Blood loss in coronary artery bypass grafting on minimally invasive extracorporeal circulation – a single-centre experience and retrospective analysis

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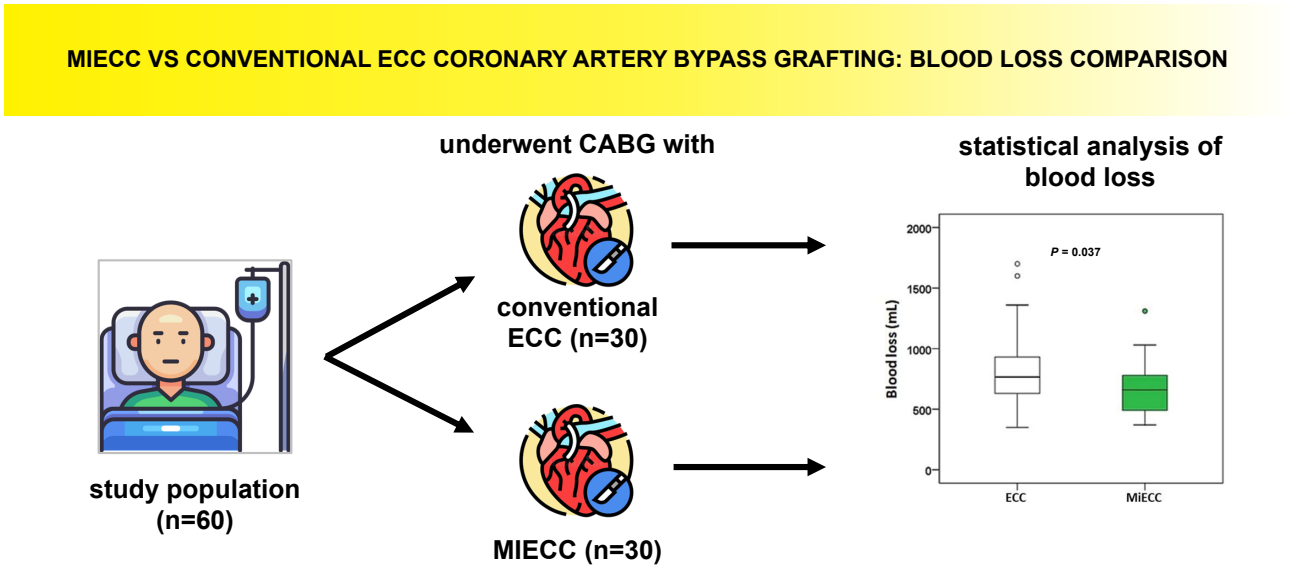
Background. Minimally-invasive extracorporeal circulation (MiECC) is confirmed to mitigate the post-perfusion syndrome resulting in better outcomes in operated patients compared to the conventional cardiopulmonary bypass (ECC).
Aims. To determine whether there is a clinical benefit of lower blood loss in patients operated on MiECC compared to ECC. To provide a detailed construction of modified MiECC and its perfusion management.
Methods. Retrospective analysis of the clinical data of 60 patients undergoing coronary artery bypass grafting on MiECC or ECC. The primary outcome was to compare the following variables in the 2 groups: intraoperative and 30-day mortality and cardiovascular death, myocardial infarction and cerebral stroke (MACCE). Secondary outcomes included surgical revision for bleeding or tamponade, intraoperative and postoperative blood loss and the consumption of packed red blood cell units. We modified our MiECC by connecting a cardiotomy suction.
Results. There was no mortality, major adverse events or surgical revisions in either group. No difference was found for intraoperative blood loss. The MiECC group had significantly lower overall postoperative blood loss (660 mL vs 765 mL, *P*=0.037). Total consumption of packed red blood cell units was insignificantly higher in the ECC group (n=30 vs n=20, *P*=0.490).
Conclusion. MiECC is a safe alternative to conventional ECC in routine procedures such as CABG. Its improved biocompatibility was reflected by better preservation of hemostasis in this study.



