Iran Red Crescent Med J. 2018 May; 20(5):e66187. doi: 10.5812/ircmj.66187.

Published online 2018 September 10. **Research Article**

Modified Ultrafiltration in Coronary Artery Bypass Grafting: A Randomized, Double-Blinded, Controlled Clinical Trial

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Received 2018 January 12; **Revised** 2018 March 19; **Accepted** 2018 July 17.

Abstract

Background: Modified Ultrafiltration (MUF) has been used in Cardiopulmonary Bypass (CPB) operations to prevent hemodilution and remove pro-inflammatory cytokines. It has been studied in pediatric operation settings. However, evidence exists regarding its application in adults' Coronary Artery Bypass Grafting (CABG) operation.

Objectives: The present study investigated MUF and its effects on inflammatory cytokine response, hemodilution and rotational thromboelastometry outcomes in adults' CABG operation.

Methods: In a randomized controlled trial, 56 elective CABG patients that had referred to the Rajaie Cardiovascular Medical and Research Center (Tehran, Iran) during year 2017 were randomly assigned to two groups, including control and MUF groups. Preoperative and postoperative clinical parameters were recorded. Serum level of inflammatory cytokines after clamp removal, after Cardiopulmonary Bypass (CPB) (MUF in the MUF group) and 24 hours after Intensive Care Unit (ICU) entrance, and Rotational Thrombo-elastometry (ROTEM) indices, pre-operation, and post-operation, were measured.

Results: The two groups were similar in clinical perioperative parameters, including hemodynamics, transfusions, ROTEM indices, mechanical ventilation and CPB time, and ICU stay. The levels of inflammatory mediators were significantly increased after CPB in both groups. Interleukin (IL)-6, -8 and -10 measures were equal between the two groups in all trial measurement points. The MUF group demonstrated a significantly lower level of Tumor Necrosis Factor (TNF)-α compared with the control group after CPB (1.55 $\pm$ 0.29 versus 1.77 $\pm$ 0.35 log10 pg/mL, respectively; P = 0.031). Hemoglobin (9.55 $\pm$ 0.96 versus 8.29 $\pm$ 0.57 g/dl, P < 0.001) and hematocrit % (29.96 $\pm$ 3.23 and 24.72 $\pm$ 1.62, P < 0.001) levels were significantly higher in the MUF group compared with the control, after CPB.

Conclusions: Modified Ultrafiltration eliminates extra liquids and TNF-α from circulation in adults CABG operation, without affecting the hemostatic indices and improves hemoglobin level. It does not remove anti-inflammatory cytokine IL-10 from circulation.

Keywords: Cytokine, Hematocrit, Hemoglobin, Inflammatory Response, Modified Ultrafiltration, Thromboelastography

1. Background

Cardiopulmonary Bypass (CPB) is associated with postoperative complications, such as inflammatory response, hemodilution, pericardial effusion, edema, and pulmonary dysfunction (1-6). Inflammatory cytokine response usually occurs in response to ischemia/reperfusion injuries and subsequent oxidative stress (7-20). Moreover, contact of the blood with the surface of the perfusion system and graft materials causes further activation of cytokine-producing cells (13, 21, 22). These finally lead to systemic inflammatory response, following cardiopulmonary bypass operations, which simulates the cytokine storm phenomena (13). Ultrafiltration is recommended for removing excess free fluid and inflammatory mediators in patients with Coronary Artery Bypass Grafting (CABG) (23-27). Modified Ultrafiltration (MUF) has been reported in recent studies as a safe and effective method for im-

proved elimination of the extra fluid and inflammatory mediators from circulation, after CPB. Despite reports on the efficacy of MUF in improving hemodilution and inflammatory mediators in pediatric CPB settings (28-30), debates exist over its effectiveness in the elimination of inflammatory factors in adults (24). Current knowledge on the application of MUF in CPB operations is mostly based on data from a few very small trials with a handful of patients, and larger studies are required to give a solid conclusion about its effectiveness during CPB. Specifically, concerns exist over the safety of MUF, since despite its effects on removing excess liquid and effective hemoconcentration, it could result in hemostatic disturbances and complicate bleeding control.

Control of hemostasis, hemodilution, and inflammation process are the main strategies in the management of CABG-related mortality and morbidity and it is necessary to have well-designed and accurate studies for the assessment of the efficacy of MUF among patients undergoing a CABG operation. There is some evidence available on MUF effectiveness among adult patients and most related studies were performed on the pediatric population. Moreover, most studies are done only with very low sample numbers.

