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Is Zero-Balance Ultrafiltration an Effective Clinical Method for SIRS Prevention During Extracorporeal Circulation in Adults Heart Diseases Correction?

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ABSTRACT

Background: Ultrafiltration, which is currently considered as a standard method to remove the excess water administered during cardiopulmonary bypass (CPB), aims to minimize the adverse effects of hemodilution, such as tissue edema and blood transfusion. Three ultrafiltration techniques can be used before, during and after CPB procedure, including conventional ultrafiltration (CUF), zero-balance ultrafiltration (Z-BUF), and modified ultrafiltration (MUF) at the end of CPB.

The aim of study: The present research attempts to revise the efficiency of Z-BUF ultrafiltration method, laboratory results, and clinical impacts.

Material and methods: 94 adults (54 men and 40 women) with acquired heart diseases undergoing a single cardiac surgical procedure in condition of cardiopulmonary bypass (clamp aortic 89, 9± 38, 8 min. and pump 135,14 ± 45,17 min.) were divided into 3 groups.

1st group (no ultrafiltration) - 34 patients with classic cardiac surgery, 2nd with the use of zero-balance ultrafiltration (ZBUF) group - 37 patients with classic cardiac surgery, and 3rd group ZBUF with mini invasive cardiac surgery - 23 patients.

ZBUF was performed by removing in the ratio of 3 l/m^2 ultra filtrate using a hemoconcentrator with priming volume 133 ml. For myocardial protection, "Bretschneider" solution 1500 ml for the first doze and 1000 ml for the second doze in case of necessity was used, or blood cardioplegia with St. Thomas II (15 mL/kg) was also performed. Patient blood samples were taken before CPB (T1), immediately following CPB (T2), and 12 hours following the procedure (T3). There were no significant differences in diagnosis, age, sex, clinical status (Euroscore 1st-1,313, 2nd-1,891, 1,214 in a 3rd).

Results: Laboratory data demonstrate the presence of SIRS in all groups (high levels of leucocytes or reticulocytes, the presence of C reactive protein positive in 10, 5% cases of 1st gr., 10, 2% cases of 2nd gr. and 10,9% in 3rd gr.). The length of mechanical ventilation was statistically lower in 3rd ZBUF group, and in 1st group than in 2nd ZBUF group: 7,21 ± 2,1 hour - 3rd gr., 9,40 ± 2,7 hour -1st, and 19,82 ±3,8 hour -2nd. The length of stay in ICU was statistically higher in 2nd ZBUF group (3,62 ± 1,5 days) versus (2,62 ± 1,1 days) control 1st group P = 0,03, but approximately equal with 3rd gr. (3,04±0,76 days).

Conclusions: This study demonstrated that ZBUF ultrafiltration is an efficient method that can be used during CPB in the adults and helps to remove significant amounts of body water that seriously affects the clinical results. The use of ultrafiltration in our study, unfortunately, could not prevent organ dysfunction during the postoperative period and, however we think that it should have been used for volemic control in patients who underwent extracorporeal circulation. These results suggest with certainly, that Z-BUF improves the pulmonary function even in case of severe lung injury and may be an effective tool in attenuating the CPB derived inflammatory process. We think that in cases of SIRS signs before intervention and all complicated cases it is necessary MUF application that will improve the clinical results.

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Introduction

Surgical treatment of majority acqiured heart diseases usually uses cardiopulmonary bypass and normovolemic hemodilution. The lowest level of hematocrit tolerable by patients without any danger for them varies according to the opinions of many authors from 20 to 25% depending on the type of pathology and patients personal particularities [1, 2].

These limits of hematocrit ensure the secure transport of oxigen and prevent hemolisis. But the decrease of the number of red blood cells induces erytrocyte desagregation and reduce blood flow in capillars. As a result the decreased resistence before and post capillars facilitates increase of total body weight [3,4].

High incidence of the increase of capillar permeability after pump in adult patients, especially the old ones is at least partially result of postpump syndrome, but more commonly by postcardiotom syndrome. The majority of clinics in the world at present use normothermia and mild hemodilution.

