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Effects on Cerebral Oxygen Balance in Coronary Artery Bypass Grafting: A Comparison of Conventional and Minimal Extracorporeal Circulation

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Abstract

Objective: *To investigate the cerebral oxygen balance difference between minimal extracorporeal circulation (MECC) and conventional extracorporeal circulation (CECC) during coronary artery bypass grafting.*

Methods: *20 patients undergoing coronary artery bypass grafting with cardiopulmonary bypass (CPB) were divided into two groups, the CECC group (n=10) and the MECC group (n=10). Blood withdrawn from radial artery and right jugular vein were analyzed at the following timepoints: during the anesthesia induction (T1), before CPB (T2), the initiation of CPB (T3), aorta cross-clamped (T4), after temperature decreased (T5), during stable hypothermia (T6), initiation of rewarming (T7), aorta unclamped (T8), after weaning of CPB (T9), end of the operation (T10).The artery oxygen content (CaO_2) and cerebral oxygen extraction ratio (OER) were calculated. The mean artery pressure (MAP), hemoglobin (Hb), nasopharyngeal temperature (NPT), and pump perfusion flow were recorded during the operation.*

Results:
(1) MAP and Hb of MECC group were significantly higher than those in the CECC group from T3 to T10 (P<0.05); perfusion flow in MECC group during CPB was significantly lower than those in CECC group (P<0.05); NPT in MECC group was significantly higher than those in CECC group (P<0.05).
(2) During T3-T4 and T8-T9, jugular venous oxygen saturation in CECC group was significantly lower than those in MECC (P<0.05); OER in CECC group was significantly higher than those in MECC group (P<0.05).
(3) The arterial lactic acid and venous lactic acid in these two groups were decreased gradually from T3 to T10. Thearteriovenous difference in lactic acid in CECC group were higher than those in MECC group during T3-T4 and T8-T9 (P<0.05).

Conclusion: *Patients undergoing coronary artery bypass grafting with MECC enjoy more stable blood pressure, less intense hemodilution and lighter temperature disturbance than those with CECC, which indicating a better cerebral oxygen balance in CABG.*

Keywords: Conventional Extracorporeal Circulation, Minimal Extracorporeal Circulation, Coronary Artery Bypass Grafting, Cerebral Oxygen Balance

Introduction

Standard coronary artery bypass grafting (CABG) surgery employs an arrest of the heart with cardioplegia, providing a motionless, bloodless surgical field, and optimal conditions for the construction of coronary anastomoses. Due to the intractable adverse effects of cardiopulmonary bypass (CPB) like inflammatory response and neurologic dysfunction, pump-oxygenator circuits and cardioplegia techniques plateaued throughout the 1990s [1-5]. The off-pump coronary artery bypass (OPCAB), meaning CABG without the use of cardiopulmonary bypass, was then developed, and chosen by many practitioners because of the improvement in inflammatory response, myocardial injury, renal function, and coagulation function [6-8]. However, this technique is not only limited by the skills of surgeons and anesthesiologists, but also the patient's circumstances [9-11].

The mini-CPB or minimal extracorporeal circulation (MECC) was introduced to minimize these flaws. The MECC consists of a membrane oxygenator, a centrifugal pump, an arterial filter, and heparin-coated tubing that reduces the priming volume by 450ml [12]. It helps improve the biocompatibility, mitigate the inflammatory reactions, reduce postoperative bleeding by protecting the coagulation system, protect myocardium by reducing myocardial damage, reduce neurologic damage, as well as provide a motionless and bloodless surgical condition. MECC is an easy and safe procedure for coronary artery bypass graft surgery [9]. In selected patients, the advantages of MECC equal those of OPCABG [9,13-17].

