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The combined use of HA380 hemoperfusion in cardiopulmonary bypass alleviates postoperative inflammatory response and organ dysfunction following cardiac surgery.

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Objective: To evaluate the efficacy of the HA380 hemoperfusion device in attenuating systemic inflammatory response during cardiopulmonary bypass (CPB)-assisted cardiac surgery and its influence on perioperative clinical outcomes.

Methods: This trial enrolled 65 patients who underwent elective cardiac surgery with CPB. Patients were randomly divided into two groups: the experimental group (HP group, n=34) used the HA380 hemoperfusion device throughout CPB; the control group (n=31) underwent conventional CPB only. Serum levels of IL-1β, IL-6, IL-8, IL-10, TNF-α, and CRP were measured at: preoperatively (T0), immediately postoperatively (T1), 24h (T2) and 48h (T3) post-surgery. Surgical data, postoperative ICU indicators (duration of intubation, vasoactive-inotropic score [VIS], drainage volume, urine output, ICU stay duration), and first-day postoperative blood routine, liver and kidney function, and coagulation indicators

were recorded. Differences between the two groups were compared.

Results: There were no statistical differences in baseline data between the two groups (P>0.05). Inflammatory factor analysis showed that serum levels of IL-1β, IL-6, IL-8, and IL-10 in the HP group were significantly lower than the control group (P<0.05) at T1 and T2. However, no significant differences were observed in TNF-α and CRP levels between the two groups at any time point (P>0.05). Regarding clinical indicators, the HP group exhibited a lower VIS on postoperative day 1 (P<0.05); significant reductions in levels of white blood cells, neutrophils, ALT, urea, and creatinine were observed than the control group (P<0.05). ICU intubation time, drainage volume, and urine output on the first postoperative day, ICU stay duration, hemoglobin, platelet, bilirubin, and other indicators showed no intergroup differences ($P > 0.05$).

Conclusion: The combined application of the HA380 blood perfusion device during CPB-assisted cardiac surgery effectively clears medium molecular weight inflammatory mediators (IL-1β, IL-6, IL-8, IL-10), significantly reduces early postoperative systemic inflammatory response, and helps improve early postoperative hemodynamic stability (reducing the need for vasoactive drugs) and short-term liver and kidney function indicators. However, no significant reduction was observed in ICU mechanical ventilation time and ICU stay duration. HA380 demonstrates promise as an adjunct anti-inflammatory therapy, though its long-term benefits and impact on postoperative recovery optimization require further investigation.

Keywords: Cardiopulmonary bypass; Blood perfusion device; Cardiac surgery; Inflammatory response.

INTRODUCTION

In 1953, Gibbon successfully implemented the first cardiopulmonary bypass (CPB) procedure for repairing atrial septal defects, marking the beginning of a new era in direct heart surgery[1]. During the CPB process, various factors such as the contact of blood with non-biological materials, sustained non-pulsatile blood flow, blood dilution, hypothermia, and systemic anticoagulation of the body may lead to potential pathophysiological change [2]. Major CPB-related complications include bleeding, low cardiac output syndrome, arrhythmias, respiratory failure, renal failure, neurological dysfunction or neuropsychiatric changes, fluid and electrolyte disturbances, hemolysis, and systemic inflammatory response[3]. Among these, the systemic inflammatory response triggered by CPB has been a focus of research in this field due to its prevalence and significant clinical impact[4-5].

To improve patient prognosis, reducing the inflammatory response during CPB has become an important research goal, leading to the development of various intervention strategies. In terms of drug interventions: early postoperative use of glucocorticoids has been shown to significantly alleviate inflammation after CPB[6]; broad-spectrum protease inhibitor Ulinastatin can stabilize lysosomal membranes and inhibit the release of lysosomal enzymes, thereby reducing the release of inflammatory mediators[7]; and infusion of phosphodiesterase III

inhibitor Milrinone during CPB can lower the production levels of interleukin-6 (IL-6) and interleukin-1β (IL-1β) in patients undergoing coronary artery bypass grafting (CABG), helping to improve left ventricular function[8]. Regarding equipment technology, researchers are dedicated to improving the materials of CPB circuit components (such as tubing), oxygenators, and ultrafilters, aiming to reduce the activation of blood components and the release of inflammatory factors caused by the equipment itself [9-11]. In recent years, the combination of hemoperfusion (HP) technology with CPB in cardiac surgery has been proposed as a new research direction and potential approach to address the inflammation issues associated with CPB.

