

# Cardiopulmonary Bypass Management Using High-volume Continuous Hemofiltration in Patients with Comorbidities

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## Abstract

**Objectives:** To evaluate the effectiveness of hemofiltration during longstanding cardiopulmonary bypass (CPB) in patients with comorbidities.

**Materials and Methods:** Prospective randomized clinical trial included 38 male patients with ex-pecting duration of CPB >120 minutes due to comorbid pathology. Standard anesthesia protocol was carried out. Study includes two groups: first group (controlled, n=20) included standard CPB, 2<sup>nd</sup> group (analyzed, n=18) included perfusion with high-volume hemofiltration using polyionic buffered solution 80 mL/min during all CPB time. Hemofiltration has been also supported by ultra-filtration for hydro-balance maintenance at the level of 8-10 mL/kg. Laboratory tests, respiratory and renal complications, drainage blood loss,

hemostasis disorders, requiring hemostatics and blood transfusion, intensive care unit (ICU) and in-hospital were evaluated. Nonparametric methods-Mann-Whitney U test for independent samples and Wilcoxon signed-rank test for dependent samples were used.

**Results:** IL-6 level in 2<sup>nd</sup> group was significantly lower ( $p=0.0017$ ) and did not exceed 7.4 pg/mL. C-RP, metalloproteinase and procalcitonin levels were lower too, but not statistically significant. Lactate level in analyzed group was in reference range, while in control group after perfusion it in-creased to  $8.3\pm 4.2$  mmol/L. Renal dysfunction, requiring dialysis, was diagnosed in six (20,7%) patients from controlled group vs two patients (6.1%) from analyzed group. Respiratory insufficiency



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developed in three patients (10.3%) only in controlled group. In-hospital stay was significantly lower in analyzed group and so was the ICU length. Polyorganic insufficiency syndrome occurred in three patients (10.3%) from the controlled group.

**Conclusion:** High-volume hemofiltration using polyionic

buffered solution for longstanding CPB reduces damaging effects of traditional roller pump and reduces risks of organic dysfunction in postoperative period.

**Keywords:** Cardiopulmonary bypass, hemofiltration, systemic inflammatory response

## Introduction

Despite the development of new technologies and cardiopulmonary bypass (CPB) techniques, its negative effects still remain significant<sup>(1)</sup>. Systemic inflammatory response makes serious contribution to the pathophysiology and it depends on surgical trauma, blood and artificial surfaces interactions during extracorporeal circulation, ischemia/reperfusion, endotoxemia and etc<sup>(2)</sup>. At the same time, number of patients with organic dysfunction due to comorbidities is increasing every year. That is why preventing of inflammatory response during CPB can lower postoperative complications. For example, invention of centrifugal pumps influenced a lot CPB management in cardiac surgery. Recent studies are showing advantages of using centrifugal pumps over roller pumps<sup>(3)</sup>. But the conclusions are still controversial, since these studies included only operations with perfusion duration less than 90 minutes. The magnitude of complement activation is proportional to the duration of CPB<sup>(4)</sup>. There are several ways to reduce the inflammatory response, such as ultrafiltration, plasmfiltration, hemosorption (with polymethyl methacrylate). All of them have proven their effectiveness, but still there is a lack of data in using these methods. Also Rabie Soliman et al. in his research discovered that hemofiltration can cause lactate level in serum<sup>(5)</sup>. Currently, there are no guidelines to the CPB management during surgeries with different perfusion time. Correlation between mediators of inflammatory response level during and after CPB and the incidence of organic insufficiency is not evaluated in any studies.

## Materials and Methods

Prospective randomized clinical trial with 38 male patients included with CPB duration over 120 minutes during concomitant heart surgery. Inclusion criteria: patients with coronary artery disease and/or heart valve disease with the history of atrial fibrillation and comorbidities (chronic pyelonephritis, chronic obstructive pulmonary disease, diabetes mellitus), requiring coronary artery bypass grafting (CABG) surgery and/or valve surgery and “maze” procedure. Patients who underwent urgent surgery were excluded from the trial. The study was approved by the local ethic committee; informed consent was signed by all patients. Standard anesthesia protocol was carried out. Study includes two groups: First group (controlled, n=20) included standard CPB, 2<sup>nd</sup> group (analyzed, n=18) included perfusion with high-volume hemofiltration using polyionic buffered solution 80 mL/min during all CPB time. Hemofiltration has been also supported by ultrafiltration for hydro-balance maintenance at the level of 8-10 mL/kg. For the study we are using Maquet hemoconcentrators with priming volume 65 mL and membrane surface 0.7 m<sup>2</sup> and as a substitute solution MultiBic bicarbonate buffer solution with potassium concentration 4 mmol/L was used. Hemofiltration ends after weaning from CPB.