Different bypass technologies lead to individualized intraoperation management. Cerebral oxygen balance during surgery is crucial to patients' neurological function protection and prognosis. Regional cerebral oxygen saturation (rSO_2) obtained from a near-infrared reflectance spectroscopy (NIRS) was proved to be correlated significantly with heart rate, mean artery pressure (MAP), central venous pressure, arterial carbon dioxide tension, arterial oxygen pressure, and base excess (BE); and is correlated positively with PaO_2, MAP, and BE [18,19]. As the NIRS-based cerebral oximeter only detect oxygen saturation in a thin superficial layer, it can neither measure global cerebral oxygenation, nor differentiate between arterial and venous blood [20]. In this work, we investigated the cerebral oxygen balance impact brought by MECC, compared the cerebral oxygen balance by monitoring a variety of indicators in patients who underwent coronary artery bypass grafting with these CPB technologies [21].

Materials and Methods

Study Patients: Patients diagnosed with coronary CECC were be classified into the CECC group (n=10); patients undergoing MECC were classified into the MECC group (n=10). The surgeons, anesthesiologists, and perfusion doctors were specifically designated. General patients' information is listed in Table 1.

Table 1: Preoperative Patient Data

	CECC (n=10)	MECC (n=10)
Sex ratio (M/F)	4.0	2.3
Age (years)	59.8 ± 5.3	63.2 ± 5.0
Weight (kg)	72.6 ± 4.8	69.8 ± 4.3
hypertension (%)	60	50
Diabetes (%)	30	10
Unstable angina pectoris (%)	40	50
left ventricular ejection fraction (%)	53.8 ± 4. 8	54.7 ± 5.5

Extracorporeal Circulation Protocol The MECC system (Jostra AG, Harlingen, Germany) consisted of a Rota flow® centrifugal pump (Jostra, Germany), a Quadro® arterial microemboli filter (Jostra, Germany), and a Quadrox® membrane oxygenator (Jostra, Germany), as shown in Figure 1A. All the components were entirely Bioline® coated (Jostra, Germany) [22]. The CECC system consisted of a roller pump (SIII, Stokert Shiley, Germany), a membrane oxygenator, a venous reflux chamber with a priming volume of 4000 ml (TERUMO, Japan), a blood filter (Kewei, Dongguan, China), and a non-heparin coated piping kit (Tianjin Plastics Research Institute, China), as shown in Figure 1B. Details of these systems are listed in Table 2 [23].

Table 2: Comparison of CECC and MECC system

	CECC system	MECC system
Contact area (m^2)	12	3
Blood storage chamber	Yes	No
Priming volume (mL)	1500	500
Heparin coating	Yes	Yes
Heparin (IU/kg)	400	150
ACT requirement (s)	>480	200-250
Water tank temperature required during rewarming (°C)	40	38

