Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Original article | Published 11 February 2022 | doi:10.4414/SMW.2022.w30101
Cite this as: Swiss Med Wkly. 2022;152:w30101

Initial experience with minimally invasive extracorporeal circulation in coronary artery bypass graft reoperations

Paul Philipp Heinisch[ab*], Maks Mihalj[a*], Elif Haliguer[a], Brigitta Gahl[a], Bernhard Winkler[a], Philipp Venetz[c], Hansjoerg Jenni[a], Patrick Schober[d], Gabor Erdoes[e], Markus M. Luedi[e], Joerg C. Schefold[f], Alexander Kadner[a], Christoph Huber[g], Thierry P. Carrel[a]

[a] Department of Cardiovascular Surgery, University Hospital Bern, University of Bern, Switzerland
[b] Department of Congenital and Pediatric Heart Surgery, German Heart Center Munich, Technische Universität München, Munich, Germany
[c] Department of Intensive Care Medicine, Luzerner Kantonsspital, Luzern, Switzerland
[d] Department of Anaesthesiology, Amsterdam UMC, Vrije Universiteit Amsterdam, Netherlands.
[e] Department of Anaesthesiology and Pain Medicine, University Hospital Bern, University of Bern, Switzerland
[f] Department of Intensive Care Medicine, University Hospital Bern, University of Bern, Switzerland
[g] Department of Cardiovascular Surgery, Geneva University Hospital, University of Geneva, Switzerland
[*] Equally contributing first authors

Summary

AIMS OF THE STUDY: Minimally invasive extracorporeal circulation (MiECC) is an established alternative to conventional extracorporeal circulation (CECC) in coronary artery bypass graft surgery (CABG), but data on its use in cardiac reoperations are limited. We aimed to analyse perioperative morbidity and mortality in adult patients undergoing reoperations for isolated CABG using either CECC or MiECC circuits at our centre.

METHODS AND RESULTS: In a single centre retrospective observational study of all adult patients undergoing cardiac reoperations for isolated CABG between 2004 and 2016, we identified 310 patients, and excluded those who received concomitant cardiac procedures (n = 205). Of the remaining 105 patients, 47 received isolated redo-CABG using MiECC, and 58 received CECC. Propensity score modelling was performed, and inversed probability treatment analysis was used between the treatment groups. Primary endpoint was 30-day all-cause mortality. Secondary endpoints included major adverse cardiac or cerebrovascular events or need for conversion to CECC. Groups were comparable, apart from a higher incidence of NYHA class III or higher in CECC group (33.5% vs 8.6%, p= 0.004). Shorter times for operation, cardiopulmonary bypass and aortic cross-clamp were observed in the MiECC group. The incidence of postoperative atrial fibrillation was significantly lower with MiECC (22.1%, p = 0.012). No significant difference was observed in all-cause 30-day mortality between the MiECC and CECC groups (6.8% vs. 8.3%, p = 0.81).

CONCLUSION: We found no difference in overall mortality between CECC and MiECC in patients undergoing reoperation for isolated CABG. Furthermore, we found no indication of differences in most outcomes between extracorporeal circuit types. In the case of redo-CABG, MiECC could provide an alternative strategy.

Correspondence:
Paul Philipp Heinisch, MD
Department of Cardiovascular Surgery
University Hospital Bern
Freiburgstrasse 18
CH-3010 Bern
ppheinisch[at]
googlemail.com

Introduction

In patients with severe coronary artery disease, surgical revascularisation using conventional extracorporeal circulation (CECC) circuits currently is the preferred perfusion technique for cardiopulmonary bypass (CPB) in most centres worldwide [1]. Through the continuous technological improvements of CECC in the past decades [2], the peri- and postoperative outcomes have been improving despite the increasing prevalence of high-risk patients. As a result, the use of CECC in coronary artery bypass graft surgery (CABG) is currently considered the "gold standard" with respect to safety, efficacy, and quality of surgical revascularisation [3, 4].

ABBREVIATIONS

BMI	body mass index
CABG	coronary artery bypass graft surgery
CECC	conventional extracorporeal circulation
CPB	cardiopulmonary bypass
ICU	intensive care unit
IPTW	inversed probability treatment weighing
LVEF	left ventricular ejection fraction
MACCE	major adverse cardiac and cerebrovascular events
MI	myocardial infarction
MiECC	minimally invasive extracorporeal circulation
NYHA	New York Heart Association
redo	reoperations

However, the use of CECC circuits has been associated with various degrees of systemic inflammatory response syndrome (SIRS), possibly contributing to adverse clinical outcomes. With the aim to reduce pathophysiological CECC-induced adverse effects, such as triggering of complement cascades by artificial surfaces, haemodilution resulting from higher priming volumes, and pressure changes within the cardiotomy reservoir [5–7], efforts have been made in recent years to reduce these adverse effects, through the continuous improvement of the CPB circuits. This led to the concept of minimally invasive extracorporeal circulation (MiECC) circuits [8]. MiECC is a closed system with a smaller extracorporeal volume, reduced artificial surfaces, smaller priming volume and reduced air-blood contact [3].

The concept of off-pump coronary artery bypass grafting (OPCAB) was developed with a similar intention, to reduce CECC-related adverse effects. Although some data indicate that adverse pathophysiological effects of CECC can be partially avoided by OPCAB in coronary surgery, especially in patients with multiple comorbidities, porcelain aorta, or in patients undergoing reoperation for CABG (redo-CABG) [3, 9], it may lead to incomplete revascularisation [2, 4, 7, 10], and longer intensive care unit (ICU) and hospital stays [2].

Several studies compared the clinical effects of MiECC with CECC and reported conflicting results [1]. Whereas some evidence supports decreased postoperative blood loss with reduced need for blood transfusion [3, 7] and a decrease in some perioperative adverse events (e.g., SIRS with resulting organ dysfunction) in CABG surgery using MiECC circuits when compared with CECC circuits, other studies could not confirm these findings [1, 7]. However, there is evidence supporting MiECC circuits and OPCAB to improve perioperative outcomes after CABG, compared with CECC [3]. Therefore a growing number of centres including ours, use MiECC circuits or OPCAB as preferred choices not only in elective isolated CABG cases, but also in high-risk patients in an elective or emergency setting, as well as patients undergoing aortic valve surgery [11–13].