Key words: coronary artery bypass grafting, extracorporeal circulation, minimal invasive, blood loss

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INTRODUCTION

Coronary artery bypass grafting (CABG) is a cardiac surgery procedure routinely performed worldwide and has its place in indications for coronary revascularisation alongside percutaneous coronary intervention. The utilization of the cardiopulmonary bypass (CPB) became an inseparable standard for the majority of these procedures. However, decades of research have shown that the use of CPB is burdened by pathophysiological consequences[1,2] such as induction of the systemic inflammatory response syndrome (SIRS) (ref.[3]), coagulopathy[4,5], platelet dysfunction[6,7], hemodilution[8] and microemboli formation[9]. These changes are then accompanied by post-operative organ dysfunction, bleeding, neurological damage, arrhythmias, depression of myocardial function, and others as part of the post-perfusion syndrome. The off-pump CABG addresses that by the complete exclusion of the CPB, although it also has its limitations and may not be suitable for all patients or surgeons. The minimally-invasive extracorporeal circulation (MiECC) has become a modern alternative to the latter in recent years. It was firstly introduced in practice in 1999; this new version of CPB soon proved its superior biocompatibility and beneficial effect as mitigation of the negative impact of CPB on the human organism[10-12], improving outcomes[13] and lowering the mortality in cardiac surgery procedures[14]. The MiECTiS (Minimal Invasive Extracorporeal Technologies International Society) defined the MiECC system as a shortened closed circuit with biologically inert artificial surfaces, reduced priming volumes, a centrifugal pump, a membrane oxygenator, a heat exchanger, a cardioplegia system, a venous bubble trap or venous air-removing device, and a shed blood management system[15]. Increasing evidence is reflected in the recommendations for the use of the MiECC in EACTS/EACTA guidelines on cardiopulmonary bypass in adult cardiac surgery 2019 (ref.[16]).

From 2016 our institution has routinely conducted revascularization procedures using the MiECC and by 2018 our system had undergone technological development into the type III MiECC circuit, modified by incorporation of the cardiotomy suction. In our construction, the suction is activated on demand, and blood is collected in a parallel soft-shell bag and later returned to the venous line prior to the venous bubble trap facilitated by the suction force generated by negative pressure in the venous line of the main circuit driven by the centrifugal pump (Fig. 1). This configuration allows blood recuperation without using any hard-shell reservoir, maintaining the principles of a closed circuit.

This study compares clinical outcomes of CABG using MiECC and conventional ECC, focusing on safety, major adverse events, bleeding, and transfusion needs. Further, it describes the MiECC circuit construction and key principles of perfusion and surgical management.

METHODS

We conducted a retrospective analysis of the clinical data of 60 patients undergoing elective CABG on either MiECC or ECC between the years 2020–2022. Patients enrolled in the study were operated on by the same two surgeons in order to exclude differences in surgical technique and to reduce the bias of the analysis. The selection criteria were isolated CABG, patient age 18–80 years. Exclusion criteria were re-do procedures, severe preoperative left ventricular dysfunction (EF<30%), severe preoperative organ dysfunction (chronic kidney disease KDIGO G3b and higher, creatinine >200 μmol/L or dialysis; liver enzyme elevation more than 3-times normal, bilirubin >35μmol/L, spontaneous elevation of INR >1.7; chronic pulmonary disease GOLD 3 and higher or long-term use of steroids for lung disease). Patients were divided into the MiECC (n=30) and ECC (n=30) groups. To adress potential factors influencing safety and bleeding, an analysis was conducted on preoperative demographic and biometric data, medications affecting coagulation or platelet aggregation, and intraoperative factors like the duration of the operation, cardiopulmonary bypass (CPB), and the number of coronary bypasses performed.

Study outcomes

The primary outcome was to compare the groups in intraoperative and 30-day mortality, cardiovascular death, myocardial infarction and cerebral stroke (MACCE). Secondary outcomes included surgical revision for bleeding or tamponade, intraoperative and postoperative blood loss and the consumption of packed red blood cells unites in the first 7 postoperative days.

