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CO2 field-flooding devices offer potential value for cardiopulmonary bypass procedures for CHD performed via a right-side small incision approach

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Abstract

Objective This study sought to evaluate the value of a CO_2 field-flooding device in cardiopulmonary bypass (CPB) surgical procedures for congenital heart disease (CHD) performed via a right-side small incision approach.

Methods Between April 2022 and December 2023, 234 children with simple CHD who underwent CPB via a right-side small incision approach were separated into a control group ($n=93$) without the use of a CO_2 field-flooding device and a treatment group ($n=141$) in which this device was added to the traditional surgical manual exhaust. Demographic, perioperative, arterial blood gas (ABG), and laboratory test data were then compared between these groups of patients.

Results There was a significant difference in abnormal electrocardiogram (ECG) after aorta de-clamping during CPB, and interventions for abnormal ECG after aorta de-clamping during CPB between the control and treatment groups (17(18.3%) vs.14(9.9%), $P=0.048$;12(85.7%) vs.7(50%),$P=0.013$). The treatment group exhibited a lower pH (7.34 ± 0.07 vs. 7.36 ± 0.06, $P=0.039$) and a higher $PaCO_2$ (43.08 ± 7.36 vs. 38.86 ± 5.65 mmHg, $P=0.042$) at the time of 30 min after initiation of CPB. A significant reduction in postoperative CK-MB was observed in treatment group (41.20 ± 17.88 vs. 56.57 ± 22.99 U/L, $P=0.002$). Lower 3-day postoperative CRP levels were also observed in the treatment group relative to control (5.77 ± 0.48 vs. 9.45 ± 0.98 mg/L, $P<0.001$). The S100ß concentration in the relevant patient cohort increased significantly from the time just after induction, intubation, and installation of the right central venous line to the time of admission to CCU (71.61 ± 11.83 vs. 124.04 ± 38.80, $P=0.01$) and at the time of 24 h after operation (71.61 ± 11.83 vs. 101.97 ± 30.31, $P=0.01$). No differences on S100β serum concentration level were found at the time of installation of the right central venous line between two groups. But there were statistically significant differences in S100β serum concentration level at the time of admission to CCU between control group and treatment group. (161.19 ± 6.62 vs. 86.89 ± 9.69 pg/ml, $P=0.01$). Similar results were observed at the time of 24 h after operation. (127.62 ± 19.44 vs. 76.33 ± 10.40, $P=0.01$).

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Conclusion These data suggest that the CO_2 field-flooding device can safely be used when performing CPB surgical procedures via a right-side small incision approach to treat CHD without hypercapnia. The use of such a CO2 field-flooding device at a flow rate of 5 L/min may help protect against cardiac and nervous system damage in children undergoing CHD surgery.

Keywords Congenital heart disease, CO2 field-flooding, CPB, Right-side small incision, S100β

Background

Congenital heart disease (CHD) ranks as the most common birth defect in China, with surgical treatment for this condition generally necessitating cardiopulmonary bypass (CPB) assistance [1].

During CPB surgical procedures, air can be pumped into circulation by the heart during the early stages of rebeating, which can result in air embolism formation. If severe, this can impair the function of peripheral or central organs, potentially even leading to patient death [2].

Standard de-airing strategies that are used to evacuate air from the heart following open heart CPB surgery include left ventricle filling and venting, the placement of the patient in the Trendelenburg position, needle aspiration, and mechanical ventilation. Even using this approach, however, large volumes of air can remain. In China, people are paying more attention to the aesthetic requirements and do not want to see surgical scars in the anterior chest. Therefore, for some simple CHD surgery (including ASD, VSD, PAPVC, and PAVC) with relatively small surgical risk, we try to correct it through a small right axillary incision. Advances in CPB surgery performed to treat CHD via the right-side small incision approach entail a smaller, deeper surgical field, increasing the difficulty of evacuating air as compared to traditional de-airing maneuvers.

The use of carbon dioxide (CO_2) to flood the surgical field can reduce intracardiac air incidence by ~85% owing to the fact that CO_2 is 1.5-fold more dense and 25 times more soluble than air such that dependent areas of the surgical field are preferentially filled with CO_2, with a corresponding reduction in micro-emboli size [3, 4].