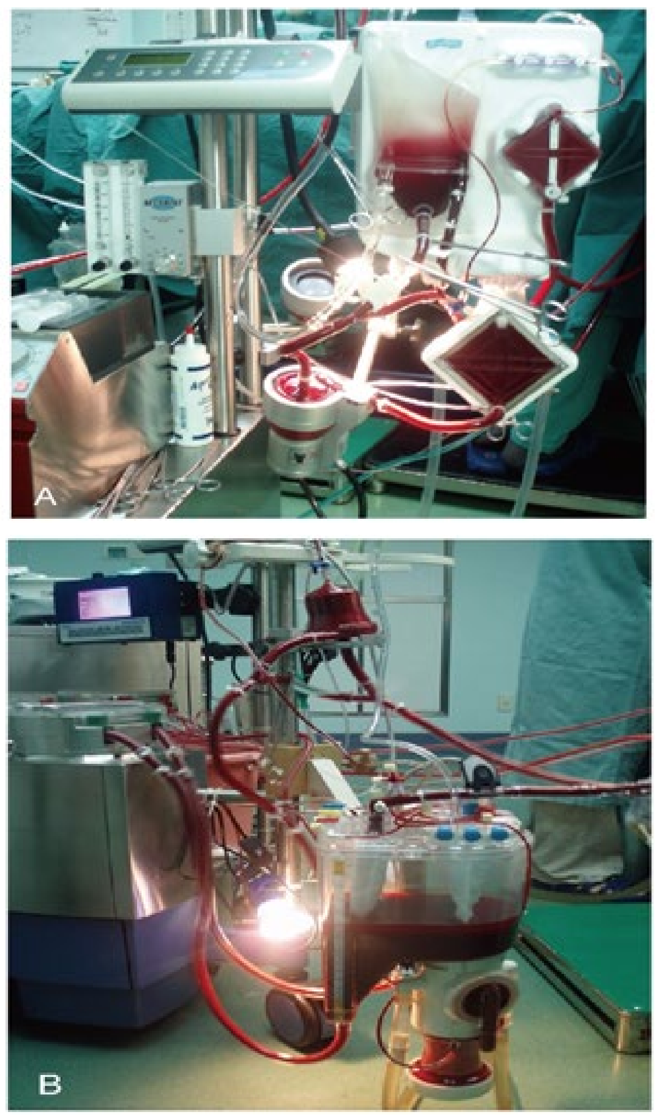

Figure 1: The minimal extracorporeal circulation system (A) and conventional extracorporeal circulation system (B).

Jugular Bulb Catheterization

The jugular bulb is a dilatation in the rostral internal jugular vein right below the jugular foramen [24]. In normal patients, bilateral jugular bulb saturations are equal and probably represent drainage from all parts of the brain [25,26]. Continuous monitoring of the jugular venous oxygen saturation ($SjvO_2$), which is sampled from this position, can be used as an indicator of cerebral oxygenation (20-22) for accuracy, the catheterization is performed as previously described [27]. A 5F double-lumen central venous catheter (Yixinda, Shenzhen, China) is carefully placed in the right jugular vein towards the brain. During the operation, patient's head was kept still, to prevent the catheter displacement. To withdraw blood samples for analysis, 5ml blood should be taken first, followed by a slow withdraw of 2ml blood [27].

Anesthesia Procedure

The anesthesia procedure consists of:

1. Intramuscular injection of morphine 10 mg and penehyclidine hydrochloride 0.1 mg, as preoperative medications
2. Intravenous injection of midazolam 0.05-0.1 mg/kg, etomidate 0.2 0.3 mg/kg, vecuronium bromide 0.15-0.2 mg/kg, and sufentanil 1.5-2 mcg/kg, for induction and endotracheal intubation
3. Propofol 1-4 mg/(kg.h), sufentanil 1 2 mcg/(kg.h) for anesthesia maintenance
4. Midazolam and vecuronium bromide were given intermittently. Invasive blood pressure was established in the left radial artery before induction. A three-lumen venous catheter was placed in the right jugular vein, adjacent to the jugular bulb catheterization. Before CPB, the mechanical ventilation parameters were as follows: tidal volume 8-12 ml/kg, respiratory rate 8-12 times/min, inhale/exhale ratio 1:2.

Data Process

Serial blood samples were analyzed during the anesthesia induction (T1), before CPB (T2), the initiation of CPB (T3), aorta cross-clamped (T4), after temperature decreased (T5), during stable hypothermia (T6), initiation of rewarming (T7), aorta unclamped (T8), after weaning of CPB (T9) and end of the operation (T10). The MAP, hemoglobin (Hb), nasopharyngeal temperature (NPT), pump perfusion flow, arterial blood and jugular bulb blood gas analyses were recorded at the same time. The $SjvO_2$, partial pressure of jugular venous oxygen ($PjvO_2$), artery oxygen saturation (SaO_2), partial pressure of oxygen (PaO_2), arterial lactic acid (AL), and venous lactic acid (VL) were used to calculate the rest indicators with the formulas in Table 3.