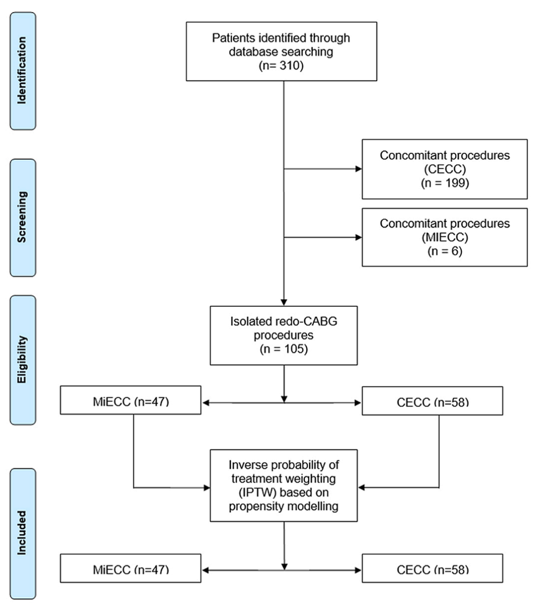
Cardiac reoperations, however, are associated with increased peri- and postoperative risk with an increased incidence of major adverse cardiac and cerebrovascular events (MACCE). These patients are traditionally operated on using the CECC circuits and so far no data exist on the use of MiECC circuits in cardiac reoperations. Specifically, in cardiac reoperations for isolated CABG, the patients are operated on either using a CECC circuit, or an OPCAB approach. Although the use of MiECC circuits in isolated redo-CABG is technically feasible, there are no data to date on its safety and efficacy. [1]. Therefore, we retrospectively investigated our experience in the use of MiECC circuits in isolated redo-CABG cases, focusing on the peri- and early postoperative outcomes, and compared these results with CECC circuits in a propensity score modelling analysis.

Methods

We analysed all adult patients who underwent a reoperation for CABG (redo-CABG) using CECC or MiECC between 2004 and 2016 at our centre. From 2004 to 2010 all isolated redo-CABG procedures were performed using the CECC circuits. As a result of the growing experience and favourable results of the MIECC circuits in isolated CABG procedures, the use of MiECC as standard of practice in all consecutive isolated re-do-CABG cases was initiated. Of 310 patients who underwent re-do-CABG, patients with concomitant cardiac procedures were excluded (199 patients using CECC circuits, 6 patients using MiECC circuits), and only those who received isolated re-do-CABG were included (fig. 1). All patients with concomitant procedures (e.g., valve or aortic surgery) in combination with redo-CABG were not eligible for MIECC. A total of 105 patients were identified, 47 in the MiECC group and 58 in the CECC group. The primary endpoint was all-cause 30-day mortality. Secondary endpoints included major adverse cardiac or cerebrovascular events (MACCE), or conversion to CECC. MACCE were defined as sudden cardiac death, perioperative myocardial infarction (MI), neurological dysfunction (defined as stroke or transient ischaemic attack), new renal dysfunction (defined as doubled baseline creatinine levels, or creatinine levels of >170 µmol/l), pulmonary arterial embolism, postoperative atrial fibrillation, or surgical re-exploration for bleeding. Perioperative myocardial infarction was defined according to the "2012 Third Universal Definition of Myocardial Infarction by the European Society of Cardiology Guidelines" as elevation of cardiac high-sensitive troponin (hs-TnT) >10 × 99th percentile upper reference limit in patients with normal baseline hs-TnT levels. In addition, the following were considered indicative of MI: new pathological Q-waves, new left bundle branch block, documented new native coronary artery occlusion in coronary angiography, imaging evidence of new loss of viable myocardium, or new regional wall motion abnormality [14].

As a pre-requisite, all patients were evaluated preoperatively using percutaneous coronary intervention (PCI) with coronary lesions (left main stenosis, complicated and multiple lesions) unsuitable for primary PCI, as a standard of

Figure 1: Study flowchart. CABG: coronary artery bypass graft; CECC: conventional extracorporeal circulation; MiECC: minimally invasive extracorporeal circulation



care at our institution. Emergency procedures with acute myocardial infarction included cases with conversion to surgical correction after failed PCI. Rdo-CABG procedures were performed using a CECC circuit or MiECC circuit, under general anaesthesia. Complete surgical revascularisation was the objective in all patients. All operations were performed by senior surgeons experienced in redo-CABG and with experience with both CECC and MiECC circuits. The study was approved by the Cantonal Ethics Committee in Bern on human research prior to commencement of the study.

Operational technique and perioperative management

Our minimally invasive cardiopulmonary circuit (MiECC) comprises a closed circuit containing the oxygenator and pump. Unlike a CECC circuit, this does not have an open venous reservoir. The tubing system is shorter than that of CECC circuits. These characteristics enable a reduction in the priming volume as compared with CECC, as well as a reduction in some adverse side effects [15].

At the time of this study, the MiECC circuit consisted of a Maquet® (Cardiopulmonary AG, Hirrlingen, Germany) minimally invasive cardiopulmonary circuit with a RotaFlow® centrifugal pump (RotaFlow, Jostra AG) and a hydrophobic oxygenation membrane (Quadrox Safeline®, Maquet, Cardiopulmonary AG, Hirrlingen, Germany). This system required 600 ml of priming, as opposed to 1800 ml for the CECC. As previously mentioned, we employed a single injection (100 ml) of crystalloid cardioplegia [16]. During MiECC, the perfusion flow was set to two litres per square metre of body surface area. All patients received an initial bolus of unfractionated heparin (400 international units per kilogram body weight) tailored to an activated clotting time of at least 480 seconds (ACT plus®, Medtronic, USA) as per institutional protocol.

Data collection

The eligible patients were identified from the internal hospital records (Dendrite Clinical Systems Ltd, Henley on-Thames, UK), and for this study relevant pre-, peri- and postoperative data obtained from existing internal hospital records. Patients were followed up for 30 days. Peri- and postoperative endpoints were defined according to the guidelines of Akins et al. [17]. Additive and logistic EuroSCOREs, and EuroSCORE II were calculated to assess the presumed risk of 30-day all-cause mortality. The additive EuroSCORE ranges from 0 to about ≥40 (as age scores linearly by 5-year increments, the score is not strictly limited). The logistic EuroSCORE and EuroSCORE II range from 0.88 or 0.5, respectively, to <100, representing the risk of perioperative death in % [11–13].