Utilizing a CO_2 atmosphere when performing cardiac surgical procedures has emerged as a standard of care in many cardiac surgery departments. As CO_2 exhibits 25-fold greater solubility in blood compared to air such that these CO_2 bubbles dissolve more rapidly in blood as compared to bubbles of air [5].

Transesophageal echocardiography (TEE) indicates that the application of CO_2 leads to the rapid disappearance of intracardiac air in a matter of minutes.[5] Utilizing a CO_2 atmosphere can increase the $PaCO_2$ while decreasing the pH and base excess (BE) [6].

Materials and methods

This study was performed with support from the Scientific Achievements Transformation Incubation Fund of Beijing Children's Hospital (ZHFY3-1-015), with approval from the ethics committee of the Beijing Children's Hospital, Capital Medical University in Beijing, China([2022]-E-083-Y). The Declaration of Helsinki was observed when performing this study.

Study group

The study cohort was comprised of pediatric CHD (including ASD, VSD, PAPVC, and PAVC) patients who were scheduled to undergo surgery in Beijing Children's Hospital, Capital Medical University, and who ultimately underwent CPB surgical procedures using a right-side small incision approach. All patients were screened from April 2022 through December 2023, leading to the selection of 234 consecutive patients. Individuals eligible for inclusion were: 1) ≤ 18 years of age, 2) undergoing CPB, 3) individuals who provided written informed consent, and 4) individuals without any prior history of serious cardiac complications. Patients were excluded if they: (1) refused to participate in the study, (2) were undergoing reoperation, or (3) were found to exhibit other forms of cardiac malformations or systemic disease on preoperative examination. Patients were separated into a control group ($n = 93$) that underwent normal de-airing and a treatment group ($n = 141$) in which a CO_2 field-flooding device was added to these normal de-airing procedures. The specific details of demographics data including sex, age, weight, chromosomal abnormalities, cardiac malformations and details of the performed surgical procedures were included in Table 1.

Procedure description

All of the patients included in this study underwent CPB surgery performed via a right-side small incision approach. CPB was established via a standard technique using a membrane oxygenator, non-pulsatile flow, ascending aorta, and superior and inferior vena cava cannulation to establish CPB. Cardiac blood flow was blocked via the antegrade infusion of cardioplegic solution into the aortic root. All CPB procedures were performed under mild hypothermia, maintaining a core temperature of 30–34 °C during aortic cross-clamping (ACC).

Table 1 Demographics data

Variable	Control, *n* = 93	Treatment, *n* = 141	*P*-value
Sex			
Male, n (%)	50(53.8)	77(54.6)	NS[a]
Female, n (%)	43(46.2)	64(43.4)	
Age(months)	35.8 ± 12.6	35.9 ± 12.1	NS[c]
Weight(kg)	14.1 ± 8.4	14.6 ± 8.2	NS[c]
Chromosomal abnormalities, n (%)	3(3.2)	5(3.5)	NS[c]
Cardiac malformations			
ASD, n (%)	22(23.6)	37(26.2)	NS[a]
VSD, n (%)	61(65.6)	95(67.3)	NS[a]
PAPVC, n (%)	5(5.4)	8(5.7)	NS[a]
PAVC, n (%)	5(5.4)	6(4.2)	NS[a]
surgical procedures			
ASD, n (%)	22(100)	37(100)	
ASD closure, n (%)	19(86.4)	32(86.5)	NS[a]
ASD closure + MPA arterioplasty, n (%)	1(4.5)	2(5.4)	NS[a]
ASD closure + Mitral annuloplasty, n (%)	2(9.1)	3(8.1)	NS[a]
VSD, n (%)	61(100)	90(100)	
VSD closure, n (%)	55(90.2)	81(90)	NS[a]
VSD closure + ASD closure, n (%)	3(4.9)	5(5.6)	NS[a]
VSD closure + PDA ligation, n (%)	3(4.9)	4(4.4)	NS[a]
PAPVC, n (%)	5(100)	8(100)	
Correction of anomalous drainage of the right superior pulmonary vein by intra-atrial tunnel, n (%)	5(100)	8(100)	NS[a]
PAVC, n (%)	5(100)	6(100)	
Ostium primum ASD closure + Mitral valve commissural repair + Tricuspid valve leaflet plasty, n (%)	5(100)	6(100)	NS[a]