HA380 is a blood perfusion device that uses neutral macroporous adsorption resin as a carrier, with an adsorption spectrum primarily for substances with a molecular weight of 0.5-60 kDa[12]. Existing studies have shown that HA380 can effectively reduce inflammatory responses in acute inflammatory conditions such as sepsis[13], trauma[14], liver failure[15], pancreatitis[16], and severe COVID-19[17]. However, research on the application effects of HA380 and its inthe inflammatory protective role in cardiac surgery involving CPB is still insufficient.Unlike previous HA380 studies mostly focusing on sepsis or a single type of cardiac surgery, this study for the first time verifies its anti-inflammatory and short-term organ-protective effects in various CPB-assisted cardiac surgeries. This study aims to preliminarily verify the anti-inflammatory and short-term organ-protective effects of HA380 in CPB-assisted cardiac surgeries, providing a basis

for subsequent related exploration.

Therefore, this study aims to evaluate the inflammatory protective protective effects of the combined application of the HA380 blood perfusion device during cardiopulmonary bypass in cardiac surgery and to explore its potential for perioperative protection of liver and kidney organs during the perioperative period, with the goal of providing new clinical evidence for optimizing CPB management.

Methods

Research Object:

Patients undergoing elective cardiac surgery with CPB assistance in the Department of Cardiothoracic Surgery at Fuyang Hospital, Anhui Medical University, from May 2022 to July 2024 were included. Patients were randomly assigned to two groups: the Experimental Group (HP group, n=34): based on routine CPB, an HA380 blood perfusion device (Jafron Biomedical Co., Zhuhai, China) was installed in series in the CPB circuit. HP treatment was initiated after the CPB started stable operation and continued throughout the CPB period. The Control Group (Control group, n=31): received only routine CPB support, with no blood perfusion device in series in the circuit. Inclusion criteria: 1) Age ≥ 18 years; 2) Diagnosed as needing cardiac surgery under CPB (such as valve replacement/repair, coronary artery bypass grafting, congenital heart disease correction, etc.); 3) No obvious surgical contraindications. Exclusion criteria: 1) Preoperative malignancy; 2) Preoperative systemic autoimmune diseases; 3)

Severe active infections preoperatively; 4) Emergency surgery; 5) Known allergies to HP adsorbent-related materials.

Group assignment was performed using a computer-generated random number table. Eligible patients were sequentially numbered by admission order, with odd numbers assigned to the HP group and even numbers to the control group, without manual interference to ensure allocation concealment.

During the study period, valvular surgery was the main type due to limited clinical volume of coronary artery bypass grafting (only 1 eligible case). The distribution of surgical methods between the two groups was balanced (P=0.427, Table 1)."

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Fuyang Hospital, Anhui Medical University. Informed consent was obtained from each patient in writing.

Study Hypothesis and Endpoints

The prespecified hypothesis was that HA380 hemoperfusion mitigates postoperative systemic inflammation and improves hemodynamic stability/organ function by adsorbing medium-molecular-weight inflammatory mediators (10–60 kDa) during CPB. The primary endpoint was serum IL-6 level at 24 hours postoperatively (T2), a key marker of CPB-induced inflammation. Secondary endpoints included inflammatory cytokines (IL-1β, IL-8, IL-10, TNF-α, CRP) at T0–T3, 24-hour cumulative VIS, perioperative liver/kidney function indices (ALT, urea, creatinine), and clinical recovery outcomes (mechanical ventilation duration, ICU stay duration).

Anesthesia Management:

All patients in this study underwent CPB-assisted cardiac surgery, with the same strategy for anesthesia induction, maintenance, and intraoperative management. Midazolam, etomidate, rocuronium/bisbenzylisoquinolinium, and sufentanil were used for intravenous induction followed by tracheal intubation and internal jugular vein cannulation. During the procedure, intermittent doses of sufentanil and midazolam were administered, with continuous infusion of cisatracurium, dexmedetomidine, and propofol for anesthesia maintenance.