Statistical analysis

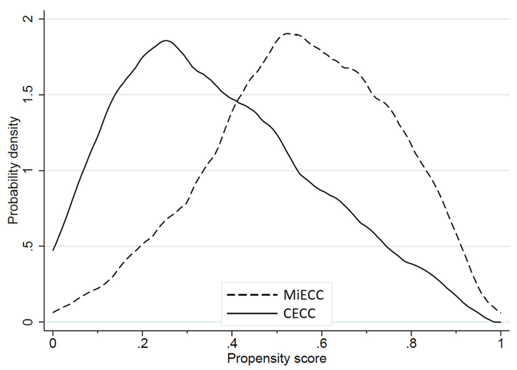
We used propensity score modelling to construct balanced treatment groups with respect to risk factors, applying inverse probability of treatment weighting (IPTW). We included age, logistic EuroSCORE I, arterial hypertension, preoperative renal disease, myocardial infarction within 90 days before surgery and presence of three vessel coronary artery disease as covariates into a logistic regression as propensity model. The tails of the of propensity score were trimmed at both ends of the distribution in both groups at the more centred of the 2.5 and 97.5 percentile of the groups, representing areas of suspected residual confounding. Continuous variables were summarised as means ± standard deviation (SD) in the case of normal distribution and as geometric means with SDs calculated on the log scale and back-transformed if the distribution was skewed. Comparisons were calculated using linear or Poisson regressions, respectively. Dichotomous variables are expressed in absolute numbers and percentages, with comparisons conducted using logistic regression. After IPTW, robust SDs were used in all analyses. Statistical analysis was performed by a biostatistician (BG) using Stata V 16.0 (StataCorp, College Station, TX, USA).

Results

Unadjusted baseline data (before IPTW analysis) are summarised in supplementary table S1–S3 (in the appendix). Operative data were significantly indifferent between the groups. After IPTW, both groups were comparable in terms of all baseline covariates used for propensity score estimation. IPTW improved covariate balance between treatment groups. Figure 2 shows the Kernel density analysis of the probability to receive MiECC in either group, indicating good overlap of the groups.

After IPTW, a total of 105 patients were identified for analysis: 47 patients (44.8%) underwent isolated redo-CABG using ab MiECC circuit and 58 patients (55.2%) underwent isolated redo-CABG using a CECC circuit (fig. 1). The baseline groups were comparable; the cohorts of interest differed significantly only in the prevalance of New York Heart Association class III or IV, which was less common in the MiECC group (8.6%, n = 4 compared with 33.5%, n = 19 in the CECC group (p = 0.004). Mean age was 65.3 ± 14.6 years for the MiECC group and 65.5 ± 9.3 years for the CECC group (p = 0.954). Both groups had high incidence of MI within 90 days before surgery, at 41.1% and 39.6%, respectively (p = 0.893), and there was high prevalence of three-vessel coronary artery disease in both groups (69.0% and 68.9%, respectively, p = 0.991). The estimated operative risk calculated as EuroSCORE II was 4.3% and 4.2%, respectively (p = 0.711). The preoper-

Figure 2: Kernel density analysis of the probability to receive MiECC in either group shows a good overlap of the groups. Regions outside the more centred 2.5th and 97.5th percentile (red vertical lines) were trimmed off to eliminate residual confounding [16]. CECC: conventional extracorporeal circulation; MiECC: minimally invasive extracorporeal circulation



ative left ventricular ejection fraction (LVEF) averaged almost 52.2 ± 12.4% in the MiECC group and 51.2 ± 15.2% in the CECC group (p = 0.726). The most frequent cardiovascular risk factors in both groups were hypercholesterolaemia and arterial hypertension. The number of years since last surgery was similar in both groups, with the mean of 10.6 years for the MiECC group and 11.4 years for the CECC group (p = 0.257), with previous CABG surgery being the most common in both groups, at 84.3% and 83.0%, respectively (p = 0.873). Further patient baseline data are summarised in table 1.

The intraoperative data are presented in table 2. The numbers of distal anastomoses in the MiECC and CECC groups were comparable at 2.4 ± 0.6 and 2.6 ± 0.8, respectively (p = 0.191). There was a statistically significant shorter duration of surgery, duration on CBP support, and duration of aortic cross-clamp in the MiECC group (p <0.05). More emergency surgeries and more patients under intra-aortic ballon pump (IABP) support prior to surgery were observed in the CECC group (12.8% vs 19.2%, and 12.2% vs 16.3%, respectively), although statistically not significant.

Table 1:
Preoperative patient baseline data after propensity score matching and after inverse probability of treatment weighting (IPTW).

Patient baseline data	MiECC (n = 47)	CECC (n = 58)	Difference	p-value
Age in years	65.3 ± 14.6	65.1 ± 9.3	–0.012	0.954
Female	5 (10.6%)	8 (13.1%)	–0.075	0.742
Diabetes on insulin	10 (21.5%)	7 (12.8%)	0.235	0.250
Arterial hypertension	39 (82.5%)	45 (76.7%)	0.144	0.493
Hypercholesterolaemia	38 (80.9%)	50 (8578%)	–0.144	0.568
Smoking	29 (61.9%)	35 (60.8%)	0.023	0.916
Height in metres	1.71 ± 0.09	1.73 ± 0.10	0.133	0.498
Weight in kilograms	82.1 ± 13.4	81.0 ± 17.3	–0.070	0.719
Obesity (BMI >30 kg/m^2)	15 (32.4%)	13 (22.9%)	0.215	0.307
Impaired kidney function	15 (32.0%)	17 (29.0%)	0.066	0.756
Peripheral arterial disease	10 (21.8%)	8 (14.3%)	0.200	0.372
Carotid disease	7 (13.9%)	6 (10.2%)	0.112	0.598
COPD	3 (6.2%)	3 (5.3%)	0.041	0.819
MI 90 days prior to surgery	19 (41.1%)	23 (39.6%)	0.030	0.894
CAD: 1-vessel	5 (11.4%)	6 (10.8%)	0.020	0.931
CAD: 2-vessels	9 (19.6%)	12 (20.4%)	–0.018	0.936
CAD: 3-vessels	32 (69.0%)	40 (68.9%)	0.003	0.991
NYHA Class ≥III	4 (8.6%)	19 (33.5%)	–0.602	0.004
CCS Class ≥3	22 (47.4%)	26 (45.7%)	0.034	0.876
LVEF in %	52.2 ± 12.4	51.2 ± 15.2	–0.068	0.726
Additive EuroSCORE I	7.3 ± 3.1	7.3 ± 2.8	–0.001	0.995
Logistic EuroSCORE I (%)	8.0 (6.3–10.2)	7.7 (6.2–9.5)	–0.158	0.416
EuroSCORE II (%)	4.3 (3.4 –5.4)	4.2 (3.3–5.4)	–0.015	0.711
Years since last cardiac surgery	10.6 (7.8–14.5)	11.4 (9.7–13.3)	0.294	0.257
Type of previous surgery:				
– CABG	40 (84.3%)	48 (83.0%)	0.033	0.873
– AVR	2 (3.5%)	4 (6.9%)	–0.149	0.425
– Aortic root replacement	3 (5.8%)	1 (1.8%)	0.208	0.321
– AVR + ascending aorta replacement	0 (0.0%)	3 (4.4%)	—0.267	0.413
– ASD repair	3 (6.5%)	0 (0.0%)	0.388	0.059
– VSD repair	0 (0.0%)	2 (3.8%)	–0.276	0.188