2. Objectives

The present study was performed for the assessment of the efficacy of modified ultrafiltration on control of hemostasis, inflammation, and coagulation process among adult patients undergoing CABG operation compared to conventional ultrafiltration.

3. Methods

3.1. Study Design

This study was a double-blinded, randomized clinical trial, performed on patients undergoing CABG operation at the Rajaie Cardiovascular Medical and Research Center (Tehran, Iran) during the year 2017. The study center was a governmental medical center, which is a referral center and serves a mixed population of patients from around the country. The study protocol was approved by the institutional research ethics committee and registered at Iranian Registry of Clinical Trials (IRCT) with the registration code of IRCT2017042127617N3. Simple randomization was used to allocate the patients to two groups, as previously described (13). Patients signed an inform consent form before recruitment. The CPB time was required to be between 50 and 120 minutes and the number of grafts must have been up to three or four. Patients with active cardiac disorders affecting post-CABG recovery period, history of a sternotomy, cardiac arrest or using a defibrillator in CABG operation, preoperative infection or coagulation disorders and left ventricular ejection fraction below 35%, were excluded. Study participants were randomly allocated to two groups: MUF and control. Anesthesia type and bypass pumps characters were the same between the study groups. During the CABG operation, patients in both groups received Conventional Ultrafiltration (CUF) and patients in MUF were continued on modified ultrafiltration. Clinical findings were measured using a vital sign monitoring system and recorded in a questionnaire.

Sample size was calculated using the following formula:

$$n = [(Z_{\alpha/2} + Z_{\beta})^2 \times \{2(ó)2\}]/(\mu_1 - \mu_2)^2$$

Where n was the sample size required in each group, μ_1 was mean hemoglobin level in the MUF group and had the value of 12.4, μ_2 demonstrates mean hemoglobin level in the common ultrafiltration group and equaled 14.6, $\mu_1 - \mu_2$ was clinically significant difference, which was equal to 2.2 and ó is standard deviation of the hemoglobin level, which was 2.9. $Z_{\alpha/2}$ for 5% level of significance was 1.96 and Z_{β} for 80% power was 0.84. The calculated sample size (n) was 27 for each group.

3.2. Laboratory Analysis

Blood samples were drawn and sent to the laboratory before and after the operation. Hemostasis parameters for rotational thromboelastometry were measured on a Rotational Thromboelastometry (ROTEM) device (ROTEM, Basel, Switzerland), according to the standard operating procedure of the device. Blood biochemistry parameters were measured on an automated biochemistry analyzer (Hitachi, Tokyo, Japan) using reagents, standards, and calibrators from the Pars Azmoun Company (Pars Azmoun Ltd., Tehran, Iran). These devices are run regularly for clinical analysis of the samples and laboratory devices are calibrated daily for ensuring their appropriate operation, using internal and external standards from manufacturers as well as Reference Health Laboratory of the Iranian Ministry of Health.

Blood samples for assessment of inflammatory mediators were gathered at three- time points: first sample, one minute after unclamping of the aorta clamp, secondary sample, after MUF (end of bypass), and the third sample 24 hours after ICU entrance. Circulating cytokines interleukin (IL)-6, -8, -10 and Tumor Necrosis Factor (TNF)-α were measured using cytokine assay kits, all from Biorbyt (Cambridge, UK), according to the manufacturer's guide.

Table 1. Comparing the Demographic Information of the Modified Ultrafiltration (MUF) Group Versus the Control Group

Variables	MUF	Control	P Value
Age (years)	60.3 ± 8.1	58.43 ± 8.77	0.44
Gender (referent: male), %	74	85	0.23
Height (centimeters)	166.11 ± 7.21	166.11 ± 7.84	0.99
Weight (kilograms)	75.85 ± 8.13	72.01 ± 18.90	0.33
Body area (m^2)	1.86 ± 0.08	1.85 ± 0.20	0.94

Table 2. Comparing Perioperative Characteristics of the Modified Ultrafiltration (MUF) Versus the Control Group

Variables	MUF	Control	P Value
CBP time (minutes)	82.11 ± 26.72	82.64 ± 31.48	0.95
Clamping time (minutes)	42.14 ± 14.53	40.23 ± 14.89	0.64
Operation time (hours)	4.83 ± 0.86	4.82 ± 0.75	0.98
Mechanical ventilation time (hours)	8.04 ± 4.84	8.45 ± 3.85	0.74
ICU stay (hours)	64.63 ± 48.87	59.98 ± 35.67	0.69

Abbreviations: CBP, cardiopulmonary bypass; ICU, intensive care unit.