Notes: *aChi-squared test;bFisher's exact test;cMann–Whitney U test;dTwo-sample t-test*

Abbreviations: *ASD Atrial septal defect; VSD Ventricular septal defect; PAPVC, Partial anomalous pulmonary venous connection; PAVC Partial atrioventricular canal; MPA Main pulmonary artery; NS, not significant*

The surgical de-airing procedures in our team comprise left atrium (LA) de-airing, left ventricle (LV) and the aortic root de-airing, and right atrium (RA) de-airing. Taking VSD repair as an instance, after the VSD repair is completed, the LA drainage tube placed via the Patent foramen ovale (PFO) is withdrawn. A forceps is inserted through the incision of the PFO into the LA to maintain the temporary opening of the PFO. Water is injected through this incision for LA de-airing, and the anesthesiologist is requested to perform lung inflation. After the air in the LA is completely exhausted, the PFO is sutured and closed. Before the aorta de-clamping, the perfusion needle at the aortic root is extracted, and de-airing of the LV and the aortic root is conducted through the incision of the perfusion needle. Before the aorta de-clamping, simulate the cardiac pulsation by squeezing the LV with fingers or forceps, Meanwhile, the anesthesiologist is required to assist with lung inflation. A large number of bubbles can be seen emerging through the incision of the perfusion needle. While performing lung inflation, the aortic cross-clamp is slowly released. When no bubbles are seen emerging from the incision of the perfusion needle and good bleeding is observed, the aortic cross-clamp can be completely released and the lung inflation operation is stopped. Additionally, RA de-airing is performed before closing the incision of the RA, the Cardiopulmonary Perfusionist is required to briefly control the venous end of the pipeline. The large amount of air bubbles can be seen emerging through the incision of the RA. When good blood return is observed at the incision of the RA, the suture thread is tightened, the incision of the RA is completely closed, and then the incision of the perfusion needle is sutured. Thus, all cardiac de-airing operations are completed. The same surgical team performed all procedures. After surgery, patients were transferred to the cardiac intensive care unit (CCU) where they were treated by the same care team until being transferred out of the CCU, with relevant clinical indices being recorded.

Patient medical records were reviewed to obtain demographic and perioperative clinical data including sex, age, weight, chromosomal abnormalities, CPB time, ACC time, CCU stay, mechanical ventilation time, abnormal electrocardiogram (ECG) after aorta de-clamping during CPB (including abnormal elevation of ST segment, ventricular fibrillation, atrial fibrillation, and other arrhythmias), and interventions for abnormal ECG (including defibrillation, sewing temporary pacing leads, apply isoproterenol, unplanned rapid bolus injection of vasoactive drugs).

Analyzed arterial blood gas (ABG) data included pH, $PaCO_2$, BE, and lactic acid (Lac) levels measured at Baseline in the OR (T1), 30 min after initiation of CPB (T2), and Admission to the CCU (T3).

Laboratory tests included analyses of renal, liver, and myocardial damage-related markers, levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), serum creatinine (Scr), and Creatine kinase-MB (CK-MB). Preoperative laboratory test data were collected 3 days prior to surgery(T0), while postoperative data were collected 1 day post-surgery(T4). C-reactive protein (CRP) levels were analyzed on days 1 (T4) and 3 after surgery(T5).

We selected 23 patients separately in the control and treatment group, aiming to analyze the influence of CO2 field flooding on micro-embolism-induced brain damage. We collected 46 patients' blood samples to assess the change level of S100β protein.S100β was regarded as a marker of brain damage.