Cardiopulmonary Bypass:

The Control Group: Conventional cardiopulmonary bypass and ultrafiltration were used. The Experimental Group: Based on conventional cardiopulmonary bypass and ultrafiltration, the HA380 blood perfusion device was connected in series. Routine preoperative administration of ulinastatin and methylprednisolone was performed; during the transition, the perfusion flow was maintained at 2.0-2.4 L/(m^2·min); mean arterial pressure at 55-75 mmHg; mixed venous oxygen saturation at (75±10)%; temperature during surgery was maintained at 28-34℃ according to surgical needs; full blood heparinization (3 mg/kg), and extracorporeal circulation commenced after achieving an Activated Clotting Time of Whole Blood (ACT) >480s. Dynamic monitoring of hematocrit (Hct) and arterial and venous blood oxygen saturation was performed during the transition, with periodic checks of ACT, blood gas analysis, and electrolytes. After completing cardiac procedures, blood was rewarmed to 36.5°C, myocardial contraction was

strong, and circulatory indicators were stable before weaning from extracorporeal circulation.

HA380 Hemoperfusion in the CPB Circuit: The HA380 hemoperfusion device was connected in series to the CPB circuit, specifically positioned between the oxygenator and the venous reservoir. Hemoperfusion was initiated 10 minutes after CPB stabilization to avoid hemodynamic fluctuations during the initial bypass phase, with the flow rate synchronized with the CPB flow (2.0–2.4 L/(m^2·min)) and maintained throughout the entire CPB period until the termination of cardiopulmonary bypass. No additional modifications to the CPB circuit were required, and no device-related complications (e.g., coagulation, flow obstruction) were observed during the procedure.

Collection and Processing of Experimental Specimens:

Venous blood was collected from patients preoperatively (T0), postoperatively at 0h (T1), 24h (T2), and 48h (T3), promptly centrifuged to obtain serum, and stored at -80°C. Venous blood collected preoperatively and on the first postoperative day was sent to the hospital's laboratory for routine blood tests and liver and kidney function tests.

Detection Methods for Inflammatory Indicators:

The inflammatory factors IL-1β, IL-6, IL-8, IL-10, TNF-α, and CRP studied in the experiment were detected using the ELISA method. The specific method is as follows: serum levels of IL-1β, IL-6, IL-8, IL-10, TNF-α, and CRP were measured using an ELISA kit (Beyotime, Shanghai, China). A standard curve was created

according to the instructions of the kit, and the OD values of the sample wells were measured at 450 nm using a microplate reader, followed by calculation and analysis based on the formula.

Statistical Methods:

IBM SPSS 25.0 statistical software (SPSS Statistics V25; IBM Corporation, Somers, NY, USA) was used for data analysis. Continuous data were expressed as mean ± standard deviation (x±s), and categorical data were expressed as count (percentage) [n(%)]. Independent samples t-test was used for inter-group comparison of continuous data when parametric test conditions were met, otherwise Mann-Whitney U test was used; χ^2 test was used for inter-group comparison of categorical data. For repeated measurement indicators such as inflammatory factors at multiple time points (T0, T1, T2), two-way mixed-design ANOVA was used to analyze inter-group (intervention factor), intra-group (time factor) effects and their interaction effects. Before statistical analysis, normality was verified by Shapiro-Wilk test and homogeneity of variance by Levene test. Regarding multiple comparisons: The preset primary outcome indicators of this study were IL-1β, IL-6, IL-8, and IL-10, with inter-group differences showing a consistent downward trend (lower in the HP group than in the control group) and uniform result directions, so no formal multiple comparison correction was performed, as the consistent effect direction can reduce the risk of false positive results. A P value < 0.05 was considered statistically significant.

Results

Patient demographics and clinical characteristics

A total of 65 patients were included, with an average age of 64.43 ± 12.94 years. There were 34 patients in the HP group and 31 patients in the control group, with no statistically significant differences in baseline characteristics (including age, gender, BMI) between the two groups. All surgeries were completed with the assistance of CPB, and there were no statistically significant differences between the two groups in terms of surgical methods, preoperative left ventricular ejection fraction (LVEF), surgical duration, extracorporeal circulation time, preoperative cardiac function classification, presence of diabetes before surgery, or presence of atrial fibrillation before surgery (Table 1).