Table 3: Calculated Parameters and Formulas

Description	Formula
Artery oxygen content(ml/dl)	$CaO_2 = (Hb \times 1.39 \times SaO_2 + 0.003 \times PaO_2)$
Cerebral oxygen extraction ratio (%)	$OER = (CaO_2 - CjvO_2)/CaO_2$
Jugular venous oxygen content (ml/dl)	$CjvO_2 = (Hb \times 1.39 \times SjvO_2 + 0.003 \times PjvO_2)$
Arteriojugular lactic acid difference (mmol/L)	ADVL = VL-AL
Hb: Hemoglobin; SaO_2: artery oxygen saturation; PaO_2: partial pressure of oxygen; $SjvO_2$: jugular venous oxygen saturation; $PjvO_2$: partial pressure of jugular venous oxygen; AL: arterial lactic acid; VL: venous lactic acid.	

Statistical Processing

Continuous variables are reported as mean ± standard deviation. Categorical variables are reported as frequency and proportion. The statistical analysis has been performed by chi-square test for categorical variables and Student's t test and Mann Whitney test for continuous variables, utilizing Prism (Version 8, GraphPad Software, Inc). The difference was considered s statistically significant when P value <0.05.

Results

Changes in MAP, Hb, NPT, and Pump Perfusion Flow

MAP: From T3 to T9, the MAP in the MECC group was significantly higher than that in the CECC group (P <0.05). In the MECC group, MAP from T4 to T8 were significantly lower than that of T2 (P <0.05), but MAP were > 60 mmHg in all cases. In the CECC group, MAP from T3 to T9 were significantly lower than that of T2 (P <0.05). See Figure 2A.

Hb: Hb in both groups decreased after T3 (P <0.05). From T3 to T10, the Hb in MECC group was significantly higher than that in the CECC group (P <0.05). Hb from T3 to T9 in the CECC group were all < 8 g/dL. Hb in the MECC group from T1 to T10 were all > 8 g/dL. See Figure 2B.

NPT: From T5 to T7 the values in MECC group were significantly higher than those in the CECC group P <0.05. The temperature of stable hypothermia ranged from 30 to 32 °C in CECC, and 34 to 35 °C in MECC. See Figure 2C.

Pump Perfusion Flow: The perfusion flow of the CECC group ranged from 2.4 to 2.8 L/(min.m^2), and 2.0 to 2.4 L/(min.m^2) in the MECC group. From T3 to T8, the perfusion flow in MECC group were significantly lower than those in the CECC group P <0.05 See Figure 2D.