MiECC: minimally invasive extracorporeal circulation circuit group; CECC: conventional extracorporeal circulation circuit group; BMI: body mass index; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; CAD: coronary artery disease; NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society; LVEF: left ventricular ejection fraction; CABG: coronary artery bypass grafting; AVR: aortic valve replacement; ASD: atrial septal defect; VSD: ventricular septal defect

Values are mean ± SD or number (percentage).

Table 2:
Intraoperative data after propensity score matching and after inverse probability of treatment weighting (IPTW).

Intraoperative data	MiECC (n = 47)	CECC (n = 58)	Difference	p-value
Emergency surgery	6 (12.8%)	11 (19.2%)	–0.174	0.437
Preoperative IABP	6 (12.2%)	9 (16.3%)	–0.118	0.628
Operation duration in minutes	226.0 ± 66.5	256.8 ± 89.4	0.434	0.028
CBP time in minutes	86.5 ± 40.1	108.5 ± 57.3	0.444	0.024
Aortic cross-clamping time in minutes	36.7 (32.3–41.6)	51.8 (46.7–57.5)	9.989	0.001
Number of distal anastomoses	2.4 ± 0.6	2.6 ± 0.8	0.254	0.191

MiECC: minimally invasive extracorporeal circulation circuit group; CECC: conventional extracorporeal circulation circuit group; IABP: intra-aortic balloon pump; CPB: cardiopulmonary bypass

Values are mean ± SD or number (percentage).

The postoperative results are summarised in table 3. The adjusted 30-day mortality was in the MiECC group 6.8%, and 8.3% in the CECC group (standard mean difference –0.058, p = 0.814). There were no significant differences the ICU- and hospital stay between groups. Both groups had comparable outcomes, with a slightly lower occurrence of perioperative myocardial infarction (7.0% vs 14.5%), of renal complications (14.7% vs 22.8%), and of surgical re-exploration for bleeding (8.9% vs 16.1%) in the MiECC group, although statistically not significant. However, we observed a statistically significant lower occurrence of postoperative atrial fibrillation in the MiECC group (22.1% vs 49.3%, p = 0.012). No significant reduction of blood transfusion requirements was observed in either group.

Discussion

The present study represents the first comparative analysis of early postoperative outcomes in isolated CABG reoperations using MiECC and CECC circuits. Propensity score modelling was applied to reduce selection bias. After inverse probability of treatment weighting analyses, we observed a statistically significant lower occurrence of postoperative atrial fibrillation in the MiECC group.

The majority of patients had a previous CABG surgery and the presence of three -vessel coronary artery. In both groups, comparable numbers of distal anastomoses of 2.4 ± 0.6 and 2.6 ± 0.8 in MiECC and CECC groups, respectively, were performed, indicating complete revascularisation. Nonetheless, the time on CPB support, as well as the aortic cross-clamp time were both significantly lower in the MiECC group, as was the median duration of CPB time and aortic cross clamp time. While all procedures were performed by senior surgeons, standard practice for all cardiac reoperations at our institution, the differences between the groups may be explained by higher prevalence of emergency cases in the CECC group (19.2% vs 12.8%), as well as the significantly higher rate of NYHA class III or higher (33.5% vs 8.6%). This difference may have also contributed to the significantly elevated rate of postoperative atrial fibrillation in CECC group (49.3% vs 22.1%), although a higher incidence of atrial fibrillation with conventional circuits has been observed before [19–21, 28, 29].

The elimination of air-blood contact may theoretically be a key advantage of MiECC and may explain the potentially reduced early postoperative inflammatory response after interventions compared with CECC. Coating and reduction of overall size in MiECC minimises the foreign surface area, which is one of the main triggers for SIRS [21–24]. In clinical practice, this translates into superior myocardial protection with significantly reduced levels of cardiac injury markers, lower incidence of postoperative atrial fibrillation, lower incidence of stroke, less haemodialysis as well as lower creatinine levels postoperatively, and better neurocognitive and lung function [19]. This improved end-organ protection may potentiate a survival advantage in MIECC, and reduce the occurrence of complications [19]. We observed a statistically significant lower incidence of postoperative atrial fibrillation in MiECC group in redo-CABG, and a non-significant reduction of perioperative MI and renal dysfunction. These differences in outcomes are comparable to results previously described [2, 9, 27].

Asteriou et al. described better outcomes using MiECC circuits in terms of morbidity and mortality in high-risk patient groups such as in reoperations and emergency cases. Furthermore, a risk reduction for development of renal dysfunction of 77% was observed when using MiECC circuits [25]. In our study, a reduction of 8.1% was observed in postoperative renal dysfunction, although this was non-significant. Christenson et al. examined the peri- and postoperative outcomes in 594 patients undergoing redo-CABG using CECC, and found the overall mortality at 30 days to be 7.3%, and incidence of postoperative complications of renal dysfunction and postoperative stroke of 11% and 2%, respectively [26]. The overall 30-day mortality of 8.3% in the CECC group in our study correlates with

Table 3:
Postoperative data after propensity score matching and after inverse probability of treatment weighting (IPTW).