Surgical technique

An identical surgical technique was used on all patients, the left internal mammary artery was harvested as a skeletonized graft for revascularization of the left anterior descending artery, the great saphenous vein was harvested via open or endoscopic technique and was used for all the other coronary branches. Standard cannulation of ascending aorta, right atrial appendage utilizing a dual-stage venous cannula and the C-vent were performed to connect the perfusion circuit, in the MiECC patients the additional ligature of the right appendage around the venous cannula was applied to eliminate any air leak into the circuit. Venous drainage was facilitated via vacuum-assisted drainage in the conventional ECC and by kinetically-assisted drainage in the MiECC. Construction of peripheral anastomoses were performed during cardioplegic heart arrest, followed by de-clamping of the aorta and construction of central anastomoses of venous bypasses on the beating heart using the side-bite clamp on the ascending aorta. Weaning of CPB was initiated after a reperfusion period (20% of cross-clamp time). After weaning and de-cannulation of the CPB, Protamine administration and hemostasis, epicardial pacing wire and 3 pericardial 8Fr Redon drains were inserted prior to the closure of the wound and additional similar drains were introduced

into pleural cavities, if these were opened during the procedure. Redon drains were kept in the wound for 48–96 h and were extracted no sooner than 48 h post-operation, if 1-hour blood loss was less than 50 mL in 2 consecutive measurings.

Anesthetic management

The patient was kept on an empty stomach a minimum of 6 hours prior to the surgery. Premedication is Bromazepam 3 mg in the evening, Morphin 10 mg i.m. with Midazolam 5 mg i.m. in the morning before the surgery. Anesthesia is managed by Sufentanil 0.5–0.75 μg/kg/h combined with Propofol 0.5–1.0 mg/kg/h, supplemented by inhalation anesthesia with Sevoflurane 1–2% in 50% O_2 and 50% air. During the CPB, Sevoflurane can be used to deepen the anesthesia via the evaporator in the circuit. Rokuronium is used for muscle relaxation. Anticoagulation for CPB is managed by systemic administration of unfractionated Heparin 3 mg/kg (300 U/kg) and 1 mg/kg into the priming of CPB, the target kaolin-activated ACT is above 400 s. Boluses are added in the case of drops in the ACT levels. If there are signs of heparin resistance with no increase of ACT levels after repeated boluses, the Antithrombin III concentrate 500–1000 IU is administrated. After decannulation of CPB, Protamin in a dose of 1 mg per 100 units of Heparin is administrated in a maximum single dose of 500 mg for neutralization of anticoagulation. In case of persisting elevated ACT levels after neutralization of Heparin, additional Protamin is administrated at a dose of 30–50 mg. Further corrections of hemostatic disorders are guided selectively based on Trombelastography.

MiECC construction and perfusion management

The construction of the MiECC circuit is schematically shown in Fig. 1. Model S5 Stockert non-pulsatile centrifugal pump system (Stockert S5, SCP system, Sorin group) drives the cardiopulmonary bypass with the oxygenator Terumo FX 15E with 1.5 m^2 surface area and integrated arterial filter, X-coating, bubble trap in venous line and soft-shell reservoir connected in the circuit prior to the venous bubble trap. A cardiotomy suction is connected to the system driving blood into a separate soft shell bag. The suction is activated on demand and powered by a small roller pump. The blood collected by the suction is returned to the circuit into the venous line prior to the venous bubble trap. The construction meets the parameters of MiECC type III. Priming volume is 600–800 mL containing 200 mL of 20% Mannitol and balanced crystaloid. CPB is performed on target hematocrit close to ≥28% in normothermia and systemic heparinisation 300 U/kg and target ACT ≥ 400 s. Pump-flow is regulated to maintain >65% of systemic venous O_2 saturation and to maintain the flow 2.2–2.4 L/min/m^2. Antegrade St.Thomas cold blood cardioplegic solution in ratio 4:1 (St. Thomas, Adreapharma, Czech Republic) with 800 mmol/L KCl and 600 mmol/L $MgSO_4$ and blood is administrated via C-vent in initial dose 10 mL/kg and repeated in 30 min intervals by dose 5 mL/kg. Conventional monitoring of venous oxygen saturation, hemoglobin, hematocrit (Terumo CDI550), Spectrum M4 (Medtronic) is used during the perfusion and can be augmented by the extended monitoration of pO_2, pCO_2, K, HCO_3 via the CDI 510H (Terumo CDI 550) cuvette.