3.3. Statistical Analysis

Study data were entered and analyzed using IBM SPSS Statistical Software, version 20.0 (IBM Corp., Armonk, N.Y., USA). The qualitative variables were presented with frequency and percentages, and the quantitative variables were presented with mean and standard deviation. This study used independent student *t*-test, Chi-square, and repeated measure analyses for comparing quantitative and qualitative variables between the two study groups. All P values less than 0.05 were considered as significant results.

4. Results

Study design and flow is depicted in Figure 1. Demographic information of the patients is presented in Table 1.

Data on clinical parameters are presented in Tables 2 and 3. Systolic blood pressure after CPB in the MUF group was significantly higher than the control group. Mean postoperative diastolic blood pressure in six hours and thirty-six hours after the operation was significantly higher in the MUF group in comparison with the control group. Mean central venous pressure upon ICU entrance in patients of the MUF group was significantly lower than patients of the control group (Table 3).

Epinephrine inotrope infusion in the operation room and ICU did not significantly differ between MUF and control groups. Norepinephrine usage in the operation room was similar between MUF and control groups. Mean transfusion in the operating room, and the ICU was similar between the two groups (Table 4).

Patients of both groups needed a temporary pacemaker and this rate was similar between MUF and control groups (0.028 versus 2.28; P = 0.49). Frequency of operation room return for hemorrhage control was similar be-

Table 3. Comparing the Hemodynamic Parameters Among Patients of Modified Ultrafiltration (MUF) Group Versus the Control Group

Variables	MUF	Control	P Value
HR (per minutes)			
Before operation	74.52 ± 18.66	82.36 ± 9.34	0.056
After CPB	83.37 ± 12.08	83.26 ± 9.34	0.52
IET	89.27 ± 9.09	88.11 ± 7.98	0.64
6 hours after IET	91.41 ± 10.95	85.95 ± 8.96	0.11
12 hours after IET	84.60 ± 10.95	84.22 ± 9.31	0.91
24 hours after IET	83.36 ± 8.64	86.40 ± 8.89	0.27
36 hours after IET	79.25 ± 2.47	88.15 ± 7.62	0.15
48 hours after IET	86.45 ± 3.69	85.87 ± 7.23	0.82
SBP (mmHg)			
Before operation	113.35 ± 21.11	106.30 ± 34.21	0.34
After CPB	113.07 ± 15.97	103.46 ± 13.15	0.018
IET	117.14 ± 13.84	116.42 ± 13.94	0.72
6 hours after IET	118.14 ± 10.59	117.22 ± 8.22	0.67
12 hours after IET	115.39 ± 10.57	122.25 ± 13.39	0.07
24 hours after IET	116.82 ± 11.33	120.78 ± 10.85	0.19
36 hours after IET	117.80 ± 16.05	117.05 ± 9.62	0.96
48 hours after IET	122.06 ± 11.01	120.18 ± 5.92	0.58
DBP (mmHg)			
Before operation	64.82 ± 10.73	68.51 ± 10.01	0.36
After CPB	68.78 ± 8.22	65.67 ± 6.44	0.12
IET	69.95 ± 7.82	62.23 ± 6.60	0.001
6 hours after IET	72.53 ± 9.66	63.36 ± 6.60	0.001
12 hours after IET	65.92 ± 10.73	68.51 ± 10.01	0.36
24 hours after IET	68.78 ± 8.22	68.51 ± 10.01	0.12
36 hours after IET	69.95 ± 7.82	62.33 ± 6.60	0.001
48 hours after IET	72.53 ± 9.66	63.36 ± 21.96	0.16
CVP (cmH_2O)			
Before operation	9.11 ± 2.91	9.55 ± 1.86	0.51
After CPB	9.26 ± 2.45	7.92 ± 2.56	0.055
IET	8.85 ± 3.98	11.71 ± 3.98	0.11
6 hours after IET	10.71 ± 3.01	11.85 ± 3.54	0.19
12 hours after IET	12.64 ± 3.14	11.64 ± 3.39	0.26
24 hours after IET	12.82 ± 3.39	11.89 ± 3.09	0.29
36 hours after IET	13.01 ± 3.80	11.81 ± 2.41	0.22
48 hours after IET	14.53 ± 3.33	12.27 ± 3.22	0.096