## Statistical Analysis

Main clinical data, such as age, weight, CPB duration and others were comparable in both groups (Table 1). Envelope randomization was carried out. Laboratory tests (WBC, Hb, Plt, IL-6, IL-10, lactate, procalcitonin,

C-RP) were evaluated, as well as respiratory and renal complications, drainage blood loss, hemostasis disorders, requiring hemostatics and blood transfusion, ICU and in-hospital.

All operations included in this study in both groups were concomitant, such as coronary artery bypass surgery with the valve repair or replacement and atrial fibrillation surgery, and all of them required long CPB and cross-clamping time (Table 2). Data in both groups was comparable. All results presented as mean value  $\pm$  standard deviation ( $\sigma$ ). To evaluate the diversity significance between all parameters Student's t-test was used. P-level  $<0.05$  was considered as significant.

## Results

IL-6 level was significantly lower in analyzed group ( $p=0.0017$ ) and did not exceed 7.4 picogram per mL, while

IL-10 level was comparable in both groups (Table 3). Also procalcitonin, C-RP levels were lower, but not statistically relevant. Lactate level remained normal, while in control group it has been increased to  $8.3\pm 4.2$  mmol/L after perfusion. Transfusion rate were the same in both groups, but patients from analyzed group didn't require any hemostatic therapy. There was no need in inotropic and vasopressor medications in the analyzed group by the end of the first postoperative day, all patients were extubated in first postoperative hours. Renal dysfunction, requiring dialysis, was diagnosed in 6 (20.7%) patients from controlled group vs. two patients (6.1%) from analyzed group. Respiratory insufficiency developed in three patients (10.3%) only in controlled group. In-hospital stay was significantly lower in analyzed group and so was the ICU length. Polyorganic insufficiency syndrome occurred in three patients (10.3%) from the controlled group.

## Discussion

The use of CPB in major cardiac surgery initiates an acute inflammatory response that is complex, unpredictable and can cause significant morbidity and mortality, especially during long-standing procedures. Pathophysiology of CPB negative effects can be summarized as generalized inflammatory response,

**Table 1.** Clinical data

	Control group (n=20)	HVH group (n=18)
Age, years	69.3 $\pm$ 11.3	72.1 $\pm$ 12.7
Weight, kg	74.9 $\pm$ 9.4	71.9 $\pm$ 12.6
HF (NYHA class), n (%):		
II	11 (55)	10 (55.6)
III	9 (45)	8 (44.4)
Comorbidities:		
Renal failure (RIFLE), n (%)	6 (30)	5 (27.8)
R	2 (10)	2 (11.1)
I	3 (15)	2 (11.1)
F	1 (5)	1 (5.55)
Respiratory failure, n (%) (A.G.Dembo chronic respiratory insufficiency classification <sup>(6)</sup> )	8 (40)	7 (38.9)
I	2 (10)	1 (5.6)
II	4 (20)	4 (22.2)
III	2 (10)	2 (11.1)
Diabetes mellitus, n (%)*	8 (40)	7 (38.9)
EuroSCORE 2, %	4.3	3.7

HVH: High-volume hospital, HF: Heart failure, NYHA: New York Heart Association, n: Number of the patients

**Table 2.** Operative data

	Control group (n=20)	HVH group (n=18)
CABG + MV replacement + RFA, n (%)	6 (30)	5 (27.8)
CABG + MV repair + RFA n (%)	7 (35)	9 (50)
CABG + MV replacement + LV aneurysm repair + RFA n (%)	1 (5)	1 (5.5)
AV and MV replacement + RFA n (%)	4 (20)	1 (5.5)
AV replacement + CABG + RFA n (%)	2 (10)	2 (11.1)
CPB duration, min	182 $\pm$ 44	176 $\pm$ 52
Cross-clamp time, min	145 $\pm$ 27	142 $\pm$ 39
Surgery duration, min	330 $\pm$ 56	340 $\pm$ 60
Intraoperative blood loss, mL	725 $\pm$ 55	730 $\pm$ 65

HVH: High-volume hospital, CABG: Coronary artery bypass grafting, MV: Mitral Valve, RFA: Radiofrequency ablation, LV: Left ventricular, AV: Atrioventricular, CPB: Cardiopulmonary bypass, n: Number of the patients

ischemia-reperfusion injury, endotoxemia, and operative trauma. Also the longer cardiopulmonary bypass was, the more expressed inflammatory response was<sup>(7)</sup>. At the same time, number of patients with organic dysfunction is increasing every year, as well as CPB duration during complex concomitant surgery. That is why techniques to minimize the negative effects of inflammatory response during CPB, allowing to reduce or remove alterative factors during perfusion, remain relevant<sup>(8)</sup>.