Conventional ECC construction and perfusion management

Model S5 Stockert non-pulsatile roller pump system (Stockert S5, Sorin group) drives the cardiopulmonary bypass with the oxygenator Terumo FX 25 with 2.5 m^2 surface area, hardshell reservoir, integrated arterial filter, and X-coating). The priming volume is 1200–1700 mL

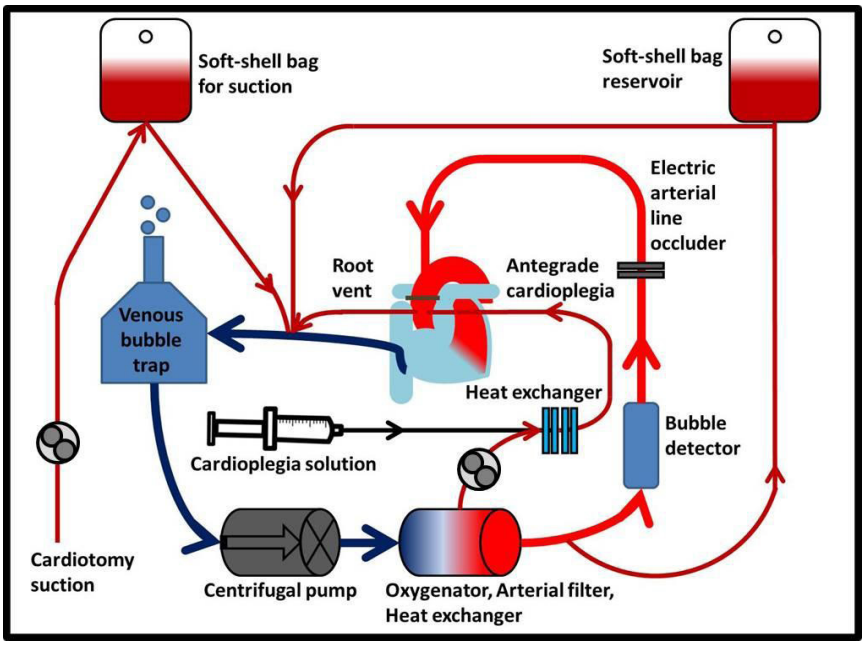

Fig. 1. Schematics of MiECC circuit. Construction meets the criteria of type III minimal-invasive extracorporeal circulation. Additionally the cardiotomy suction is incorporated into the device and is activated optionally on demand.

Table 1. Patient characteristics.

Variable	ECC (n=30)	MiECC (n=30)	*P*
Male	23 (76.7%)	26 (86.7%)	0.317
Age (years)	67.1 ± 6.9	64.7 ± 8.9	0.242
Weight (kg)	89.7 ± 15.6	89.3 ± 14.4	0.915
BMI	29.4 (20.5–37.0)	29.8 (22.5–38.6)	0.779
BSA (m^2)	2.03 ± 0.19	2.02 ± 0.18	0.837
EURO score II (%)	1.25 (0.55–4.18)	1.06 (0.50–2.69)	0.383

mean ± SD; median (min–max).

Table 2. Preoperative medication.

Medication	ECC		MiECC		
	n	%	n	%	*P*
Low Molecular Weight Heparin	0	0.0%	4	13.3%	0.112
Anopyrine 100 mg less than 7 days preop.	24	80.0%	26	86.7%	0.488
Clopidogrel 75 mg less than 7 days preop.	5	16.7%	2	6.7%	0.424
Ticagrelol 90 mg/2x less than 5 days preop.	3	10.0%	8	26.7%	0.095
Apixaban less than 2 days preop.	1	3.3%	0	0.0%	1.000
Dabigatran less than 2 days preop.	0	0	0	0	-

Table 3. Operation characteristics.