Postoperative data	MiECC (n = 47)	CECC (n = 58)	Difference	p-value
30-day all-cause mortality	3 (6.8%)	5 (8.3%)	–0.058	0.814
Postoperative mechanical support (IABP)	7 (14.6%)	9 (15.3%)	–0.018	0.940
ICU stay in days	1.6 (1.2–2.2)	1.8 (1.4–2.3)	0.053	0.352
Hospital length of stay in days	10.5 (9.0–12.2)	11.2 (9.9–12.7)	0.436	0.707
MACCE				
– Postoperative myocardial infarction	3 (7.0%)	8 (14.5%)	–0.244	0.324
– Neurological dysfunction (stroke or TIA)	3 (6.3%)	3 (5.1%)	0.049	0.808
– Renal dysfunction	7 (14.7%)	13 (22.8%)	–0.206	0.365
– Pulmonary artery embolism	1 (1.6%)	0 (0.0%)	0.166	0.287
– Atrial fibrillation	10 (22.1%)	29 (49.3%)	–0.563	0.012
CK total (U/l)	606 (458–802)	783 (623–982)	70.193	0.255
CK MB (µg/l)	18.6 (13.1–26.6)	31.9 (23.5–43.2)	4.016	0.196
Total blood transfusion units	3.7 (2.9–4.8)	4.2 (3.3–5.3)	0.170	0.177
Transfused packed red blood cells units	2.7 (2.1–3.4)	2.3 (1.8–3.0)	–0.139	0.278
Transfused platelet units	1.3 (1.0–1.6)	1.3 (1.1–1.6)	0.016	0.195
Transfused FFP units	2.0 (1.4–2.8)	2.2 (1.6–3.1)	0.052	0.123

MiECC: minimally invasive extracorporeal circulation circuit group; CECC: conventional extracorporeal circulation circuit group; IABP: intra-aortic balloon pump; ICU: intensive care unit; MACCE: major cardiac and cerebrovascular events; TIA: transient ischaemic attack; CK: creatinine kinase; FFP: fresh frozen plasma concentrate

Values are mean ± SD or number (percentage).

mortality rates described by Christenson et al, although more patients experienced NYHA class III or higher, and a higher rate of emergency cases and of patients requiring IABP support prior to surgery. As these were not included in the propensity score modelling, because it would further decrease the sample size and power of the study, these results should be interpreted cautiously, and further analyses are needed to make any recommendations [26].

So far the clinical benefits of MiECC have not been investigated in a large randomised trial. The current ongoing CoMICS Trial is looking at conventional versus minimally invasive extra-corporeal circulation in patients undergoing cardiac surgery. CoMICS is a multicentre randomised controlled trial including approximately 3500 patients. CoMICS will compare the effectiveness and cost effectiveness of MiECC versus CECC in patients undergoing cardiac surgery requiring extra corporeal circulation. The aim is to inform clinical understanding and influence surgical practice by providing high quality evidence to support or refute the use of MiECC for patients undergoing cardiac surgery. The estimation of the cost-effectiveness of MiECC versus CECC is an major goal of the study. Patient enrolment is still ongoing and results are currently pending [30]

Existing comparative studies of MiECC versus CECC in myocardial revascularisation report lower early postoperative morbidity and mortality with MiECC [1, 31, 32]. A meta-analysis including 2770 patients demonstrated that MiECC significantly decreases mortality, when compared withconventional extracorporeal circulation circuits (0.5% vs 1.7%, p = 0.02) [31]; however, cardiac reoperations were excluded. To the best of our knowledge, no data exist on the use of MiECC in reoperations for myocardial revascularisations, and our study represents first comparative analysis in the use of MiECC and CECC circuits in isolated redo-CABG.

In conclusion, using propensity score estimation, there was no statistically significant difference in overall 30-day mortality in patients undergoing isolated redo-CABG using MiECC versus CECC. We noted significantly a reduced rate of atrial fibrillation in the MiECC group. MiECC may offer an alternative feasible strategy in isolated redo-CABG.

Limitations of this study

Several limitations deserve discussion. As a retrospective single centre analysis, with all its inherent limitations, the data span a period of 12 years from a single institution. Because CECC circuits were routinely utilised for all cardiac reoperations for CABG at our facility until 2010, and MiECC circuits were subsequently been employed, a potential therapeutic bias exists. To reduce this, the same inclusion period was used for the MiECC group, i.e., from 2010 to 2016. However, our institution's treatment techniques, patient demographics, and therapeutic procedures have remained constant over the years. All cardiac reoperations at our institution are performed by experienced senior surgeons, thus minimising the intra- and inter-observer variability.

As we were limited by the number of patients treated for redo-CABG in our institution in the observation period, we did not perform an *a priori* sample calculation but rather used the data of all available patients. With the available sample size, we had 80% power to detect a 26% reduction in the rate of atrial fibrillation at a 0.05 alpha level. Propensity score modelling was performed for six variables considered relevant by the authors, further modelling by emergency status and by NYHA class ≥III between the groups would have significantly reduced the sample size. To minimise the confounding bias, patients were matched using propensity score modelling. The Kernel density analysis shows the overlap between the groups. Potential unmeasured or hidden co-variables may still exist, however, as the analysis showed low values for several outcome variables, calling for further studies in this field.

Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. JCS reports departmental grants (full disclosure) from Orion Pharma, Abbott Nutrition International, B. Braun Medical AG, CSEM AG, Edwards Lifesciences Services GmbH, Kenta Biotech Ltd, Maquet Critical Care AB, Omnicare Clinical Research AG, Nestle, Pierre Fabre Pharma AG, Pfizer, Bard Medica S.A., Abbott AG, Anandic Medical Systems, Pan Gas AG Healthcare, Bracco, Hamilton Medical AG, Fresenius Kabi, Getinge Group Maquet AG, Dräger AG, Teleflex Medical GmbH, Glaxo Smith Kline, Merck Sharp and Dohme AG, Eli Lilly and Company, Baxter, Astellas, Astra Zeneca, CSL Behring, Novartis, Covidien, and Nycomed outside of the submitted work. The money was paid into departmental funds. There was no personal financial gain. – TC is one of tree inventors of the cardioplegia solution (Cardioplexol). The patent belongs to the University Hospital Bern and the University of Bern. – All other authors declare no conflict of interest.