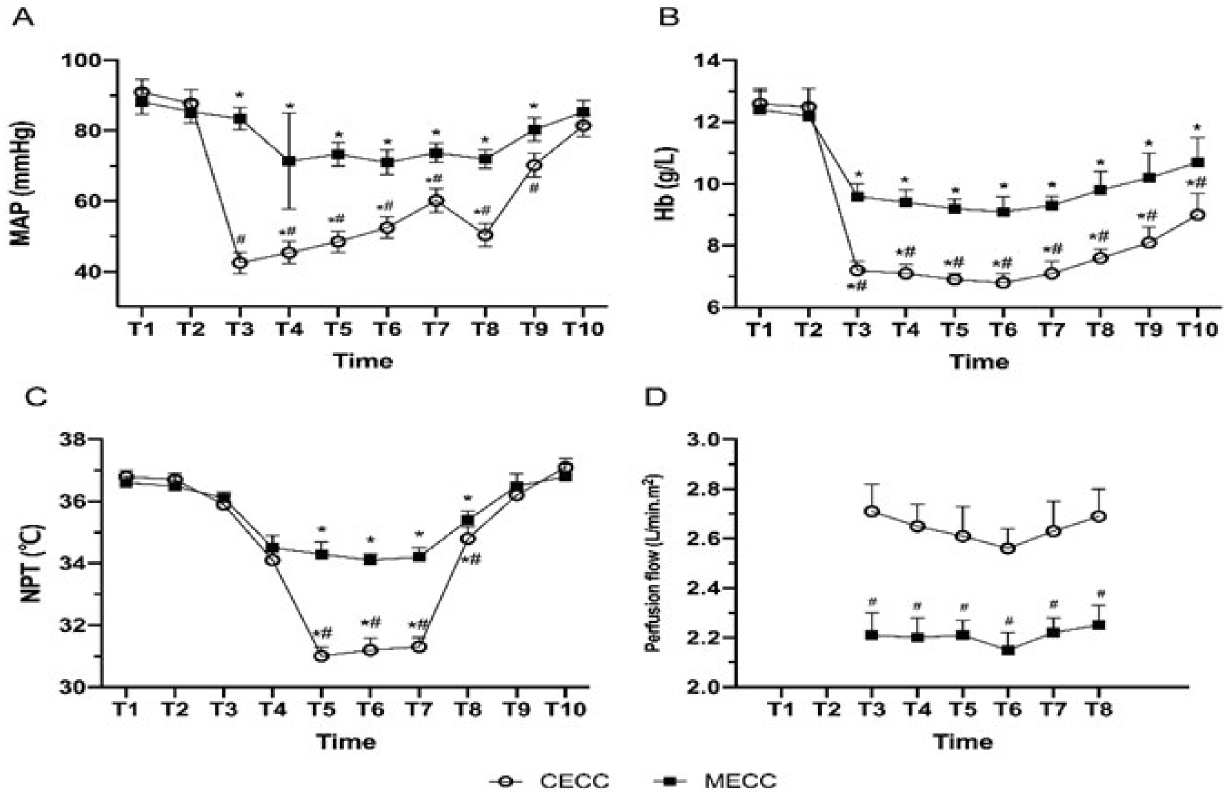

Figure 2: Records of MAP (A), Hb (B), NTP (C) and perfusion flow (D) during the surgery in CECC and MECC groups. Serial values were recorded at consecutive timepoints: the anesthesia induction (T1), before CPB (T2), the initiation of CPB (T3), aorta cross-clamped (T4), after temperature decrease (T5), during stable hypothermia (T6), initiation of rewarming (T7), aorta unclamped (T8), after weaning of CPB (T9) and end of the operation (T10). *P<0.05 indicates a statistically significant difference when compared to the value of T2 in the same group, and #P<0.05 indicates a statistically significant difference comparing the values at the same time between groups. MAP, mean artery pressure; Hb, hemoglobin; NPT, nasopharyngeal temperature; CPB, cardiopulmonary bypass; CECC, conventional extracorporeal circulation; MECC, minimal extracorporeal circulation.

Changes of Cerebral Oxygen Metabolism

$SjvO_2$: In the CECC group, $SjvO_2$ in T3, T4, and T7 to T9 were significantly lower than that in T2 ($P < 0.05$). $SjvO_2$ in the CECC group, from T3 to T10 (except for the stable hypothermia phase, T6), were significantly lower than those in the MECC group $P < 0.05$. The peak of both groups at T6 were (CECC: 73.7 ± 9.9%; MECC: 73.5 ± 8.7%). In the CECC group, $SjvO_2$ reached its nadir at T4 and T8. $SjvO_2$ in the MECC group from T1 to T10 were all > 50%. See Figure 3A.

CaO_2: In both the MECC and CECC groups, CaO_2 decreased significantly from T3 to T10, compared to T2 ($P < 0.05$). A noticeable decreasing trend can be found in the MECC and CECC group. CaO_2 in the MECC group from T3-T10 were significantly higher than those in the CECC group $P < 0.05$. See Figure 3B.