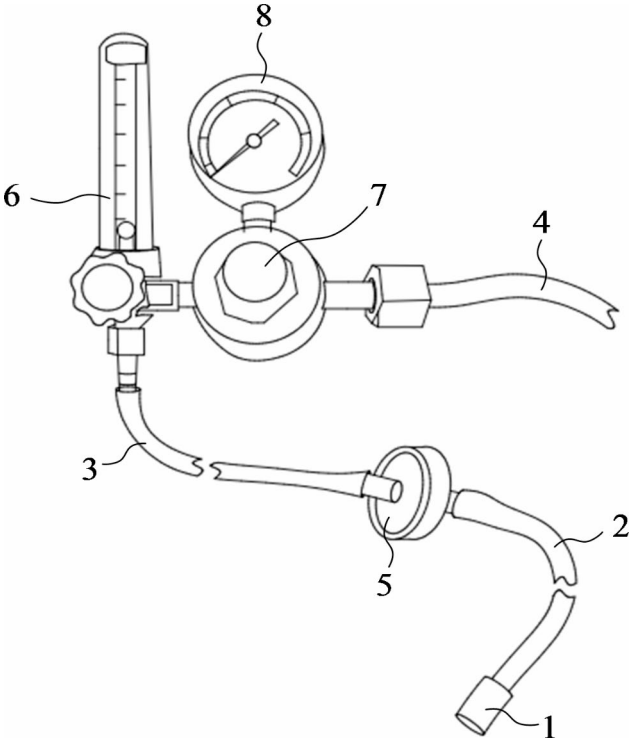

Fig. 1 Schematic diagram of CO2 field-flooding device. **Notes:** 1. The diffusion head of the CO2; 2 and 3. General medical aspirator tube; 4. Air source connecting pipe; 5. Gas filter; 6. flow meter; 7. Pressure valve; 8. Gas pressure indicator

CO2 field-flooding device

A medical CO_2 gas source, pressure gauge, and self-produced CO_2 field-flooding device were connected, ensuring that the connections were tight before beginning the procedure. (Fig. 1). The diffusion head of the CO_2 field-flooding device is used for the dispersal of CO_2, as it is inserted into the surgical incision just beneath the chest retractor. CO_2 flow was measured using a standard flowmeter for medical CO_2, starting a flow rate of 5 L/min beginning 5 min before CPB and ending after CPB was complete.

S100β protein measurements

To analyze the changes in S100ß protein level, blood was collected at three points. The first blood sample (P1) was taken just after induction, intubation, and installation of the right central venous line. The next sample(P2) was taken in the time of admission to CCU. The third sample (P3) was collected 24 h after operation. Blood was stored at 4 °C, allowed to clot, and after centrifugation (10 min, 3,000 rpm) collected in 2 ml EP tube. Samples of serum were stored at -80 °C for later analysis. Protein S100ß was analyzed using ELISA (Banyan Biomarkers, Alachua, FL), and the detection reference range of S100ß serum concentrations in 95% of healthy subjects is 0.015-2ng/ml.

Table 2 Perioperative clinical data

Variable	Control, *n* = 93	Treatment, *n* = 141	*P*-value
CPB time(min)	80.3 ± 32.7	76.9 ± 29.6	NS[d]
ACC time(min)	54.1 ± 24.6	48.1 ± 22.6	NS[d]
Mechanical ventilation time(h)	22.9 ± 34.6	16.2 ± 23.9	NS[a]
CCU stay(days)	2.5 ± 1.4	2.0 ± 1.6	NS[b]
Abnormal ECG after aorta de-clamping during CPB, n (%)	17(18.3)	14(9.9)	0.048[b]
Interventions for abnormal ECG after aorta de-clamping during CPB, n (%)	12(85.7)	7(50)	0.013[b]

Notes: *aChi-squared test;bFisher's exact test;cMann–Whitney U test;dTwo-sample t-test*

Abbreviations: *CPB Cardiopulmonary bypass; ACC Aorta Cross-clamping; CCU, Cardiac care unit; ECG electrocardiogram; NS, not significant*

Statistical analysis

SPSS 22.0 (SPSS, IL, USA) was used to analyze all data. Descriptive statistics are reported as means ± SD. Non-continuous data were compared with Chi-square, Yates' chi-square, and Fisher's exact test approaches, as appropriate. Normally distributed continuous variables, as identified via the Kolmogorov-Smirnov test, were compared with two-sample t-tests, while skewed data were compared with the Mann-Whitney U test for independent data and the Wilcoxon signed-rank test for correlated data. $P < 0.05$ was selected to define significance.