Funding

There was no direct funding for this study.

References

1. Ried M, Haneya A, Kolat P, Philipp A, Kobuch R, Hilker M, et al. Emergency coronary artery bypass grafting using minimized versus standard extracorporeal circulation—a propensity score analysis. J Cardiothorac Surg. 2013 Apr;8(1):59. http://dx.doi.org/10.1186/1749-8090-8-59. PubMed. 1749-8090
2. Kara I, Cakalagaoglu C, Ay Y, Al Salehi S, Yanartas M, Anasiz H, et al. Reoperative coronary artery bypass surgery: the role of on-pump and off-pump techniques on factors affecting hospital mortality and morbidity. Ann Thorac Cardiovasc Surg. 2013;19(6):435–40. http://dx.doi.org/10.5761/atcs.oa.12.02043. PubMed. 2186-1005
3. Kowalewski M, Pawliszak W, Raffa GM, Malvindi PG, Kowalkowska ME, Zaborowska K, et al. Safety and efficacy of miniaturized extracorporeal circulation when compared with off-pump and conventional coronary artery bypass grafting: evidence synthesis from a comprehensive Bayesian-framework network meta-analysis of 134 randomized controlled trials involving 22 778 patients. Eur J Cardiothorac Surg. 2016 May;49(5):1428–40. http://dx.doi.org/10.1093/ejcts/ezv387. PubMed. 1873-734X
4. Kowalewski M, Pawliszak W, Malvindi PG, Bokszanski MP, Perlinski D, Raffa GM, et al. Off-pump coronary artery bypass grafting improves short-term outcomes in high-risk patients compared with on-pump coronary artery bypass grafting: meta-analysis. J Thorac Cardiovasc Surg. 2016 Jan;151(1):60–77.e1. http://dx.doi.org/10.1016/j.jtcvs.2015.08.042. PubMed. 1097-685X
5. Edmunds LH Jr. Blood-surface interactions during cardiopulmonary bypass. J Card Surg. 1993 May;8(3):404–10. http://dx.doi.org/10.1111/j.1540-8191.1993.tb00384.x. PubMed. 0886-0440
6 Edmunds LH. Inflammatory response to cardiopulmonary bypass. Ann Thorac Surg.1998;66:S12–6–discussionS25–8.
7. Winkler B, Heinisch PP, Gahl B, Aghlmandi S, Jenni HJ, Carrel TP. Minimally Invasive Extracorporeal Circulation Circuit Is Not Inferior to Off-Pump Coronary Artery Bypass Grafting: Meta-Analysis Using the Bayesian Method. Ann Thorac Surg. 2016;0: http://dx.doi.org/10.1016/j.athoracsur.2016.08.067. PubMed. 0003-4975