OER: In the CECC group, the OER from T3 to T4 increased and reached the first peak at T4 (42.4 ± 4.1%), which were both significantly higher than T2 $P < 0.05$; while the OER from T5 to T6 decreased and reached the nadir at T6 (24.7. ± 2.7%), which were both significantly lower than T2 $P < 0.05$. At T7 the value reached its second peak (43.9 ± 4.1%). As for the MECC group, values from T5 to T10 were significantly lower than that of T2 ($P < 0.05$), and reached the nadir at T6 (25.5 ± 2.9%). OER in the MECC group at T4, 5, 7-10 were significantly lower than those in the CECC group ($P < 0.05$). See Figure 3C.

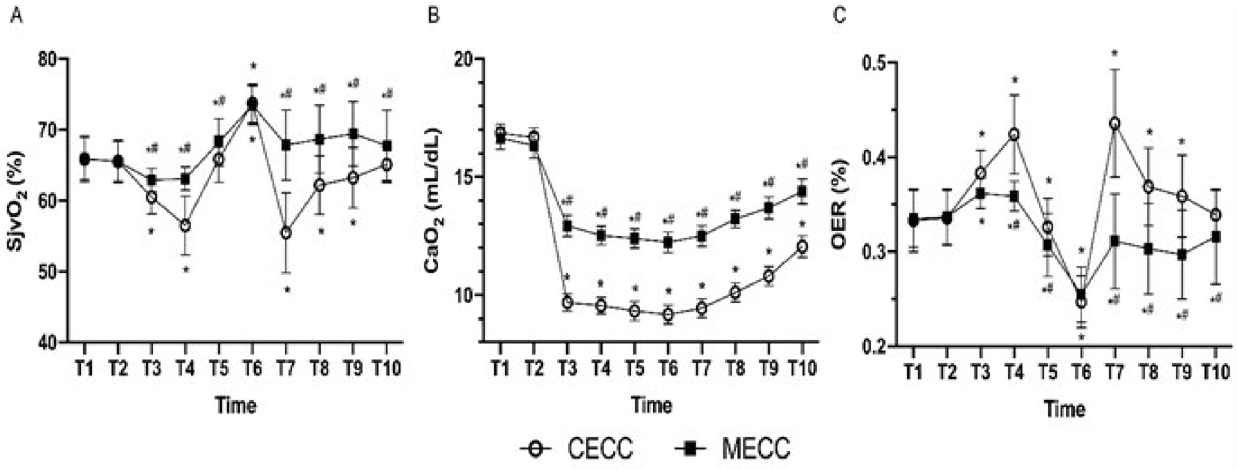

Figure 3: Records of $SjvO_2$ (A), CaO_2 (B), and OER (C) during the surgery in CECC and MECC groups. Serial values were recorded at consecutive timepoints: the anesthesia induction (T1), before CPB (T2), the initiation of CPB (T3), aorta cross-clamped (T4), after temperature decrease (T5), during stable hypothermia (T6), initiation of rewarming (T7), aorta unclamped (T8), after weaning of CPB (T9) and end of the operation (T10). *$P<0.05$ indicates a statistically significant difference when compared to the value of T2 in the same group, and #$P<0.05$ indicates a statistically significant difference comparing the values at the same time between groups. $SjvO_2$, jugular venous oxygen saturation; CaO_2, artery oxygen content; OER, cerebral oxygen extraction ratio; CPB, cardiopulmonary bypass; CECC, conventional extracorporeal circulation; MECC, minimal extracorporeal circulation.

Changes of Lactic Acid Metabolism

AL and VL: In both the MECC and CECC groups, AL and VL from T3 to T10 were increased gradually and were significantly higher than T2 ($P <0.05$). Comparing the two groups, T7-T10 in AL and T3-T10(except T6) in VL were higher in the CECC group ($P <0.05$). See Figure 4A, 4B.

ADVL: ADVL from T3 to T5 and T7 to T10 in CECC group were significantly higher than those in MECC group $P <0.05$. There was no significant difference between the two groups at T6. The trend was consistent with the OER, and opposite to the $SjvO_2$. The line chart is shown in Figure 4C.