Low body patient weight, moderate hipotermia and long pump time increase the total water body weight. The bypass technique optimization (centrifugal pump, pulsatile flow), priming minimization, diuretics use, hemodialysis after the operation and hemofiltration during the operation are the important strategies for “capillary leakage” phenomenon prevention.

Ultrafiltration is a process of filtration of semipermeable membrane in which water and particles with molecular weight lower than the diameter of the membrane holes go through. One of facultative conditions is the restituation of the ultrafiltrated volume by the same water input in the venous reservoir of the pump. It is zero balanced ultrafiltration. Conventional (CUF) and zero-balanced ultrafiltration (ZBUF) are commonly perform during cardiopulmonary bypass. Modified ultrafiltration is used just after the end of the cardiopulmonary bypass. For the first time CUF was used in 1976 by Romagnoli A. and colleagues (coll.) for preventing low hematocrit caused by the aspiration in the extracorporeal circuit the significant amount of cristaloid cardioplegia and or/ cristaloid solution for the external heart cooling and described in detail by Darup J. and coll. 1979 [5,6].

ZBUF was as first introduced by Journois D. and col. in 1996, and principially is the same like conventional ultrafiltration (hemofilter and ultrafiltration during pump) [7].

The main characteristic of this method is that it can get rid of inflammatory mediators effectively but cannot concentrate blood at the end of pump. The third variant of ultrafiltration during the operations, the revolutionary method, proposed by Martin Elliott et coll. from “Great Ormond Street (GOS) Hospital for sick Children” London, UK, modified ultrafiltration (MUF) – (ultrafiltration after pump) gives the possibility to treat postperfuzional oedems during the acute postoperatory period at the beginning in children, and later in adults [8].

As successfully demonstrated Jarnois et coll.the combination of ZBUF and MUF effectively eliminate toxins and SIRS factors and at the same time concentrate the red blood [7].

Usually conventional ultrafiltration (CUF) is performed during rewarming. The favorable results of ultrafiltration are the storage of fibrinogen and other coagulating factors, with the increase of thrombocytes concentration, as a result the necessity of homolog blood transfusion during operation decreases.

The third variant is ultrafiltration in postsurgical period. This procedure is usually used for hypervolemia treatment in intensive care unit. By the improvement of the renal function both the cardiac and pulmonary functions are improved with the decrease of cardiac preload and pulmonary oedema.

The hemoconcentrator can be used in any place of extracorporeal circuit (ECC) circuit, replacing the usual shunt of oxigenator, but are thousand variants placement of it. The obligatory condition is the accurate air debubbling from ultrafiltration circuit to prevent microembolization. The inlet line of the hemoconcentrator can be placed as both in the arterial and venous lines (oxigenator tubings). But if it is placed in the venous line has a very big disadvantage because the air bubbles can block the membranes of oxigenator. So it is common practice to place the inlet line of the hemoconcentrator in the arterial tubing of the oxigenator and the outlet line in the venous tubing or in the venous reservoir of the extracorporeal circuit, the last variant being more preferable.

When the inlet line of the haemofilter is placed in the arterial tubing of ECC circuit, the flow is enough for the high ultrafiltration rate (high transmembrane pressure) and it is no necessary to connect the external vacuum to the ultrafiltrate port . In case the inlet line is placed in the venous tubing of ECC a roller pump is used. Using the external vacuum a more efficient rate of ultrafiltration can be assured. Conventional ultrafiltration (CUF) usually begins in the period of rewarming of CPB but ZBUF ultrafiltration most often starts at the beginning of pump. See: (Tab.1).

Table 1: Parameters of ZBUF

Study	Filter types	Start time of Z-BUF	Ultrafiltration volume
De Baar M [9]	Minntech	After CPB	40 mL/min/m²
Tallman RD [10]	Minntech	15min after CPB	3L/m²
Li Gang [11]	Terumo	After CPB	300-400ml/ min
Li Yu-mei [12]	Terumo	After aortic cross-clamp	50ml/kg
Zheng Min [13]	Terumo	After aortic cross-clamp	60ml/kg
Zhao Ju [14]	Gambro	No report	300ml

In the course of blood filtration the ultrafiltrate is eliminated through the membranes of hemoconcentrator.