8. Jenni H, Rheinberger J, Czerny M, Gygax E, Rieben R, Krähenbühl E, et al. Autotransfusion system or integrated automatic suction device in minimized extracorporeal circulation: influence on coagulation and inflammatory response. Eur J Cardiothorac Surg. 2011 May;39(5):e139–43. http://dx.doi.org/10.1016/j.ejcts.2010.11.082. PubMed. 1873-734X
9 Dohi M, Miyata H, Doi K, Okawa K, Motomura N, Takamoto S, et al. The off-pump technique in redo coronary artery bypass grafting reduces mortality and major morbidities: propensity score analysis of data from the Japan Cardiovascular Surgery Database†. Eur J Cardiothorac Surg 2015;47:299–307–discussion307–8. doi: http://dx.doi.org/10.1093/ejcts/ezu081. .
10. Kowalewski M, Pawliszak W, Raffa GM, Malvindi PG, Kowalkowska ME, Zaborowska K, et al. Safety and efficacy of miniaturized extracorporeal circulation when compared with off-pump and conventional coronary artery bypass grafting: evidence synthesis from a comprehensive Bayesian-framework network meta-analysis of 134 randomized controlled trials involving 22 778 patients. Eur J Cardiothorac Surg. 2015;49(5):1448–40. http://dx.doi.org/10.1093/ejcts/ezv387. PubMed. 1010-7940
11. El-Essawi A, Breitenbach I, Haupt B, Brouwer R, Baraki H, Harringer W. Impact of minimally invasive extracorporeal circuits on octogenarians undergoing coronary artery bypass grafting. Have we been looking in the wrong direction? Eur J Cardiothorac Surg. 2017 Dec;52(6):1175–81. http://dx.doi.org/10.1093/ejcts/ezx156. PubMed. 1873-734X
12. Starinieri P, Declercq PE, Robic B, Yilmaz A, Van Tornout M, Dubois J, et al. A comparison between minimized extracorporeal circuits and conventional extracorporeal circuits in patients undergoing aortic valve surgery: is 'minimally invasive extracorporeal circulation' just low prime or closed loop perfusion? Perfusion. 2017 Jul;32(5):403–8. http://dx.doi.org/10.1177/0267659117691814. PubMed. 1477-111X
13. Winkler B, Heinisch PP, Zuk G, Zuk K, Gahl B, Jenni HJ, et al. Minimally invasive extracorporeal circulation: excellent outcome and life expectancy after coronary artery bypass grafting surgery. Swiss Med Wkly. 2017 Jul;147(2728):w14474. http://dx.doi.org/10.4414/smw.2017.14474. PubMed. 1424-3997
14. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, White HD; Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, et al. Third universal definition of myocardial infarction. Circulation, vol. 126, American Heart Association, Inc; 2012, pp. 2020–35. doi: http://dx.doi.org/10.1161/CIR.0b013e31826e1058.
15 Immer FF, Ackermann A, Gygax E, Stalder M, Englberger L, Eckstein FS, et al. Minimal extracorporeal circulation is a promising technique for coronary artery bypass grafting. Ann Thorac Surg 2007;84:1515–20–discussion1521. doi: http://dx.doi.org/10.1016/j.athoracsur.2007.05.069. .
16. Kairet K, Deen J, Vernieuwe L, de Bruyn A, Kalantary S, Rodrigus I. Cardioplexol, a new cardioplegic solution for elective CABG. J Cardiothorac Surg. 2013;8 S1:120. http://dx.doi.org/10.1186/1749-8090-8-S1-P120. 1749-8090
17. Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL, et al.; STS; AATS; EACTS. Guidelines for reporting mortality and morbidity after cardiac valve interventions. Ann Thorac Surg. 2008 Apr;85(4):1490–5. http://dx.doi.org/10.1016/j.athoracsur.2007.12.082. PubMed. 1552-6259
18. da Costa BR, Gahl B, Jüni P. Tools & techniques—statistics: propensity score techniques. EuroIntervention. 2014 Oct;10(6):761–7. http://dx.doi.org/10.4244/EIJV10I6A130. PubMed. 1969-6213
19. Anastasiadis K, Murkin J, Antonitsis P, Bauer A, Ranucci M, Gygax E, et al. Use of minimal invasive extracorporeal circulation in cardiac surgery: principles, definitions and potential benefits. A position paper from the Minimal invasive Extra-Corporeal Technologies international Society (MiECTiS). Interact Cardiovasc Thorac Surg. 2016 May;22(5):647–62. http://dx.doi.org/10.1093/icvts/ivv380. PubMed. 1569-9285
20. Anastasiadis K, Asteriou C, Antonitsis P, Argiriadou H, Grosomanidis V, Kyparissa M, et al. Enhanced recovery after elective coronary revascularization surgery with minimal versus conventional extracorporeal circulation: a prospective randomized study. J Cardiothorac Vasc Anesth. 2013 Oct;27(5):859–64. http://dx.doi.org/10.1053/j.jvca.2013.01.010. PubMed. 1532-8422
21 Immer FF, Ackermann A, Gygax E, et al. Minimal extracorporeal circulation is a promising technique for coronary artery bypass grafting. Ann Thorac Surg 2007;84:1515–20–discussion1521. doi: http://dx.doi.org/10.1016/j.athoracsur.2007.05.069. .
22. Immer FF, Pirovino C, Gygax E, Englberger L, Tevaearai H, Carrel TP. Minimal versus conventional cardiopulmonary bypass: assessment of intraoperative myocardial damage in coronary bypass surgery. Eur J Cardiothorac Surg. 2005 Nov;28(5):701–4. http://dx.doi.org/10.1016/j.ejcts.2005.08.019. PubMed. 1010-7940
23. Biancari F, Rimpiläinen R. Meta-analysis of randomised trials comparing the effectiveness of miniaturised versus conventional cardiopulmonary bypass in adult cardiac surgery. Heart. 2009 Jun;95(12):964–9. http://dx.doi.org/10.1136/hrt.2008.158709. PubMed. 1468-201X
24. Benedetto U, Luciani R, Goracci M, Capuano F, Refice S, Angeloni E, et al. Miniaturized cardiopulmonary bypass and acute kidney injury in coronary artery bypass graft surgery. Ann Thorac Surg. 2009 Aug;88(2):529–35. http://dx.doi.org/10.1016/j.athoracsur.2009.03.072. PubMed. 1552-6259
25. Asteriou C, Antonitsis P, Argiriadou H, Deliopoulos A, Konstantinou D, Foroulis C, et al. Minimal extracorporeal circulation reduces the incidence of postoperative major adverse events after elective coronary artery bypass grafting in high-risk patients. A single-institutional prospective randomized study. Perfusion. 2013 Jul;28(4):350–6. http://dx.doi.org/10.1177/0267659113479135. PubMed. 1477-111X
26. Christenson JT, Schmuziger M, Simonet F. Reoperative coronary artery bypass procedures: risk factors for early mortality and late survival. Eur J Cardiothorac Surg. 1997 Jan;11(1):129–33. http://dx.doi.org/10.1016/S1010-7940(96)01030-5. PubMed. 1010-7940
27. Axelsson TA, Mennander A, Malmberg M, Gunn J, Jeppsson A, Gudbjartsson T. Is emergency and salvage coronary artery bypass grafting justified? The Nordic Emergency/Salvage coronary artery bypass grafting study. Eur J Cardiothorac Surg. 2016 May;49(5):1451–6. http://dx.doi.org/10.1093/ejcts/ezv388. PubMed. 1873-734X
28. El-Essawi A, Hajek T, Skorpil J, Böning A, Sabol F, Ostrovsky Y, et al. Are minimized perfusion circuits the better heart lung machines? Final results of a prospective randomized multicentre study. Perfusion. 2011 Nov;26(6):470–8. http://dx.doi.org/10.1177/0267659111419035. PubMed. 1477-111X
29. Panday GF, Fischer S, Bauer A, Metz D, Schubel J, El Shouki N, et al. Minimal extracorporeal circulation and off-pump compared to conventional cardiopulmonary bypass in coronary surgery. Interact Cardiovasc Thorac Surg. 2009 Nov;9(5):832–6. http://dx.doi.org/10.1510/icvts.2009.206466. PubMed. 1569-9285
30. Angelini GD, Reeves BC, Evans J, Culliford LA, Collett L, Rogers CA, et al.; COMICS investigators, The COMICS investigators. Conventional versus minimally invasive extracorporeal circulation in patients undergoing cardiac surgery: protocol for a randomised controlled trial (COMICS). Perfusion. 2021 May;36(4):388–94. http://dx.doi.org/10.1177/0267659120946731. PubMed. 1477-111X
31. Anastasiadis K, Antonitsis P, Haidich AB, Argiriadou H, Deliopoulos A, Papakonstantinou C. Use of minimal extracorporeal circulation improves outcome after heart surgery; a systematic review and meta-analysis of randomized controlled trials. Int J Cardiol. 2013 Apr;164(2):158–69. http://dx.doi.org/10.1016/j.ijcard.2012.01.020. PubMed. 1874-1754
32. Haneya A, Philipp A, Diez C, Ried M, Puehler T, Camboni D, et al. Comparison of two different minimized extracorporeal circulation systems: hematological effects after coronary surgery. ASAIO J. 2009 Nov-Dec;55(6):592–7. http://dx.doi.org/10.1097/MAT.0b013e3181be2f5c. PubMed. 1538-943X

Appendix: Supplementary tables

Table S1:
Preoperative patient baseline data before propensity score matching and before inverse probability of treatment weighting (IPTW).