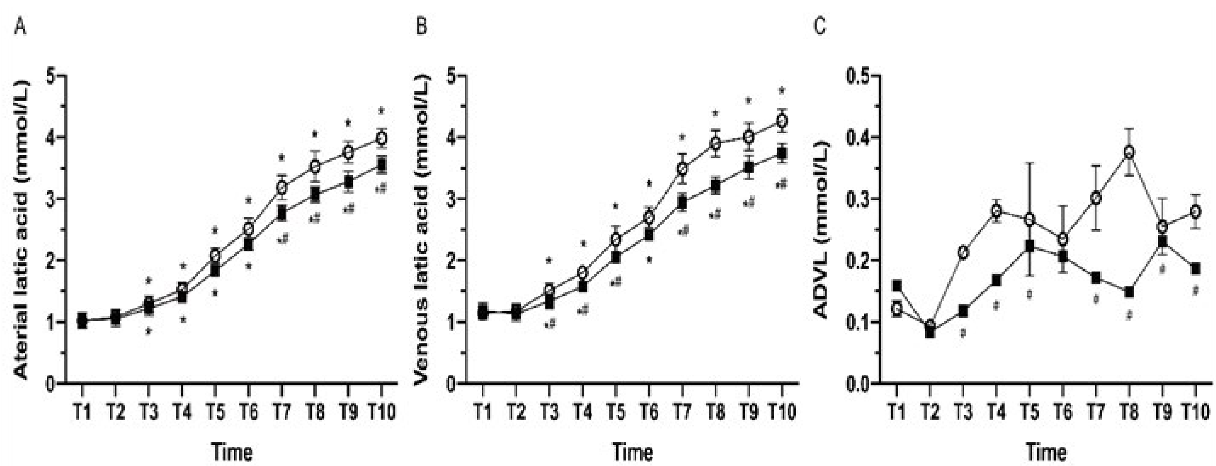

Figure 4: Records of arterial lactic acid (A), venous lactic acid (B), and ADVL (C) during the surgery in CECC and MECC groups. Serial values were recorded at consecutive timepoints: the anesthesia induction (T1), before CPB (T2), the initiation of CPB (T3), aorta cross-clamped (T4), after temperature decrease (T5), during stable hypothermia (T6), initiation of rewarming (T7), aorta unclamped (T8), after weaning of CPB (T9) and end of the operation (T10). *$P<0.05$ indicates a statistically significant difference when compared to the value of T2 in the same group, and #$P<0.05$ indicates a statistically significant difference comparing the values at the same time between groups. ADVL, arteriojugularlactic aciddifference; CPB, cardiopulmonary bypass; CECC, conventional extracorporeal circulation; MECC, minimal extracorporeal circulation.

Discussion

In this work, 20 cases of CABG surgery under CECC and MECC were retrospectively analyzed by comparing a series of cerebral oxygen related indicators. As MECC is little performed in China, the data collected in this work is limited but precious. To our knowledge, this is the first exploration focused on cerebral oxygen balance with different extracorporeal circulation techniques. Since NIRS-baseed cerebral oximeter detects rSO_2 with several flaws, we believed indirectly observing cerebral oxygen through hemodynamics and blood gas tests might be more easy-operating and overall reflected, as evidence showed strong correlation with indicators like rSO_2 and MAP, PaO_2 and BE [18-21].

Similar to the previous studies, improvements from MECC also showed benefits in our observation [13-15]. As the circulation circuit is much shortened, blood dilution is remarkably reduced. A more stably maintained vascular tension and milder MAP fluctuation were observed, which was likely triggered by the mitigated drop-off in catecholamine concentration. The MAP in the MECC group was >60 mmHg at moments. It is reported that patients with a MAP maintaining at 70-90 mmHg during CABG surgery had better prognosis than those at 50-70 mmHg [28]. MAP maintaining at 60-90 mmHg could avoid hypoperfusion cerebral ischemia and ensure cerebral oxygen supply [20,29]. The reduced blood dilution with MECC led to a higher hematocrit during the entire CPB period, ensuring sufficient oxygen supply to the brain and other vital organs. In addition, heparin-coated circuit reduces the tube-wall absorption of propofol, which helps ensure the depth of anesthesia, thus reducing cerebral oxygen consumption caused by insufficient anesthesia depth [30].