Table 1. Demographic and clinical characteristics of the patient

Parameters	HP（n=34）	Control（n=31）	*p*-value
Gender			0.878
Male	16	14	
Female	18	17	
Age,（years）	67.12±9.23	61.48±15.69	0.088
BMI（kg/m^2）	24.04±3.6	23.67±3.47	0.672
Surgical procedures			0.427
Valve surgery *	32	29	
Coronary artery bypass	0	1	

grafting			
Atrial myxoma removal	1	1	
Atrial septal defect repair	1	0	
Left ventricular ejection fraction（LVEF）	55.65±9.33	56.97±10.26	0.589
Operation time（h）	5.67±1.06	5.19±1.06	0.071
Cardiopulmonary circulation time（min）	154.38±61.89	132.68±43.89	0.106
Diabetes mellitus			1
Yes	2	2	
Not	32	29	
With atrial fibrillation			0.085
Yes	17	9	
Not	17	22	
Preoperative cardiac function grading			0.839
2	14	12	
3	20	19	

*Continuous data are expressed as mean ± standard deviation (x±s). Normally distributed data were analyzed by independent samples t-test, and non-normal data by Mann-Whitney U test. Categorical data were analyzed by χ^2 test. $P<0.05$ was considered statistically significant.

*, Valve surgery includes the replacement or shaping of mitral, tricuspid, and aortic valves.

Comparison of inflammatory indicators between two groups of patients

We tested the inflammatory-related indicators at different time points for the two groups of patients. Statistical analysis found that there were no statistically significant differences in the inflammatory-related indicators between the two groups at pre-operation (T0) and 48 hours post-operation (T3). However, at 0 hours post-operation (T1) and 24 hours post-operation (T2), the levels of IL-1β, IL-6, IL-8, and IL-10 in the HP group were lower than those in the control group, and the differences were statistically significant. For TNF-α and CRP indicators, there were no statistically significant differences between the two groups at all time points (Table 2). All inflammatory factors increased from T0 to T2 and then began to decrease at T3 (Figure 1).

Table 2. Inflammatory index results of the two groups

T0		*p*	T1		*p*	T2		*p*	T3	
P	Control	value	HP	Control	value	HP	Control	value	HP	
4.04	16.45±4.02	0.198	19.1±6.88	24.45±11.38	**0.028**	19.7±9.08	29.81±13.26	**0.001**	17.62±5.73	2
.36	5.56±1.28	0.598	6.44±1.67	8.44±3.02	**0.002**	8.27±3.36	10.78±4.87	**0.02**	7.2±2.13	8
±164	568.12±13	0.09	745.1±203.	880.92±278	**0.0**	848.65±281	1144.52±43	**0.0**	747.63±243	8

	8.8	1	55		**27**	.37	4.55	**02**	.63	2
±130	198.81±10	0.57	296.56±99.	382.05±212	**0.0**	328.13±124	439.17±203	**0.0**	315.76±92.	3
	4.52	6	78	.57	**39**	.12	.27	**11**	02	8
±52.	148.39±40.	0.10	240.52±84.	246.74±96.	0.78	293.94±132	347.39±192	0.19	246.87±82.	2
	94	8	91	69	3	.7	.49	4	95	9
2±58	973.78±50	0.14	1557.51±54	1733.44±72	0.26	1584.39±55	1630.44±58	0.74	1331.33±31	1
	8.99	2	0.44	0.41	7	9.25	5.18	7	1.54	6

* Continuous data are expressed as mean ± standard deviation (x±s). Normally distributed data were analyzed by independent samples t-test, and non-normal data by Mann-Whitney U test (TNF-α at T2, CRP at T1). Repeated-measure data were analyzed by two-way mixed-design ANOVA, with Greenhouse-Geisser correction applied for violated sphericity. P<0.05 was considered statistically significant.

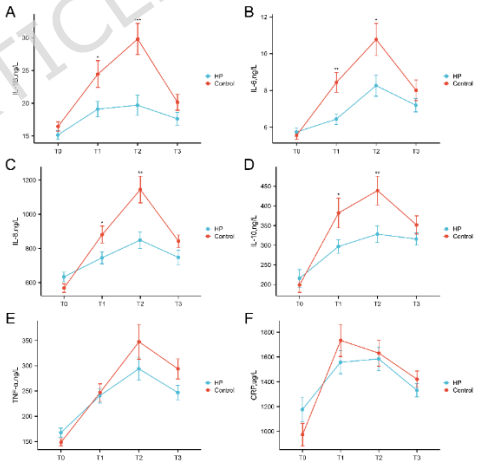

Figure 1. Inflammatory factors IL-1β (ng/L) (A), IL-6 (ng/L) (B), IL-8 (ng/L) (C), IL-10(ng/L) (D), TNF-α (ng/L) (E) and CRP (μg/L) (F) trended with time. □*, p<0.05□**, p<0.01□***, p<0.001□