Variable	ECC	MiECC	*P*
Operation time (min)	183 ± 36	170 ± 33	0.176
CPB time (min)	65 (41–123)	58 (40–104)	0.222
Constructed CABG (n)	3 (2–5)	3 (2–4)	0.474

mean ± SD; median (min-max).

according to the hematocrit, containing 200 mL of 20% Mannitol, balanced crystalloid and colloid. CPB is performed on target hematocrit close to ≥25% in tepid temperature 34–35 °C and systemic heparinisation 300 U/kg and target ACT ≥ 400 s. Pump flow is regulated to maintain >65% of systemic venous O_2 saturation and to maintain the flow 2.4–2.6 L/min/m^2. Antegrade St.Thomas cold blood cardioplegic solution in the ratio 4:1 (St. Thomas, Adreapharma, Czech Republic) with 800 mmol/L KCl and 600 mmol/L $MgSO_4$ and blood is administrated via a C-vent in an initial dose 10 mL/kg and repeated in 30 min intervals by dose 5 mL/kg. A hemoconcentration circuit BC 140 Plus (MAQUET) consisting of polyethersulfone dialysis membrane may be used as needed to remove excess fluid in the circuit during CPB. Conventional monitoration of venous oxygen saturation, hemoglobin, hematocrit (Terumo CDI550), Spectrum M4 (Medtronic) is used during perfusion and can be augmented by extended monitoring of pO_2, pCO_2, K, HCO_3 ect. via the CDI 510H (Terumo CDI 550) cuvette.

Statistical analysis

Microsoft Office Excel^R (Microsoft Corporation, Redmond, WA, USA) was used as a database for data storage. The groups of patients with ECC and MiECC were compared in quantitative parameters using the Student's t-test in the case of normally distributed variables. The Mann-Whitney U test was used in the case of non-normal distribution. The chi-squared test and Fisher's exact test were used to compare qualitative parameters. Data normality was assessed using the Shapiro-Wilk test. Quartile box graphs were used for the graphical presentation of the results, where the line inside the box represents the median, the lower and upper parts of the box represent the 1st and 3rd quartiles, and the brackets display the minimum and maximum non-outlier values. The circle symbol represents outliers and the star symbol represents the extreme values. The IBM SPSS Statistics Version 23 statistical software (Armonk, NY: IBM Corp.) was used for the data analysis. All tests were performed at the *P*-value of 0.05 significance level.

RESULTS

There were no statistically significant differences between groups of ECC and MiECC in terms of demographic and biometric data (Table 1). There was no significant difference in calculated risk (EuroSCORE II) (ECC 1.25% vs 1.06%, *P*=0.383).

Analysis of preoperative medication altering either coagulation or aggreggation is shown in Table 2. The majority of patients in both groups were still on antiplatelet therapy of Acetylsalicylic acid 100 mg by the time of the operation. Additionally, both groups contained patients on dual antiplatelet therapy, more frequently in the MiECC group. Specifically acetylsalicylic acid in combination with clopidogrel was more frequent in the ECC

Table 4. Blood loss.

Blood loss	ECC	MiECC	*P*
Intraoperative blood loss (mL)	325 (200–800)	300 (200–700)	0.425
Blood loss 24 h post-op. (mL)	560 (230–1220)	455 (280–1000)	0.128
Blood loss 24–48 h post-op. (mL)	185 (20–610)	115 (30–290)	0.001
Blood loss 48–96 h post-op. (mL)	0 (0–260)	0 (0–220)	0.211
Total blood loss (intraoperative + post-operative) (mL)	1160 (700–2500)	1015 (580–1810)	0.032
Total post-operative blood loss (mL)	765 (350–1700)	660 (370–1310)	0.037

median (min-max).

group and with ticagrelor in MiECC group. 4 patients in MiECC group were given low molecular weight heparin in less than 24 h prior to the operation. In conclusion, no statistical difference was found between groups regarding the preoperative antiplatelet and anticoagulation medication.