At the initiation of CPB (T3), $SjvO_2$ only fluctuated mildly, even though MAP has dropped by 45 mmHg, indicating that cerebral oxygen supply and demand were roughly matched [31]. Nevertheless, during the CPB (T3-T4) and aorta unclamped (T8) stages, $SjvO_2$ in the MECC group was higher than that in the CECC group, while OER and ADVL were markedly lower than those in the MECC group. These findings suggest the CECC group is risky of imbalance between cerebral oxygen supply and consumption in these two stages.

The contributing factors might include:

1. Greater decline in MAP and Hb caused by enhanced blood dilution levels in CECC, leading to insufficient cerebral oxygen supply.
2. Rapid rewarming, as in the CECC, was more likely to cause Hb desaturation and affect brain metabolism than slow rewarming [31-33].
3. Brain tissues near the large blood vesselsare preferentially rewarmed, causing excessive craniocerebral rewarming and increase of cerebral oxygen consumption [34]. When the NPT reached 37°C, the brain tissue near the large blood vessels might reached 39-40°C already.
4. The oxygen debt to be repaid during rewarming is more, due to a much lower temperature required in the CECC group during CPB stage, while a higher water tank temperature2°C (38°C for MECC and 40°C for CECC) for rewarming stage. Taken together, the cerebral oxygen supply is compromised, yet the consumption might be even higher, causing a cerebral oxygen supply-consumption imbalance. Difference in $SjvO_2$ and ADVL between two groups verified the beneficial effects mentioned above brought by MECC. By maintaining the NPT at approximately 34-35°C and rectal temperature at 36°C, MECC ensured better microvascular circulation and perfusion, lowered lactic acid production during CPB, a higher MAP, and abundant Hb for oxygen supply.

As is well known, hypothermia slows down the myocardium metabolism and enhance hypoxia tolerance for vital organs. Yet, there are also negative effects brought by low temperature, including mitochondrial dysfunctionand ion transportation dysfunction [35,36]. CPB under normothermia is reported enjoy a lower incidence of perioperative myocardial infarction, using of the intraaortic balloon pump, low output syndrome, and show little harm to other organs [37,38]. Similar to previous work, during the stable hypothermia stage (T6), $SjvO_2$ in the CECC and MECC were akin (73.7±9.9% and 73.5±8.7%, respectively), which suggest that cerebral oxygen balance of the two groups was basically identical, in spite of a higher temperature in MECC group [31]. Due to higher MAP and Hb concentration and sufficient microvascular perfusion pressure, higher temperature with MECC system is practicable as well. Also, OER of the two groups at this stage showed alike trends.

There were limitations in this study. The transcranial Doppler ultrasound was not applied to measure cerebral blood flow in our study. Combining our measurement and transcranial Doppler ultrasound might further verify brain perfusion and oxygenation. However, it was not easy to provide continuous measurements during the surgery. In addition, limited sample size might amplify the systematic error.

Conclusion

In summary, we explored the indicators with two extracorporeal circulation techniques and results showed cerebral oxygen supply and demand might not be as well matched in patients with the CECC as it did with the MECC. MECC has a smaller priming volume, lighter blood dilution effect and temperature interference, more stable blood pressure, and more ensured cerebral oxygen supply, thus indicates providing a better cerebral oxygen balance for patients underwent CABG.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The Institutional Review Board of the First Affiliated Hospital of Guangzhou Medical University approved the study protocol. The study outcomes will not affect the future patient management. This study is based on data retrieved from a hospital medical record system. All personal data have been protected and secured according to current national and international laws.

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