Patient baseline data	MiECC (n = 47)	CECC (n = 58)	Difference	p-value
Age in years	64.4 ± 12.9	66.1 ± 7.9	0.161	0.402
Female	4 (8.5%)	8 (13.1%)	–0.166	0.402
Diabetes on insulin	12 (25.5%)	8 (13.8%)	0.299	0.133
Arterial hypertension	40 (85.1%)	39 (67.2%)	0.414	0.039
Hypercholesterolaemia	38 (80.9%)	48 (82.8%)	–0.050	0.801
Smoking	32 (68.1%)	32 (55.2%)	0.265	0.179
Height in metres	1.72 ± 0.08	1.72 ± 0.09	0.026	0.498
Weight in kilograms	83.5 ± 14.8	80.4 ± 15.5	–0.203	0.306
Obesity (BMI >30 kg/m^2)	18 (38.3%)	14 (24.1%)	0.308	0.119
Impaired kidney function	20 (42.6%)	14 (24.1%)	0.394	0.047
Peripheral arterial disease	12 (25.5%)	7 (12.1%)	0.350	0.081
Carotid disease	6 (12.8%)	7 (12.1%)	0.021	0.914
COPD	4 (8.5%)	4 (6.9%)	0.061	0.757
MI 90 days prior to surgery	24 (51.1%)	16 (27.6%)	0.483	0.015
CAD: 1-vessel	4 (8.5%)	8 (13.8%)	–0.166	0.402
CAD: 2-vessels	6 (12.8%)	16 (27.6%)	–0.364	0.069
CAD: 3-vessels	37 (78.7%)	34 (58.6%)	0.430	0.031
NYHA Class ≥ III	5 (10.6%)	18 (31.0%)	–0.493	0.016
CCS Class ≥ 3	22 (46.8%)	24 (41.4%)	0.109	0.577
LVEF in%	51.8 ± 12.5	52.1 ± 13.3	0.020	0.920
Additive EuroSCORE I	7.4 ± 3.0	7.1 ± 2.5	–0.130	0.505
Logistic EuroSCORE I (%)	8.4 (6.6–10.7)	7.3 (6.0–8.8)	–0.516	0.000
EuroSCORE II (%)	4.8 (3.7–6.1)	3.9 (3.3–4.5)	–0.424	0.000
Years since last cardiac surgery	10.0 (7.4–13.5)	11.3 (9.7–13.2)	0.554	0.020
Type of previous surgery:				
– CABG	39 (83.0%)	49 (84.5%)	–0.041	0.835
– AVR	2 (4.3%)	4 (6.9%)	–0.114	0.566
– Aortic root replacement	3 (6.4%)	1 (1.7%)	0.243	0.247
– AVR + ascending aorta replacement	0 (0.0%)	2 (3.4%)	–0.252	0.652
– ASD repair	3 (6.4%)	0 (0.0%)	0.383	0.058
– VSD repair	0 (0.0%)	2 (3.4%)	–0.252	0.185

MiECC: minimally invasive extracorporeal circulation circuit group; CECC: conventional extracorporeal circulation circuit group; BMI: body mass index; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; CAD: coronary artery disease; NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society; LVEF: left ventricular ejection fraction; CABG: coronary artery bypass grafting; AVR: aortic valve replacement; ASD: atrial septal defect; VSD: ventricular septal defect

Values are mean ± SD or number (percentage).

Table S2:
Intraoperative data before propensity score matching and before inverse probability of treatment weighting (IPTW).

Intraoperative data	MiECC (n = 47)	CECC (n = 58)	Difference	p-value
Emergency surgery	7 (14.9%)	7 (12.1%)	0.083	0.673
Preoperative IABP	5 (10.6%)	7 (12.1%)	0.045	0.819
Operation duration in minutes	233.3 ± 70.7	249.8 ± 73.6	0.229	0.248
CBP time in minutes	89.6 ± 37.2	102.5 ± 41.9	0.324	0.104
Aortic cross-clamping time in minutes	38.4 (34.143.2)	49.5 (44.655.0)	7.451	0.000
Number of distal anastomoses	2.4 ± 0.6	2.5 ± 0.9	0.069	0.732

MiECC: minimally invasive extracorporeal circulation circuit group; CECC: conventional extracorporeal circulation circuit group; IABP: intra-aortic balloon pump; CPB: cardiopulmonary bypass

Values are mean ± SD or number (percentage).

Table S3:
Postoperative data before propensity score matching and before inverse probability of treatment weighting (IPTW).

Postoperative data	**MiECC (n = 47)**	**CECC (n = 58)**	**Difference**	**p-value**
30-day all-cause mortality	3 (6.4%)	3 (5.2%)	0.052	0.791
Postoperative mechanical support (IABP)	7 (14.9%)	6 (10.3%)	0.138	0.484
ICU stay in days	1.7 (1.3 to 2.2)	1.7 (1.4 to 2.2)	0.033	0.025
Hospital length of stay in days	10.6 (9.1 to 12.4)	11.7 (10.3 to 13.4)	0.651	0.155
MACCE				
– Postoperative myocardial infarction	3 (6.4%)	6 (10.5%)	–0.148	0.459
– Neurological dysfunction (stroke or TIA)	3 (6.5%)	3 (5.4%)	0.050	0.804
– Renal dysfunction	7 (15.2%)	10 (17.9%)	0.072	0.722
– Pulmonary artery embolism	1 (2.2%)	0 (0.0%)	0.224	0.283
– Atrial fibrillation	10 (21.7%)	29 (50.0%)	0.585	0.004
CK total (U/l)	597 (466767)	782 (619989)	76.798	0.000
CK MB (µg/l)	18.5 (13.525.2)	31.6 (23.941.8)	4.474	0.000
Total blood transfusion units	3.6 (2.84.6)	4.1 (3.45.0)	0.232	0.000
Transfused packed red blood cells units	2.7 (2.33.3)	2.3 (1.92.8)	0.199	0.022
Transfused platelet units	1.2 (1.01.5)	1.3 (1.11.6)	0.042	0.041
Transfused FFP units	2.2 (1.62.9)	2.1 (1.62.7)	0.034	0.002

MiECC: minimally invasive extracorporeal circulation circuit group; CECC: conventional extracorporeal circulation circuit group; IABP: intra-aortic balloon pump; ICU: intensive care unit; MACCE: major cardiac and cerebrovascular events; TIA: transient ischaemic attack; CK: creatinine kinase; FFP: fresh frozen plasma concentrate

Values are mean ± SD or number (percentage).