Results

This study enrolled 234 patients in total, including 93 and 141 in the control and treatment groups, significantly. There was a significant difference in abnormal electrocardiogram (ECG) after aorta de-clamping during CPB between the control and treatment groups (17(18.3%) vs.14(9.9%), $P = 0.048$), and interventions for abnormal ECG between the control and treatment groups (12(85.7%) vs.7(50%), $P = 0.013$), while no other demographic or perioperative clinical data differed between these groups. The perioperative clinical data were summarized in Table 2.

The results of ABG results collected during Baseline in the OR (T1), 30 min after initiation of the CPB procedure (T2) and Admission to the CCU (T3) are presented in Table 3. Relative to the control group, treatment group patients presented with a lower T2 pH (7.34 ± 0.07 vs. 7.36 ± 0.06, $P = 0.039$) and a higher T2 $PaCO_2$ (43.08 ± 7.36 vs. 38.86 ± 5.65 mmHg, $P = 0.042$).

The results of laboratory testing and associated perioperative analyses are presented in Table 4. No significant differences in preoperative (T0) laboratory test results were detected when comparing the control and treatment groups. In the control group, postoperative (T4) AST, ALT, BUN, CK-MB, and CRP levels differed significantly from preoperative (T0) values, and similarly, postoperative (T4) AST, BUN, CK-MB, and CRP levels

Table 3 ABG results at T1, T2 and T3

Variable	Control, *n* = 93	Treatment, *n* = 141	*P*-value
PaCO2(T1) (mmHg)	40.15 ± 6.96	40.52 ± 6.32	NS[b]
PaCO2(T2) (mmHg)	38.86 ± 5.65	43.08 ± 7.36	0.042[b]
PaCO2(T3) (mmHg)	35.69 ± 5.87	35.78 ± 5.98	NS[b]
pH(T1)	7.38 ± 0.06	7.38 ± 0.06	NS[b]
pH(T2)	7.36 ± 0.06	7.34 ± 0.07	0.039[b]
pH(T3)	7.32 ± 0.31	7.35 ± 0.06	NS[b]
BE(T1) (mmol/L)	-1.27 ± 2.96	-1.27 ± 2.96	NS[a]
BE(T2) (mmol/L)	-3.25 ± 3.21	-3.74 ± 3.21	NS[a]
BE(T3) (mmol/L)	-5.37 ± 1.84	-4.96 ± 2.14	NS[a]
Lac(T1) (mmol/L)	0.76 ± 0.38	0.81 ± 0.46	NS[a]
Lac(T2) (mmol/L)	1.03 ± 0.56	1.05 ± 0.65	NS[a]
Lac(T3) (mmol/L)	2.11 ± 1.33	2.02 ± 1.19	NS[a]

Notes: *T1 Baseline in the OR, T2 30 min after initiation of CPB procedure, T3 Admission to CCU;*[a]Mann–Whitney U test; [b]Two-sample t-test

Abbreviations: *ABG arterial blood gas; NS, not significant*

Table 4 Laboratory tests and associated perioperative analyses

Variable	Control, *n* = 93	Treatment, *n* = 141	*P*-value
AST(T0) (U/L)	39.14 ± 9.47	38.59 ± 11.95	NS[a]
AST(T4) (U/L)	109.78 ± 36.33	80.93 ± 33.22	0.01[a]
ALT(T0) (U/L)	18.23 ± 9.89	18.52 ± 9.54	NS[a]
ALT(T4) (U/L)	22.71 ± 15.86	19.62 ± 7.45	NS[a]
BUN(T0) (mmol/L)	4.31 ± 1.30	4.43 ± 1.33	NS[a]
BUN(T4) (mmol/L)	5.75 ± 2.09	5.38 ± 1.73	NS[a]
Scr(T0) (μmol/L)	25.75 ± 7.33	26.74 ± 8.82	NS[a]
Scr(T4) (μmol/L)	27.48 ± 15.94	27.16 ± 9.07	NS[a]
CK-MB(T0) (U/L)	24.61 ± 9.30	23.81 ± 11.63	NS[b]
CK-MB(T4) (U/L)	56.57 ± 22.99	41.20 ± 17.88	0.002[b]
CRP(T0) (mg/L)	0.90 ± 0.29	0.87 ± 0.33	NS[b]
CRP(T4) (mg/L)	38.72 ± 24.42	33.12 ± 20.49	NS[b]
CRP(T5) (mg/L)	13.9 ± 9.45	9.8 ± 5.77	< 0.001[b]