In our study main inflammatory response markers, that are always associated with long-standing CPB, were significantly lower, such as IL-6, IL-10 and others. Moreover, there were lower complication rate, less ICU and in-hospital stay, lower blood transfusion rate and there was no need in vasopressor and cardiotoxic therapy in hemofiltration group. Most of the known approaches to reduce the CPB alterative effect are using minimally invasive extracorporeal circulation,

improving of the circuit biocompatibility, using of centrifugal pumps<sup>(9-11)</sup>. But these techniques have their disadvantages too: absence of venous reservoir can increase the risk of air embolism. Also membranes in new oxygenators have better biocompatibility, but prevent blood saturation with isoflurane, so it is impossible to use inhalational anesthetics and their better protective effect on myocardium, which limits the use of this technology. High-volume continuous hemofiltration with standard roller pump CPB, that we offer, as we assume, doesn't have these disadvantages. Modified techniques of blood ultrafiltration<sup>(12,13)</sup>, hemosorption and apheresis<sup>(14,15)</sup> removes small amount of liquid, that don't let us to accomplish clinical and laboratory evaluation of inflammatory mediators through the semipermeable membrane of hemofilter, leading to indifferent elimination of both inflammatory and antipyretic mediators. And the cost price of these procedures often exceed operations'

**Table 3.** Main laboratory data in early postoperative period

Parameter	Before CPB		24 h after surgery		p
	HVH group, n=18	Control group, n=20	HVH group n=18	Control group, n=20	
Oxygenation index	342±64	376±88	406±96	269±55	0.01
Creatinine, µmol/L	107±30	89±28	88±36	288±55	0.01
Carbamide, mmol/L	4.9±2.1	6.08±3.3	5.92±2.4	15.7±5.1	0.01
Diuresis, mL/h	135±55	150±70	85±15	35±15	0.01
AST, un/L	37±9	24±15	66±28	188±32	0.01
ALT, un/L	62±22	49±31	71±21	106±18	0.02
Lactate, mmol/L	0.8±0.4	0.8±0.5	3.0±2.1	8.3±4.2	0.015
IL-6, pg/mL	7.4±3.1	6.2±3.9	5.9±1.5	19.7±3.9	<0.01
IL-10, pg/mL	8.2±2.9	7.4±4.1	11.4±2.9	12.6±3.3	0.27
Procalcitonin, ng/mL	1.4±0.6	1.1±0.7	1.25±0.5	2.1±0.3	0.09
CR-P, mg/L	9.8±3.3	7.9±5.1	15.6±6.6	22.9±8.1	0.045
WBC, x10 <sup>9</sup>	7.2±4.3	7.89±2.9	13.1±6.4	17.9±4.2	0.06
Drainage blood loss, mL	-	-	270±50	310±70	0.07
Ventilation time, min	-	-	205±70	530±120	0.01
Dopamine, µg/kg/min	2.9±0.5	2.2±0.5	0	3.3±0.5	-
Noradrenaline, µg/kg/min	0.03±0.01	0.03±0.01	0	0.05±0.05	-
ICU stay, hours	-	-	18.9±6.1	41.3±18.3	0.019
In-hospital stay, days	-	-	11.9±3.3	19.9±4.5	0.035

CPB: Cardiopulmonary bypass, HVH: High-volume hospital, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, C-RP: C-Reactive protein test, WBC: White blood cell, ICU: Intensive care unit, n: Number of the patients

cost. Moreover, roller pump, used in these techniques initiates inflammatory response by itself and damages blood cells. In our study usage of polyionic buffer solution with hydro-balance maintenance at level 8-10 mL/kg during long-standing CPB lowers these disadvantages. This study shows promising results in patients undergoing concomitant surgery with long cross-clamping time, but final results can be interpreted only after the full trial will be held.

### Ethics

**Ethics Committee Approval:** This study was approved by A.V.Vishnevsky National Medical Research Center of Surgery local committee (approval no:23).

**Informed Consent:** All patients have signed informed consent.

**Peer-review:** Externally and internally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: V.P., A.R., E.M., Concept: G.P., Design: G.P., Data Collection or Processing: V.C., E.M., Analysis or Interpretation: V.P., G.P., A.R., E.M., Literature Search: V.C., G.E., Writing: G.E.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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