Comparison of patient-related indicators in intensive care unit

There were no statistically significant differences between the two groups in terms of post-operative ICU intubation time, urine output on the first day after surgery, chest cannula drainage volume on the first day after surgery, and ICU stay duration ($p > 0.05$). However, the total amount of vasoactive-inotropic score on the first day after surgery in the HP group was significantly lower than that in the control group ($p < 0.05$) (Table 3).

Table 3. The results of intensive care-related indicators of the two groups

Parameters	HP（n=34）	Control（n=31）	*p*-value
ICU mechanical ventilation time （h）	11.37±5.6	10.69±8.52	0.704
urine output on the first day after surgery（ml）	2136.29±820.07	2109.94±644.49	0.887
chest cannula drainage volume on the first day after surgery（ml）	549.65±263.15	492.13±199.37	0.328
24-hour cumulative VIS	110.94±44.04	161.06±115.86	**0.029**
ICU stay duration（h）	51.92±24.68	47.38±24.19	0.457

* Continuous data are expressed as mean ± standard deviation (x±s). Normally distributed data were analyzed by independent samples t-test, and non-normal data by Mann-Whitney U test. P<0.05 was considered statistically significant.

VIS is calculated using the following formula: (dopamine + dobutamine) + (milrinone×10)

+ (epinephrine×100) + (norepinephrine×100).

Comparison of Clinical Laboratory Indicators in Patients

There were no statistically significant differences in preoperative blood routine (including white blood cell count, neutrophil count, hemoglobin, platelet count), biochemistry (albumin, alanine aminotransferase, bilirubin, urea, creatinine), and coagulation-related indicators (APTT, PT) between the two groups of patients. In the comparison of postoperative indicators, the HP group showed lower white blood cell count, neutrophil count, ALT, urea, and creatinine on the first postoperative day compared to the control group, with statistically significant differences ($p<0.05$). However, there were no statistically significant differences between the two groups in terms of hemoglobin, platelet count, and bilirubin on the first postoperative day (Table 4).

Table 4. Clinical laboratory index results of the two groups

Parameters	HP (n=34)	Control (n=31)	*p*-value
Preoperative			
White blood cell count (10^9/L)	5.90±1.79	5.74±1.48	0.677
Neutrophil count (10^9/L)	3.85±1.53	3.68±1.29	0.645
Hemoglobin (g/L)	126.85±17.69	122±16.37	0.257
Platelet count (10^9/L)	180.12±67.02	188.39±69.05	0.626
Albumin (g/L)	39.26±6.89	39.17±3.87	0.947

ALT (U/L)	26.56±21.52	27.32±17.69	0.877
Bilirubin (μmol/L)	16.64±7.12	18.13±8.84	0.454
Urea (mmol/L)	7.45±2.15	6.6±2.47	0.148
Creatinine (μmol/L)	66.56±17.45	64.93±19.24	0.721
Uric acid (μmol/L)	320.21±93.88	361.19±123.24	0.134
APTT (s)	36.7±15.4	33.72±6.7	0.331
PT (s)	15.79±14.01	12.83±1.74	0.256
First postoperative day			
White blood cell count (10^9/L)	10.04±2.53	11.69±3.60	**0.035**
Neutrophil count (10^9/L)	9.13±2.25	10.60±3.34	**0.040**
Hemoglobin (g/L)	97.09±14.42	96.9±10.99	0.954
Platelet count (10^9/L)	105.59±48.42	129.87±66.92	0.097
ALT (U/L)	31.68±16.89	43.10±20.10	**0.016**
Bilirubin (μmol/L)	23.63±14.77	25.16±15.23	0.683
Urea (mmol/L)	7.82±1.84	9.15±2.16	**0.010**
Creatinine (μmol/L)	74.88±14.70	86.62±25.66	**0.02**

Continuous data are expressed as mean ± standard deviation (x±s). Normally distributed data were analyzed by independent samples t-test, and non-normal data by Mann-Whitney U test. $P<0.05$ was considered statistically significant.