Abbreviations: CPB: cardiopulmonary bypass; CVP, central venous pressure in mmHg; DBP, diastolic blood pressure in mmHg; HR, heart rate in beat per minute; IET, intensive care unit (ICU) entrance time; SBP, Systolic blood pressure in mmHg.

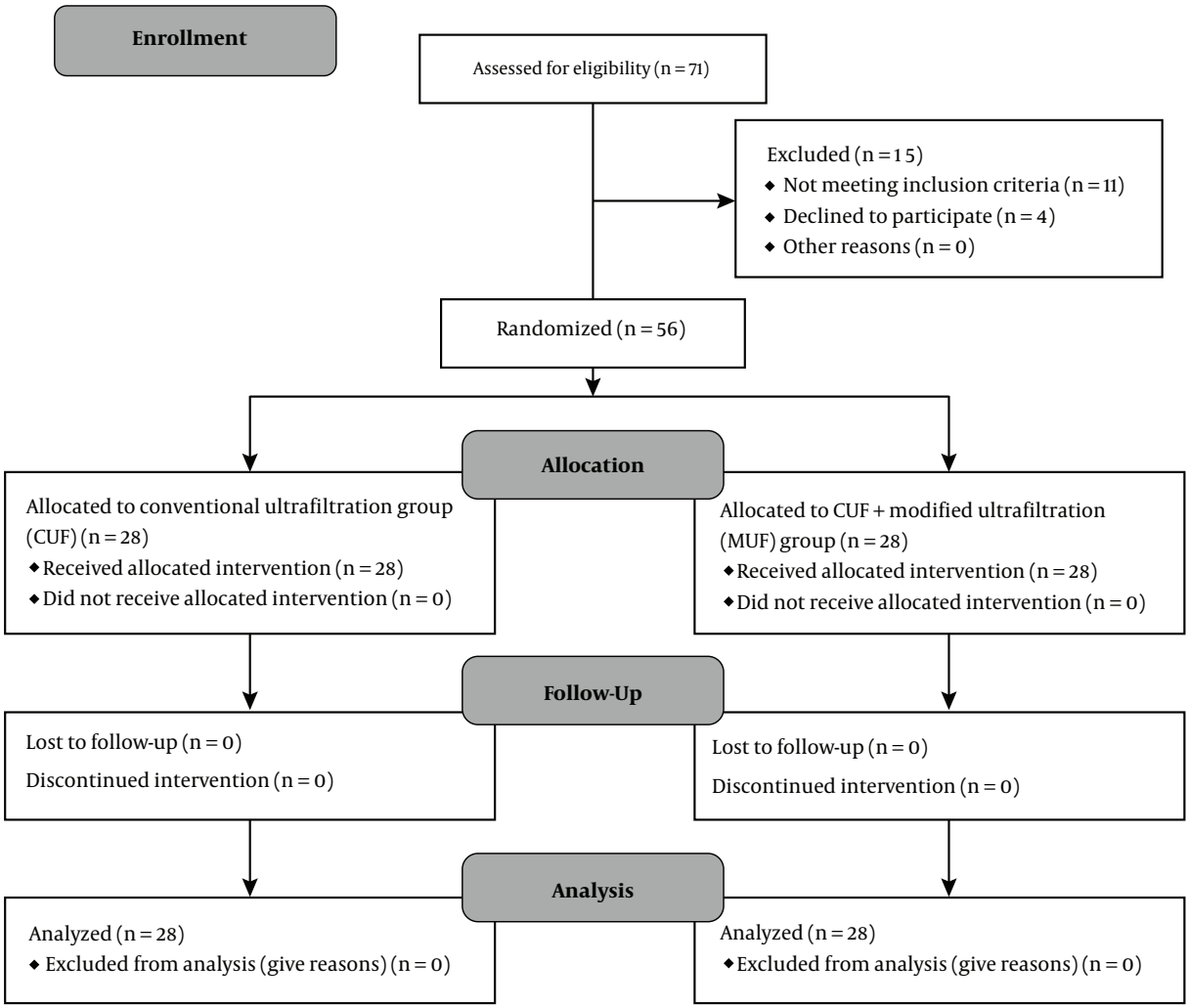

Figure 1. CONSORT flow diagram of the study

tween the study groups (1.28 versus 0.28; P = 0.99). Mean chest tube drainage volume on the second day among patients of the MUF group was significantly higher than patients of the control group (309.14 ± 2.6.45 versus 204.58 ± 101.68 milliliters; P = 0.03). Mean diuresis on the cardiac pump (614.58 ± 466.36 versus 596.0 ± 451.13 milliliters; P = 0.88) and hemofiltration on cardiac pumping (1240.74 ± 604.15 versus 1182.45 ± 658.27; P = 0.75) were similar between the MUF and control groups.

Pack cell transfusion among patients of the MUF group was similar with patients of the control group (152.77 ± 216.21 versus 239.28 ± 364.73 milliliters, respectively; P = 0.29). Fresh frozen plasma (27.77 ± 102.21 versus 0.0 ± 0.0 milliliters; P = 0.17) and platelet transfusion (25.01 ± 64.54 versus 21.42 ± 88.64 milliliters; P = 0.86) were similar between the patients of the MUF and control group. Mean creatinine, blood urea, Serum Glutamic-Oxaloacetic Transaminase (SGOT), and Serum Glutamate-Pyruvate Transaminase (SGPT) were similar at all measurement times. Hemoglobin and hematocrit values at the warm- up and postoperative times in patients of the MUF group were significantly higher in comparison with the control group (P < 0.001) (Table 5).

Mean of all cytokines was similar between the two groups at identical time points; an exception was the mean of TNF-α after the operation, which was significantly lower in the MUF group compared with the control group at the same time (1.55 ± 0.29 versus 1.77 ± 0.35 in the MUF group in comparison with the control group; P = 0.031) (Figures 2A-2D).