The groups were comparable on procedure-related data. There was no significant difference in the overall time of the operation, duration of CPB, or number of constructed peripheral anastomoses (Table 3).

In the complications analysis, zero deaths were recorded during the procedure and in the 30-days post-operation follow-up, as well as zero myocardial infarctions, cerebrovascular strokes, or surgical revisions for bleeding or cardiac tamponade in any group.

The analysis of blood loss is shown in Table 4. No difference was found in the intraoperative blood loss between the groups (ECC 325 mL vs 300 mL, *P*=0.425). In terms of post-operation bleeding, we recognised a trend of lower early post-operational blood loss in the MiECC group compared to the ECC group, however without statistical significance (455 mL vs 560 mL, *P*=0.128) in the first 24 h after surgery. The stabilisation of bleeding was more pronounced in the following second 24 h interval with significantly lower blood loss in the MiECC group (115 mL vs 185 mL, *P*=0.001). Furthermore, the MiECC group resulted into a significantly lower overall postoperative blood loss (660 mL vs 765 mL, *P*=0.037).

The total number of packed red blood cells units consumed was insignificantly higher in the ECC group (n=30 *vs* n=20, *P*=0.490), nor was there a significant difference in the numbers of patients requiring treatment by substitution of erythrocyte transfusions between groups (n=12 vs n=10, *P*=0.592).

DISCUSSION

The original construction of the MiECC circuit had no cardiotomy suction. Only the cell-saver device was available for any blood recuperation, if needed. This is additionally one of the major concerns of surgeons and often a reason why the conventional CPB is preferred to the MiECC circuit. This was addressed with the introduction of the type IV MiECC circuit, which combines the properties of the closed miniaturized system with an additional parallel stand-by circuit with a hard-shell reservoir and a coronary suction integrated into the venous line, prepared for immediate conversion into an opened circuit to facilitate blood management if required. This configuration however allows direct blood recuperation by the activation of the cardiotomy suction only when converted to a fully opened circuit and thus loses some of the principles of the MiECC circuit. In our institution, we originally operated CABG on MiECC type III with a cell-saver device prepared in stand-by for use if needed. During further development, we dispensed with the cell-saver completely as we upgraded the circuit with the cardiotomy suction with enhanced physiological properties, connected directly into the circuit prior to the venous bubble trap. The suction in our construction works separately as we collect blood from the operation field into the separate soft-shell bag without returning it to the system immediately. The collected blood is kept aside during the operation and eventually returned to the patient before the decannulation of the CPB if the volume exceeds 300 mL or the patient requires volume addition. Otherwise, this "activated" blood is excluded and counted in total operative blood loss. The suction device is powered by a roller pump. Return of the blood collected in the soft-shell bag into the circuit is facilitated by the negative pressure in the venous line generated kinetically by the centrifugal pump of the circuit. Optimally we activate the suction when the level of blood is high enough so we can drive the suction into the blood pool fully below the level of air to reduce air microembolisation. Additionally, this construction provides an option for immediate blood recuperation in critical scenarios. If the suction is used during the procedure but the blood is returned to the patient by the end of the operation, we can classify the circuit as semi-open as it preserves the principles of the closed circuit during the whole time of perfusion but returns the "activated" blood at the end.

Another important difference for the surgeon is the volume management with the MiECC system. The principle is that as soon as the CPB is initiated, the heart is unloaded by drainage of volume into the soft-shell reservoir. This volume is stored for the whole perfusion, preventing its unnecessary recirculation through the CPB. This stored heparinised blood is therefore intact, protected against the damage from recirculation through CPB, and is returned to the patient after declamp. However, the surgeon has to account for that, as there is only a limited possibility for the filling of the heart during the cross-clamp to measure the length of bypasses. The option is to keep the venous bypasses longer and fill the heart for the measuring of them all at once before the construction of central anastomosis after declamp. Measuring of left

internal mammary artery together with the selection of the target spot for the anastomosis on the left anterior descending artery should be performed as soon as it is harvested, prior to the initiation of the CPB. However, if the filling of the heart is required during the cross-clamp intermittently for every individual bypass, it can be done by the addition of crystalloids into the circuit or by returning the blood stored in the reservoir but for the price of compromising the preservation of the stored volume. In conclusion, to operate on the MiECC system it is necessary for the surgeon to adapt to these specific conditions.