Discussion:

The advent of cardiopulmonary bypass (CPB) has revolutionized cardiac surgery,

significantly improving patient survival and procedural success rates. However, the implementation of CPB is accompanied by numerous physiological changes, particularly the activation of systemic inflammatory responses, which may lead to an increase in postoperative complications and affect patient recovery[18-19].The pathophysiological mechanisms of the inflammatory response generated by CPB are composed of various factors, generally believed to be divided into two main phases. The initial phase involves blood contact with non-endothelial surfaces, causing cell damage and leading to the release of bioactive substances, such as cytokines and complement, which activate endogenous and exogenous coagulation pathways, thereby activating the fibrinolytic system and triggering an inflammatory response that consumes blood components. The secondary phase is mainly caused by surgical methods leading to fluctuations in body temperature, the infusion of blood products, blood dilution, and destruction, resulting in ischemia-reperfusion injury and endotoxemia[20-21]. This inflammatory response may lead to postoperative complications, including myocardial dysfunction, respiratory failure, renal and neurological disorders, hemorrhagic diseases, and liver function changes, ultimately resulting in multiorgan failure[2].

In the inflammatory cascade, cytokines serve as intercellular messengers produced by tissues in response to different stimuli and are often used as primary markers to assess the severity of inflammatory responses. The role of cytokines in the pathophysiology of CPB-related inflammatory responses has been extensively studied [22]. The cytokine that plays a primary role in the inflammatory response

during CPB is interleukin-1β (IL-1β), the levels of which typically increase after CPB. IL-1β is responsible for inducing the synthesis of interleukin-6 (IL-6) and works synergistically with tumor necrosis factor-α (TNF-α) to ensure the continuity of the inflammatory process. Another widely studied interleukin is IL-6, whose levels increase by 2 to 4 hours after the start of surgery. The intensity of the IL-6 response is related to the duration of the surgical procedure, making this factor extremely important in the inflammatory process [23]. Interleukin-8 (IL-8) is an effective chemokine that participates in the recruitment of neutrophils and leukocytes to the site of infection. It may exist in any tissue, and its effects may occur during infections, ischemia, trauma, and other disruptions of homeostasis [24]. Therefore, researching strategies to reduce inflammatory factors during CPB is particularly important.

This study aims to evaluate the application effects of the HA380 blood perfusion device in cardiac surgery assisted by extracorporeal circulation, particularly its impact on inflammatory responses. We randomly divided patients into two groups, with the experimental group using the HA380 blood perfusion device on the basis of conventional CPB, while the control group received only conventional CPB support. The significant decrease in IL-1β, IL-6, IL-8, and IL-10 levels in the HP group at time points T1 to T2 confirmed the adsorption efficacy of the high-capacity resin (HA380) for medium molecular weight inflammatory mediators [12]. The lower postoperative leukocyte and neutrophil counts in the experimental group compared to the control group further support this finding. In terms of

cardiac functionimprovement, the HP group showed a 31.8% reduction in the vasoactive-inotropic score (VIS) (110.94±44.04 vs 161.06±115.86, P=0.029), suggesting more stable hemodynamics. This may be due to the HA380's clearance of myocardial depressant factors (such as IL-6) and vasodilatory mediators, consistent with observations in sepsis research where blood perfusion reduced catecholamine requirements [25]. Improvements in postoperative creatinine (74.88 ± 14.70 vs 86.62±25.66 μmol/L, P=0.02), urea (7.82±1.84 vs 9.15±2.16 mmol/L, P=0.010), and ALT (31.68±16.89 vs 43.10±20.10 U/L, P=0.016) in the HP group may relate to the HA380 blood perfusion reducing free hemoglobin [26] and effectively removing pro-inflammatory cytokines and bilirubin/bile acid from hepatocytes[27]. Despite improvements in inflammatory markers, the duration of mechanical ventilation in the ICU (HP group 11.37h vs control group 10.69h, P=0.704) and ICU stay (51.92h vs 47.38h, P=0.457) were not shortened, indicating that a single anti-inflammatory intervention has limited contributions to complex the complexity of postoperative recovery.