This liquid come only from vascular flow of blood and must be recuperated from the patients interstitial space (we hope) thus decreasing the liquid overload provoked by the extracorporeal circulation. Unfortunately the ultrafiltration volume in majority of cases is the preponderant volume from the extracorporeal circuit not from the vascular volume of blood. In other words, there appears the danger of decreasing the security level of the volume in the venous reservoir, and it is common case for perfuzionist practice, because the maximum limitation of the volume for filling up the ECC takes place.

Hence, there arises the question, if in case of diminishing the level to the security limit in venous reservoir, it is necessary to add the liquid, reducing la zero one of the positive effects of ultrafiltration, persisting in such a way as the volume of liquid introduced in the reservoir of the ECC of CPB apparatus to be equal to the quantity of the evacuated ultrafiltrate (ZBUF) in the ratio recommended by the majority of authors (to 3 liters/m² of the body surface) [15].

Bruce Searles demonstrate that ZBUF (approx. 6 liters of ultrafiltrate) in pigs operated under pump 60 minutes increase cardiac recovery and pulmonary compliance. In the case then ultrafiltration line is clamped no positive signs of cardiac recovery and pulmonary function. In the case of recovery of the ultrafiltrate in ECC there are negative signs of cardiac function decrease.

Clinical effects are decrease of use blood products during pump, caused by normal hematocrit (25% and more), decrease of drainage loss, low time length of mechanical ventilation, low length time of stay in ICU and in hospital, also decrease of inflammatory agents of SIRS (there evident cause of favorable clinical effects). Unfortunately there are not investigated in trials with blind sleep lots ZBUF effects for prevent of neurocognitive deficit after cardiosurgical operations with CPB. Also it is not definitely clear SIRS effects on neurocognitive deficit.

At the end of pump patient is usually is hipervolemic that dictate the necessity of enforced diuresis and dialysis.

The aim of study is to investigate our clinical results after use of ZBUF during cardiac operations with pump on adults with acquired heart disease to prevent SIRS effects.

Subjects and Methods

Subjects

The study included 94 adult patients (54 male and 40 female) with acquired heart disease operated on heart under CPB (clamp aortic 89, 9± 38,8 min. and pump 135,14 ± 45,17 min.) and divided into 3 groups.

1st group (no ultrafiltration) - 34 patients with classic cardiac surgery, 2nd with the use of zero-balance ultrafiltration (ZBUF) group - 37 patients with classic cardiac surgery, and 3rd group ZBUF with miniinvasive cardiac surgery - 23 patients. All the patients were operated by one operating team (2 operating surgeons, 4 anestheziologists and 2 perfusionists). There were no significant differences in diagnosis, age, sex, clinical status (Euroscore 1st-1,313, 2nd-1,891, 1,214 in a 3rd). (see Table 2 & 3).

Table 2: Demografic and operation indicators

	I group without UF 34 pac.	II gr.with ZBUF- 37 pac.	III gr. with ZBUF mininvaziv operation technic 23 pac.
Age, years	63,1+-7,48 Max.86 Min.47	64+-10,12 Max.81 Min 31	58,8+-12,74 Max. 79 Min. 21
Sex male/female	18/16	22/15	14/9
Time of clamp aortic, minutes	63,6+-6,06	105,6+-8,5	101,9+-9,09
Time of pump, min	97,2+-7,6	147,8+-11,4	165+-12,9