Notes: *T0 preoperative, T4 1-day postoperative, T5 3-day postoperative;*[a]Mann–Whitney U test, [b]Yates' chi-squared test

Abbreviations: *NS, not significant*

in the treatment group differed from those at T0. Significantly lower postoperative (T4) AST values were evident in the treatment group relative to the control group (80.93 ± 33.22 vs. 109.78 ± 36.33 U/L, $P = 0.01$), and the same was true for postoperative CK-MB (41.20 ± 17.88 vs. 56.57 ± 22.99 U/L, $P = 0.002$). 3-day postoperative (T5) CRP levels were also significantly lower in the treatment group (9.8 ± 5.77 vs. 13.9 ± 9.45 mg/L, $P < 0.001$). No significant differences in other laboratory test data were detected between groups and the analyzed time points ($P > 0.05$).

It has been observed that the S100ß concentration in the total patient cohort increased significantly from the time just after induction, intubation, and installation of the right central venous line (P1) to the time of admission to CCU(P2) (71.61 ± 11.83 vs. 124.04 ± 38.80, $P = 0.01$) and at the time of 24 h after operation(P3) (71.61 ± 11.83 vs. 101.97 ± 30.31, $P = 0.01$). The differences

Table 5 The differences of S100ß serum concentration in the control and treatment groups

Results	Control, *n* = 23	Treatment, *n* = 23	*P*-value
S100β(P1)(pg/ml)	71.03 ± 9.79	72.29 ± 14.01	NS[a]
S100β(P2)(pg/ml)	161.19 ± 6.62	86.89 ± 9.69	0.01[a]
S100β(P3)(pg/ml)	127.62 ± 19.44	76.33 ± 10.40	0.01[a]

Note: [a]Mann–Whitney U test

Abbreviations: NS, not significant

of S100ß serum concentration in the control and treatment groups are presented in Table 5. No differences on S100β serum concentration level were found at the time of P1. However, there were statistically significant differences in S100β serum concentration level at the time of P2 between control group and treatment group. (161.19 ± 6.62 vs. 86.89 ± 9.69 pg/ml, $P = 0.01$). Similar results were observed at the time of P3. (127.62 ± 19.44 vs. 76.33 ± 10.40, $P = 0.01$).

Discussion

CO_2 insufflation into open surgical wounds has long been performed as a means of preventing air embolism in patients undergoing conventional open cardiac surgical procedures. The device used for open cardiac surgical procedures in most Western nations (manufactured by Cardia Innovation AB, Stockholm, Sweden), however, is often regarded by surgeons as being too large for use during minimally invasive procedures in children [7]. The vast majority of the literature focused on this topic is restricted to adult cardiac surgical patients. There is therefore a clear need for access to a sufficiently small device that can allow for the elimination of air from a small open surgical wound without disrupting the mechanics of the surgical procedure [8]. Stijn Vandenberghe described achieving a high degree of efficacy via a CO2 field flooding strategy in minimally invasive cardiac surgical procedures performed with patients in a tilted position. At 1 L/min, approximately 2.5 min were needed to fill the supine model to its maximum CO2 concentration, which was limited to a range of 48–82% in the LV. At higher flow rates, filling time and concentration were significantly improved. In a tilted model, all devices and all flow rates generated on average 99% CO2 in the ventricle. CO2 field flooding in minimally invasive cardiac surgery is highly effective if the patient is tilted. Else a flow rate of 5 L/min is recommended to achieve the same protection [9]. Our research utilized a CO2 field-flooding device with a flow rate of 5 L/min produced independently in children undergoing CPB surgery via a right-side small incision approach and achieved satisfactory clinical effects, collecting perioperative data for analysis.