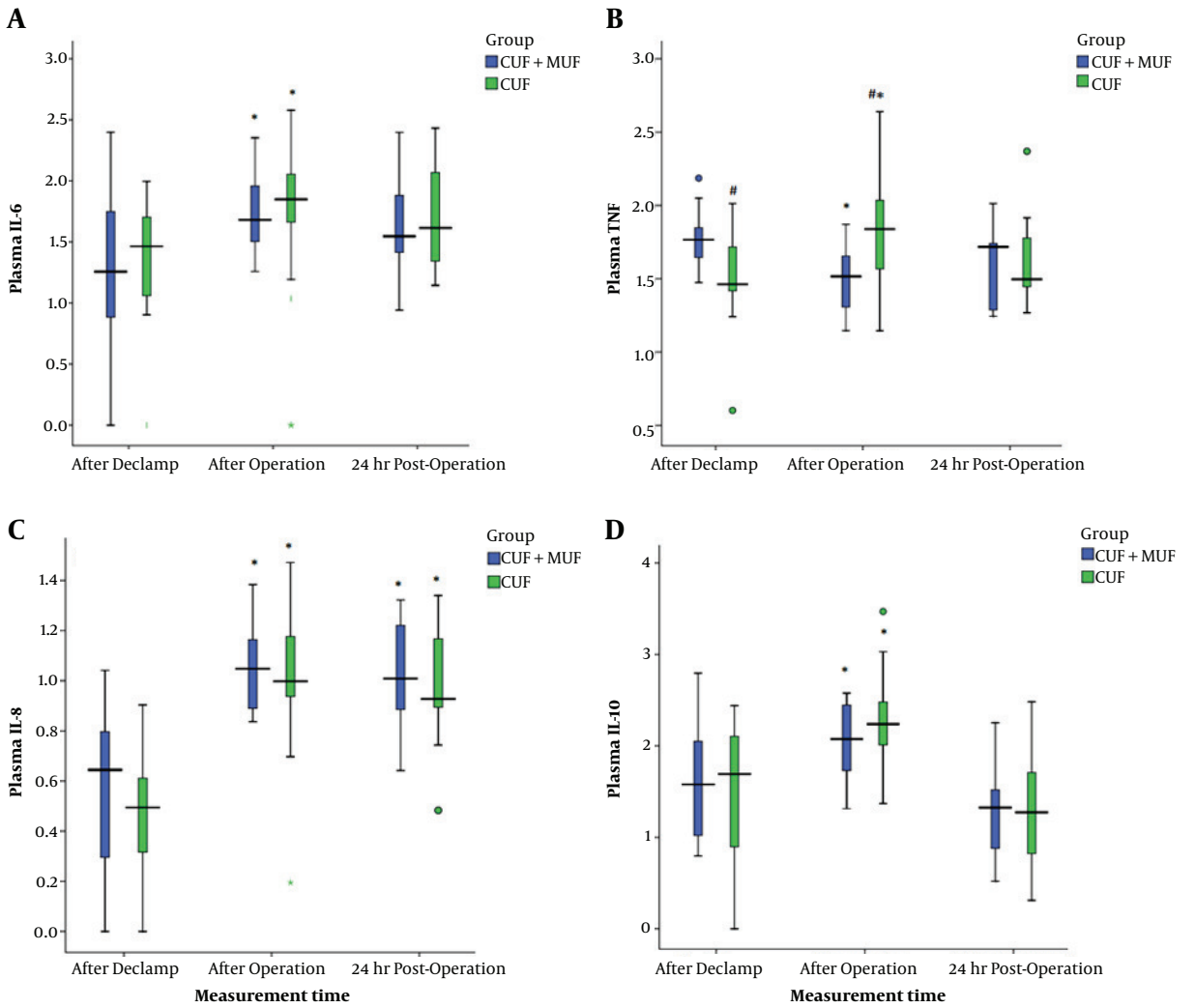

Figure 2. Level of circulatory interleukin (IL)-6 (A), tumor necrosis factor alpha (TNF-α) (B), IL-8 (C) and IL-10 (D) at three time points: after de-clamp, after operation and 24 hours after transfer to ICU. Units of measurement are in pg.mL. * $P < 0.05$ compared with measurement in Log10 pg/mL in the same group after declamp, # $P < 0.05$ compared to the measurement in the same group at the same time.

Mean of Clotting Time (CT), Clotting Firmness Time (CFT) and Maximum Clot Firmness (MCF) in coagulation pathways (INTEM and EXTEM), using the ROTEM device, were similar at different follow-up measurement points (Table 6).

5. Discussion

The present study was performed for the assessment of Modified Ultrafiltration (MUF) impacts on hemoconcentration, inflammatory, and coagulation factors that were evaluated among patients that had undergone the CABG operation. Notwithstanding that the total blood transfusion was similar between the two groups, levels of hemoglobin and hematocrit were significantly higher in the MUF group compared with the control group. Similar results were reported by other researchers (31, 32). Postoperative was systolic blood pressure in patients of the MUF group were significantly higher than the control group. Diastolic blood pressure at six and 36 hours after the operation among patients of the MUF group was significantly higher than the controls. At ICU entrance, mean central venous pressure in patients of the MUF group was significantly lower than controls. It appears that this occurs due to reversing the hemodilution effects. Use of MUF helps improve the level of hemoglobin and prevents edema. This,

Table 4. The frequency of Blood and Blood Products Transfusions Among Patients of Modified Ultrafiltration (MUF) Group Versus the Control Group[a]

Variables	MUF	Control	P Value
Packed cell in OR	5/28 (17.58)	6/28 (21.42)	0.91
Packed cell in ICU	11/28 (39.28)	5/28 (17.85)	0.14
Fresh frozen plasma in ICU	2/28 (7.14)	0/28 (0.00)	0.49
Platelet usage in OR	1/28 (3.57)	0/28 (0.00)	0.92
Platelet usage in ICU	3/28 (10.71)	2/28 (7.14)	0.90
Transamin usage in OR	1/28 (3.57)	0/28 (0.00)	0.91

Abbreviations: ICU, intensive care unit; OR, operating room.
[a] Data are expressed as frequency or relative frequency percentage of patients receiving each product in the trial groups.