Table 3: Diagnosis

Diagnosis	I gr.	II gr	III gr
Ischemic heart disease of 1 artery	4	1	
Ischemic heart disease of 2 arteries	6	3	
Ischemic heart disease of 3 arteries	7	1	
Ischemic heart disease of 4 arteries	3	1	
Rheumatic aortic valve disease	5	5	3
Aortic valve disease with tricuspid valve regurgitation	1	1	
Aortic valve disease with ischemic heart disease of 1 artery	1	1	
Aortic valve disease with ischemic heart disease of 2 arteries	2	2	
Aortic valve disease with ischemic heart disease of 3 arteries		1	
Aortic valve disease with ischemic heart disease of 4 arteries		1	
Aortic valve disease with sever mitral valve regurgitation		2	
Rheumatic mitral valve disease		5	7
Mitral valve disease with ischemic heart disease of 1 artery		1	
Mitral valve disease with tricuspid valve regurgitation		1	6
Mitral valve disease with tricuspid valve regurgitation and ischemic heart disease of 1 vessel		2	
Mitral valve disease with tricuspid valve regurgitation and ischemic heart disease of 2 vessels	1	1	
Mitral valve disease (Barlow)			1
Dilatation of ascendent aorta	1	5	2
Dilatation of ascendent aorta with ischemic heart disease of 2 vessels	1	2	
Mixom			1
Atrial septal defects			4
Total pacients	34	36	24

Surgical methods

A classic longitudinal incision was performed at the sternum median into 1 and second group: in 3rd group thoracotomy into 4th intercostal space 5cm incision were performed. In 1 and 2nd group ascending aorta and right atrium were isolated, and the aortic cannulae and venous cannulae were inserted, hence in 3rd group femoral cannulation were used. After standart heparinization (3mg per kg) respectively, to connect CPB circuit (standard for adults; composed by 3/8×1/2 inch tubing lines; total volume of priming 1000 mL). For the all groups a sodium chloride compound priming solution was used to pre-fill the circulation tubes and debubbling air. The adults membrane oxygenators ("AMG ",by firm "Eurosets") were used intraoperatively. After body temperature was cooled to 34,4+-0,6 C °C, the ascending aorta was clamped, after this antegrade perfusion for myocardial protection "Bretschneider" solution 1500 ml for the first doze, and 1000 ml for the second doze in case of necessity was used, or blood cardioplegia with St. Thomas II (15 mL/kg) were also performed. The aortic clamp time was 20-70 min. The CPB continued to operate after ascending aorta was declamped, for a duration of not less than 1/4 of the aortic blocking time. In table 4 are demonstrate all types of surgery perform in study. After surgery, patients were monitored and treated in the intensive care unit (ICU).

Table 4: Operations

Operations typ	I gr.	II gr.	III gr.
Aorto coronary bypass graft of 1 vessel (CABG 1)	6		
CABG 2	6	1	
CABG 3	8		
CABG 4	3	1	
Ascendent aorta replacement (Wheat operation)	1	4	1
Ascendent aorta replacement (Wheat) with CABG 2		1	
Aortic valve replacement	7	4	8
Aortic valve replacement (AVR) with mitral valve replacement		2	
AVR with plastie of mitral valve		1	
Mitral valve replacement (MVR) with plastie of tricuspid valve		1	
AVR with CABG 1	1	3	
AVR with CABG 2	1	5	
AVR with CABG 3		1	
AVR with CABG 4		1	
MVR		5	4
Plastie of mitral valve with ringe		1	3
MVR with plastie of tricuspid valve with ring		1	4
MVR cu plastie of tricuspid valve with ring and CABG 1		2	
MVR cu plastie of tricuspid valve with ring and CABG 2		1	
MVR with CABG 3		2	
Plastie of tricuspid valvei and plastie of ASD	1		
ASD plastie			3
Mixom excizion			1
Total pacients	34	36	24

ZBUF method

The inlet line of the hemoconcentrator with priming volume 133 ml was placed in the arterial tubing of the oxygenator (shunt) and the outlet line in the venous tubing, or in the venous reservoir of the extracorporeal circuit and ZBUF was performed in ratio 3 litres/ per m2 (of patient Body Surface Area(BSA)) ultrafiltrate at the beginning of pump (see picture 1. During surgery, blood pressure, electrocardiogram and blood oxygen saturation of patients were closely monitored. If necessary, vasoactive agents were used to reduce the adverse effect of ZBUF on hemodynamics. If systolic blood pressure dropped to <60 mmHg, 4-10 µg norepinephrine was immediately injected iv to elevate blood pressure. If no reaction on blood pressure was achieved after norepinephrine injection, the ZBUF was immediately interrupted.