The limitation of our analysis was the retrospective character and the number of patients in the compared groups. The reason being that we had to include only the patients operated in the same period of time when we were using our latest setup of the MiECC system. These patients had to be operated by the same two surgeons. As the analysis shows, both groups were comparable in preoperative as well as procedure-related data.

The medication evaluation showed a slightly higher number of patients on DAPT in the MiECC group. Currently, this trend of selection of patients for MiECC in our department is even more pronounced. During our increasing experience with this type of perfusion it eventually became a preferred type of CPB for patients on DAPT medication as our results of decreased overall bleeding in the MiECC group correlated with our personal surgical experience of better hemostatis. However, a prospective comparative analysis focused on patients on DAPT would be needed to confirm these results.

Despite different management of blood recuperation, the MiECC proved to be not inferior in terms of intraoperative blood loss. Together with no fatal events or high-risk complications in either group we consider the MiECC system in terms of safety comparable to the conventional ECC.

Improved hemostasis preservation was reflected in lower post-operative blood loss as well as in lower consumption of blood derivates in the MiECC group. However, in the ECC group, the increased substitution of erythrocytes could be explained by the combination of decreased hematocrit due to excessive priming volumes together with higher post-operative blood loss compared to the MiECC group. Our results are in agreement with the findings of Modrau et. al.[17] published in 2020 in terms of blood loss in the 1st 24-hours post-operation, where both works demonstrated a trend of decreased bleeding in the MiECC group in this period of time, however both without statistical significance. Comparable results were sooner demonstrated by Remadi et al.[18] (2006) in their prospective randomized study reflecting no difference in the operation times, lower mean postoperative bleeding rate in the MiECC group. Retrospective study conducted by Gerritsen et al.[19] in 2006 focused on similar outcomes proved not only the lower bleeding and transfusion rates in the MiECC group, but also demonstrated its superiority over the off-pump group. Additionally, our work focused also on the following time intervals in up to 96h post-operation and we found that the maximum blood loss was observed in the first 2 consecutive periods and stopped after 48 h. Furthermore in accordance with previous studies by Ellam et al.[20], Anastasiadis et al.[13], El-Essawi et al.[21], Benedetto et al.[22] and recently by Ali et al.[23] we recognized a lower consumption of blood derivates in the MiECC group.

CONCLUSION

The MiECC proved to be a safe alternative to the conventional ECC that is fit especially for routine cardiac procedures such as CABG. This type of perfusion appears to have greater benefit for patients with a higher risk of bleeding. Operating on the MiECC system provides advantages in terms of improved biocompatibility, as proved in our study by the lower bleeding rates.

ABBREVIATIONS

MiECC, Minimal invasice extracorporeal circulation; CABG, Coronary artery bypass grafting; ECC, Extracorporeal circulation; MACCE, Major adverse cardiac and cerebrovascular events; CPB, Cardiopulmonary bypass; SIRS, Systemic inflammatory response syndrome; MiECTiS, Minimal Invasive Extracorporeal Technologies International Society; EACTS/EACTA, European Association For Cardio-Thoracic Surgery/ European Association of Cardiothoracic Anesthesiologists; EF, Ejection fraction; KDIGO, Kidney Disease Improving Global Outcomes classification; INR, International Normalized Ratio; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICU, Intensive care unit; ACT, Activated clotting time; DAPT, Dual antiplatelet therapy.

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Conflict of interest statement: None declared.
Ethics statement: Additional informed consent was obtained from the patients enrolled in the study.

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