Here, the various effects of CO_2 field flooding in simple CHD patients undergoing CPB via a right-side small incision approach were analyzed in detail. Strikingly,

lower postoperative AST, CK-MB, and CRP levels were observed in the treatment group relative to the control group, and the use of the CO_2 field-flooding device was not associated with hypercapnia. Higher T2 $PaCO_2$ levels were evident in the treatment group relative to the control group, but they remained in the normal range (43.08 ± 7.36 vs. 38.86 ± 5.65 mmHg, $P = 0.048$). After the application of the CO2 field-flooding device, the incidence of abnormal ECG after aorta de-clamping during CPB surgeries in the treatment group was significantly lower than that in the control group. This might be attributed to the right sub-axillary small incision approach. Compared with median sternotomy, in the lateral thoracotomy, the entire right thoracic cavity is positioned above the heart. In such an environment with a narrow opening and a broad bottom, the air within the right thoracic cavity is more prone to enter the cardiac chambers. Nevertheless, under such conditions, the effect of using CO2 for surgical field insufflation might actually be better. And as the patient's posture changes, the position of the right coronary artery is relatively elevated, increasing the likelihood of the right coronary artery getting involved with air emboli. Our empirical findings indicate that in pediatric CPB surgeries through the right thoracotomy approach, the occurrence rate of arrhythmia after cardiac rebeating is significantly higher than that through the median sternotomy. Furthermore, the solubility of CO2 in blood and tissues is more than 25 times that of air. Even if CO2 emboli are formed, they can dissolve rapidly.

Cardiac surgery-associated kidney injury (CS-AKI) also commonly impacts CHD patients undergoing surgery [10]. While a range of strategies have been employed in an effort to protect against CS-AKI, there has not been any data published regarding the benefits of CO_2 field-flooding device in this setting. Here, both patient groups exhibited higher postoperative BUN and Scr levels relative to preoperative values, without any significant differences between groups. This thus suggests that the use of a CO_2 field-flooding device failed to provide any clear reno protective effect in these surgical patients.

During the perioperative period of cardiac CPB surgery, it is of great significance to detect brain injury at an early stage and in a timely fashion. Nevertheless, owing to anesthesia and other factors, patients are in an anesthetic and drug-induced sleep state in the early postoperative phase and are equipped with various tubes. Thus, it is extremely challenging to assess brain injury in children at the early postoperative stage in the CCU. Examinations like cranial CT and cranial MRI cannot be effectively conducted, and cognitive scales are also hardly applicable among young children. Therefore, screening for specific neuro-biomarkers capable of detecting early brain injury becomes highly significant. Among the various neuro-biomarkers currently being investigated for central nervous system (CNS) monitoring, the S100β protein appears to be one of the most promising biomarkers for detecting brain damage and predicting prognosis in children [11, 12]. The S100 proteins are a family of small, dimeric, multigenic calcium-binding proteins composed of various combinations of A1 and B subunits. They have a molecular weight of 10–12 kDa and a biological half-life of about 2 h, and were first isolated from central nervous tissue in 1965 [4, 13]. Neuronal destruction and destabilization of the blood–brain barrier are accompanied by the release of S100ß protein into the blood. S100ß can be measured within minutes after the event and detected for an extended period. It is removed from the serum via the renal clearance pathway, with a half-life of 20–25 min. S100ß protein level is a sensitive and specific marker for brain injury after stroke, head trauma, and brain damage caused by circulatory arrest or cardiac surgery with CPB. The protein has been proven a good marker of brain damage during CPB [4, 13–15]. In Mariusz listewnik's study, a group of 100 elderly patients undergoing planned mitral valve operation through median sternotomy using standard CPB was recruited, CO2 insufflation at 6 L/minute was conducted in the study group. The mean increase in the S100ß concentration was 13% lower in the group with CO2 protection than in the control group (0.988 μg/L vs. 1.125 μg/L) [4]. Martens S investigated the impact of delivering air and CO2 to the carotid arteries of pigs on the manifestation of lesions in an MRI scan and reached the conclusion that air resulted in extensive cerebral infarction, whereas CO2 did not induce any detectable lesions via MRI [16]. In our research, it was found that the S100β values measured at 2 h and 24 h after the operation in both groups of patients exhibited a significant increase. Nevertheless, in the treatment group where the CO2 surgical field filling technique was employed, the increment of the S100β value was significantly lower than that in the control group. Furthermore, upon data analysis of the two groups, a significant statistical difference was identified. We speculate that the application of the CO2 surgical field filling technique in children's CPB surgery might possess certain advantages.