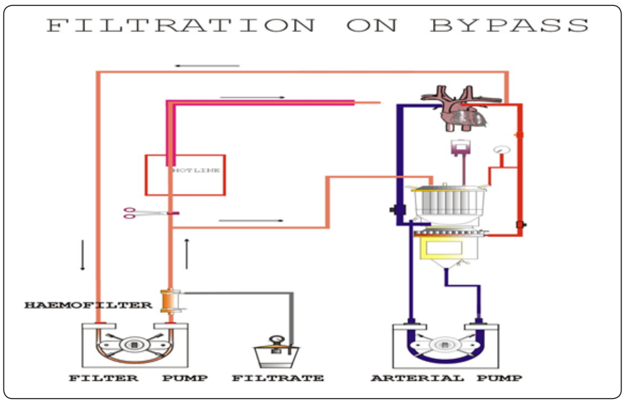

Figure 1: ZBUF

CPB management

The surgeries were performed using CPB machine "Stochert S5" ("Sorin Group"). During CPB operation, the exogenous liquid input was reduced, and the conditions maintained as follows: colloid osmotic pressure >275 mosm/l, body temperature 32-34°C, average blood pressure >40 mmHg, CPB flow 120-150 mL/kg. When the average blood pressure dropped to <40 mmHg, 4-10 μg norepinephrine was immediately iv injected to elevate blood pressure. When BE achieve ratio -4-6 mmol/l, 20-30 mL of sodium chloride compound solution was injected in ECC.

Blood samples

Patient blood samples were taken before CPB (T1), immediately following CPB (T2), 12 hours following the procedure (T3) and every day for leicocites and protein C reactive (CRP). There were no significant differences in diagnosis, age, sex, clinical status (Euroscore 1st-1,313, 2nd-1,891, 1,214 in a 3rd).

Results

Clinical (tahipnoe 20 and more respirations per minute) and laboratory data presents signs of SIRS in each group of study (increase rate of leicocytes and presence of reticulocites and PCR pozitive in 10, 5% cases in 1 gr., 10,2% cases in 2 gr., and 10,9% in 3 gr.). (seeTab. 5).

Table 5: Rezults

SIRS signs, tahipnoe laboratory data	I gr.	II gr	III gr.
Leicocytozis, % din cazuri	45.7	62	40,9
CRP % of patients	10,5	10,2	10,9
Tahipnoe in ICU % of patients	12,5	24,7	11
Time of mechanical ventilation,days	9,407 ±2,7	19,82±3,8	7,21 ±2,1
ICU stay time, days	2,62+- 1,1	3,62± 1,5 (P=0,03)	3,04+- 0,76

The length of mechanical ventilation is statistic lower in 3rd and in 2nd ZBUF groups then in 1st group (7,21 ±2,1 ore (3gr.), 19,82±3,8 ore(2nd) and 9,40±2,7 ore (1st.).

The length of stay in ICU was statistically higher in 2nd ZBUF group (3,62 ± 1,5 days) versus (2,62 ± 1,1 days) control 1st group P = 0,03, but approximately equal with 3rd gr. (3,04±0,76 days).

Conclusions

This study demonstrated that ZBUF ultrafiltration is an efficient method that can be used during CPB in the adults and helps to remove significant amounts of body water that seriously affects the clinical results. The use of ultrafiltration in our study, unfortunately, could not prevent organ dysfunction during the postoperative period and, however we think that it should have been used for volemic control in patients who underwent extracorporeal circulation. These results suggest with certainly, that Z-BUF improves the pulmonary function even in case of severe lung injury and may be an effective tool in attenuating the CPB derived inflammatory process. We think that in cases of SIRS signs before intervention and all complicated cases it is necessary MUF application that will improve the clinical results.

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