No HA380-related adverse events were observed during the study. Postoperative bleeding-related indicators (chest tube drainage volume, platelet count) and coagulation function (APTT, PT) showed no significant differences between groups (P>0.05, Tables 3 and 4), indicating that HA380 did not increase bleeding or coagulation risks. Additionally, no allergic reactions, hemolysis, or flow obstruction associated with the adsorbent were reported. These results suggest the short-term safety of HA380 in CPB-assisted cardiac surgery, though long-term

safety requires further verification in large-scale studies.

Multiple studies have similarly indicated that the combined use of HP in CPB can reduce postoperative inflammatory markers in patients and improve their prognosis[28-29]. In the study by He et al.[30], 60 patients with rheumatic heart valve disease undergoing surgical valve replacement were included to assess the efficacy of the HA380 perfusion tube in alleviating CPB-related inflammatory responses. The results showed that compared to the control group, patients receiving HA380 had significantly lower IL-6 levels ($p < 0.001$), required fewer vasoactive drugs ($p = 0.006$), had shorter ventilation times ($p = 0.007$), and shorter ICU stays ($p < 0.001$). They concluded that HA380 can effectively reduce systemic inflammatory response syndrome (SIRS) and promote postoperative recovery in adult patients undergoing CPB. The findings on HA380's role in reducing inflammatory factors align with this study, but the current study monitored inflammatory markers for up to 48 hours, and their research did not analyze IL-1β and CRP. This study did not observe differences in ICU stay or ventilation time between the two groups, which may be due to the study population's heterogeneity (the current study included more complex surgeries) or the limitations of a single anti-inflammatory treatment in addressing multiple factors. Wang J et al.[31] included a total of 117 patients with type A aortic dissection in their study, with 57 in the control group and 60 in the HA380 blood perfusion group. The results showed that the use of HA380 in CPB circuits could alleviate postoperative inflammatory responses in patients with type A dissection

and reduce major complications, and HA380 may be associated with a lower incidence of postoperative acute kidney injury (AKI). These findings support the conclusions of this study.

Several limitations of this study should be acknowledged. First, the postoperative follow-up duration was limited to 48 hours, which prevents the assessment of the long-term outcomes of HA380 hemoperfusion in patients, such as 30-day mortality, readmission rate, and chronic organ function injury. Second, this study adopted a single-center design, which was limited by the surgical procedures and patient population characteristics of a single medical center, potentially restricting the generalizability of the results. Third , a limitation of this study is the lack of cost-benefit analysis. Future research will calculate equipment, consumable, and complication treatment costs to evaluate its cost-effectiveness in specific populations. Finally, as a preliminary exploratory randomized controlled trial, the relatively small sample size not only reduced the power to detect subtle differences in clinical outcomes but also precluded subgroup analyses based on surgical types. Future studies should adopt a multi-center, large-sample design and extend the follow-up period to verify the long-term efficacy and safety of HA380 hemoperfusion in CPB-assisted cardiac surgery.

In conclusion, this study indicates that the combined use of the HA380 blood perfusion device during extracorporeal circulation in cardiac surgery can significantly reduce postoperative inflammatory responses and may improve

clinical outcomes for patients during the perioperative period. Despite some limitations, these findings provide new clinical evidence for optimizing extracorporeal circulation management, suggesting that the HA380 blood perfusion device has broad application potential as a potential intervention in cardiac surgery. Future research should continue to explore its application effects and mechanisms in different patient populations to further improve outcomes for cardiac surgery patients.

Conclusions

The combined use of HA380 in CPB can reduce the inflammatory response of patients after surgery, and has a protective effect on cardiac function, liver and kidney function in postoperative patients, and has certain application prospects.

Author contributions

Longlong Li were involved in various aspects of the work, including conception, study design, execution, data acquisition, analysis, interpretation, manuscript drafting, revising, and reviewing. Jing Li, Suli Wang and Chunyu Chen were involved in execution and data acquisition. Li Hui were involved in the detection of all inflammatory factors in the experiment. Biao Zhang were involved in including conception, study design, analysis, interpretation, revising, and reviewing. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study protocol was approved by ethics committee of Fuyang Hospital Affiliated to Anhui Medical University (Number of IRB approval: KY2022140, Date of IRB approval: Aug 26th, 2022). All enrolled patients provided written informed consent to participate in this study. The patients/participants also gave written informed consent to publish identifying details such as their age, gender, and illness. The study comply with the guidelines for human studies and the research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Competing interests

The authors declare no competing interests.

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