Limitations

Our study is actually a combination of retrospective and prospective studies. The measurement of neurotrophic marker S100β in 46 patients was part of a supplementary experiment, which indeed belongs to the prospective study. The enrollment criteria and exclusion criteria were the same as those in previous studies. As supplementary data for the entire study, there is inevitably certain limitation in the study design. To ensure that the study results were primarily attributable to the use of the CO_2 field-flooding device itself rather than other factors, only

simple CHD cases (including ASD, VSD, PAPVC, and PAVC) were selected for inclusion, for all the enrolled patients in our study, the same CPB machine was utilized, the same Cardiopulmonary Perfusionist was involved, the same CPB management plan was implemented, the same batch of CPB tubing was used, the same surgical team was engaged, etc. We made every effort to minimize the effects of other factors on the results. Naturally, there are still numerous issues in our research. The overall sample size was relatively limited, and only perioperative time points were assessed without any corresponding analyses of long-term patient outcomes. There were also no significant differences in certain clinical parameters including mechanical ventilation time and CCU stay. These results may ultimately have been biased by the relatively small sample size and mild heart disease observed herein. As the patients in this study were young, the beneficial effects of the use of the CO_2 field-flooding device may be inconsistent with similar findings in adults. To assess whether CO2 field-filling device holds clinical significance for brain protection through the neurobiological marker S100β, our research has just initiated with small sample size. Although we have achieved some promising outcomes, it still requires further validation via other approaches, such as non-invasive detection methods like near-infrared spectroscopy (NIRS), transcranial Doppler (TCD), and cognitive scales, in order to comprehend the correlation between the two. This also constitutes our future research direction. Despite these limitations, however, the present study still offers important insights of clinical relevance.

Conclusion

In summary, these results demonstrate that a CO_2 field-flooding device can be safely used when performing CPB surgical procedures via a right-side small incision approach to treat CHD without hypercapnia. The use of such a device at a 5 L/min flow rate may protect against cardiac and nervous system damage in children undergoing CHD surgery.

Abbreviations

CHD	Congenital heart disease
CPB	Cardiopulmonary bypass
CO2	Carbon dioxide
BE	Base excess
ASD	Atrial septal defect
VSD	Ventricular septal defect
PAPVC	Partial anomalous pulmonary venous connection
PAVC	Partial atrioventricular canal
MPA	Main pulmonary artery
ACC	Aortic cross-clamping
LA	Left atrium
PFO	Patent foramen ovale
PDA	Patent ductus arteriosus
LV	Left ventricle
RA	Right atrium
CCU	Cardiac intensive care unit
ECG	Electrocardiogram
ABG	Arterial blood gas
Lac	Lactic acid
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
BUN	Blood urea nitrogen
Scr	Serum creatinine
CK-MB	Creatine kinase-MB
CRP	C-reactive protein
CNS	Central nervous system

Author contributions

Zhangke Guo wrote the main manuscript text; Zhangke Guo and Zhimin Li prepared Tables 1, 2, 3 and 4 ;Song Bai, Feng Tong, Jia Zheng, Nan Ding, Xiaofeng Li prepared Figs. 1, 2, 3, 4 and 5; All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This statement confirming the approval of the study by the ethical committee of Beijing Children's Hospital, Capital Medical University in Beijing, China. ID number [2022]-E-083-Y. All patients were consented for the participation in the study.

The ethics declaration

In accordance with the Declaration of Helsinki.

Competing interests

The authors declare no competing interests.

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