence of repeat intervention with DES placement.[14] Kahn et al. have shown that more frail and elderly patients are undergoing cardiac surgery nowadays than 10 years ago. They have increased mortality and are at increased risk for prolonged ICU stay and adverse events, such as stroke, infections and acute kidney injury (AKI).[15] In their study, about 60% were isolated CABG cases, reviewed 2001–2010, and the mortality for patients defined as frail was 14%. Patients included in their study had an average EuroScore of 6%. A review of the STS database for 108 nonagenarians undergoing cardiac surgery from 2002 to 2012 showed a high prevalence of preoperative cerebrovascular disease (23.1%) and arrhythmia (55.6%). Overall, nonagenarian mortality was 13%.[3] Therefore, it is imperative to find lower-risk solutions for elderly patients undergoing CABG.

Our study reviewed 875 elderly patients, aged 75–91 years, with a EuroScore of 10.5%, who underwent isolated CABG surgery with either MECC or CECC and found significantly reduced ECCT, cross-clamp and reperfusion time, intra- and postoperative RBC transfusions, need for inotropic support and hemodialysis and stroke and delirium, as well as shorter ICU stay and reduced 30-day mortality in the MECC group. These data are mainly consistent with previously published results of analyses of other high-risk patient populations undergoing CABG. Our group is very experienced with MECC and has demonstrated favorable outcome compared to CECC in several previous publications: MECC had reduced postoperative mortality, length of stay, lower transfusion requirements, less renal and myocardial damage and a lower incidence of sternal wound infections in diabetic patients.[10] However, in those patients, the predicted perioperative risk according to the EuroScore was lower (4.9%) than in the elderly population evaluated in this study (10.5%). Another previous analysis showed that especially high-risk patients of any age with a EuroScore >10% had less myocardial damage, lower transfusion rates, less AKI and lower 30-day mortality.[9] However, this study did not reveal a significant difference in postoperative creatinine levels. Independent risk factors for 30-day mortality in elderly patients were duration of CPB, cross-clamp time and postoperative HD, which were all shorter in the MECC group. A previous analysis of younger patients identified duration of CPB, cross-clamp time, AKI and preoperative myocardial infarction as independent risk factors.[16]

These results allow us to suggest that MECC is not only a safe, but also a superior alternative for CABG in elderly patients compared to CECC.

Possible explanations for better results with MECC have been discussed in detail by prior authors.[9,10,17] Most likely, the reduction of blood-artificial surface contact and the reduction in priming volume decrease inflammatory response, hemodilution and third spacing. The lower lactate reflects better tissue perfusion and less anaerobic cell metabolism, as shown by our results in elderly as well as other populations.[10] Other approaches to reduce mortality in elderly patients undergoing CABG are off-pump coronary artery bypass grafting (OPCAB) and minimally invasive cardiac surgery CABG (MICS-CABG). Both have been widely discussed in the literature and are controversial due to limited exposure of the surgical field, less surgical control and acuity and hemodynamic instability during exposure of the posterior wall. However, the GOPCABE study group found that, in patients 75 years of age or older, there was no significant difference between on-pump and off-pump CABG with regard to death, stroke, myocardial infarction, repeat revascularization or new renal-replacement therapy within 30 days and 12 months after surgery.[18] Even further, van Boven et al. reported that, in elderly patients, MECC was associated with an improved early postoperative respiratory performance and lower transfusion rates compared to CECC or OPCAB.[19]

Our study has some limitations. This was a retrospective database analysis from one single center. The groups were not randomized or blinded and selection bias might contribute. Confounding factors might have contributed and influenced the outcome.

Concluding from our results, MECC is superior to CECC in 75-91-year-old patients undergoing CABG surgery. Especially, reduced ECCT, 30-day mortality and lengths of ICU stay, as well as lower transfusion rates, encourage the use of MECC in elderly patients.

Declaration of Conflicting Interest

The authors declare that there is no conflict of interest.

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