in turn, leads to improved hemodynamic stability, which has been reported by previous studies (22, 31). A significant change in the plasma TNF-α was observed following control, while other cytokines measured in the current study did not demonstrate a significant change. Kwak et al. reported that MUF could eliminate inflammatory mediators during CBP as measured by C-Reactive Protein (CRP) levels and improvement in postoperative function among the pediatric population undergoing cardiopulmonary bypass (33). The same has been reported by Hennein et al. (34). Moreover, previous studies on the pediatric population reported that MUF improved outcome parameters, especially led to a decrease in postoperative hemorrhage and blood product usage, increase in cardiac output, and decrease need for the ventilator, ICU stay and myocardial edema (33). Sever et al. in their longitudinal study reported that using MUF in the CABG operation, caused an increase in hemoglobin, hematocrit, and platelets counts among pediatrics (35). It is expected that using MUF during CABG operation could cause a decline in the amount of blood drainage from the chest tube. However, a study by Steffens et al. did not report improvement in the total chest tube drainage although they reported a significant decline in end of procedure net fluid balance and cell saver units processed in favor of the MUF group (36). In the present study, serum level of hemoglobin and hematocrit were significantly higher among patients of the MUF group in comparison with the control. These findings are consistent with the findings of previous studies. It appears that MUF elevates hemoglobin and hematocrit values and improves hemodynamic stability. However, its effects on inflammatory response and coagulation disorders are not conclusive. Plasma pro-inflammatory cytokines, including TNF-α, IL-4, IL-6, and IL-8, are elevated and result in a systemic inflammatory response during and after CPB (13, 37). Modified ultrafiltration was suggested for control of inflammatory response among patients undergoing CABG (37, 38). Circulatory TNF-α level was declined in the MUF group in the present study. However, the level of IL-6, IL-8, and IL-10 did not significantly change between the two groups. Hemofiltration maintains water balance, concentration of clotting factors, and improves early as well as postoperative blood loss (38). Sever et al. and Andreasson et al. in their study reported that MUF could decrease inflammatory responses via a decline in serum level of inflammatory mediators (35, 38). Papadopoulos et al. reported no significant differences in cytokines TNF-α, IL-1β, IL-6, and IL-10 between the MUF and control group during CPB, until 48 hours post-operation, however, they reported a significant decrease in Lipopolysaccharide-Binding Protein (LBP) and terminal complement complex (C5b9) (37). Also, Chew et al. reported no significant differences in circulatory cytokine levels, including TNF-α, IL-1β, IL-6, IL-10, and IL-1ra between the MUF and control group when ultrafiltration was performed using Amicon polysulfone Dia Filter 20 hemofilter (39). Grunenfelder et al. reported that MUF is associated with decreased inflammatory cytokine (IL-6, IL-8, TNF-a, and IL-2R) response as well as a reduction in adhesion molecules associated with the inflammatory response (40). Boga et al. reported no benefit for inflammatory response in modified ultrafiltration; however, this can be justified since they only measured the level of IL-6 and IL-8 (41). A notable finding in most of these studies is that they reported reduced inflammatory cytokine levels in the MUF group yet their results failed to be statistically significant, mostly due to a low sample size, while in the current study, MUF effectively eliminated TNF-α from circulation.

In another study by Papadopoulos et al., a significant post-operative inflammatory response was observed in terms of Lipopolysaccharide-Binding Protein (LBP) and terminal complement complex (C5b9) (37). They reported no change in case of IL-6, IL-10, IL-1beta, and TNF-α levels after normovolemic modified ultrafiltration (37). Furthermore, Fujita et al. reported that inflammatory cytokines did not significantly change among patients receiving MUF (42). Both of these studies had a low sample size, which makes it impossible to make judgments about the efficacy of MUF in removing cytokines from circulation, although they reported a slight but non-significant decrease in the plasma level of cytokines. The discrepancies in the TNF-α level in the serum after MUF in these studies are due to low sample size; forty patients in the study by Papadopoulos et al. (37) and only eight patients in the study by Fujita et al. (42). According to the decrease in serum level of TNF-α in patients of the MUF group compared with patients of the control group, it could be concluded that MUF can cause a decrease in inflammatory response.

Table 5. Frequency of Biochemical and Laboratory Findings of Study Participants[a]

Variables	MUF	Control	P Value
Preoperative Cr (mg/dL)	1.01 ± 0.25	0.91 ± 0.23	0.16
Cr ICU entrance (mg/dL)	0.91 ± 0.31	0.87 ± 0.27	0.21
Cr 24 after ICU entrance (mg/dL)	1.02 ± 0.26	0.94 ± 0.32	0.29
Preoperative BUN (mg/dL)	20.47 ± 9.01	18.80 ± 4.98	0.41
Postoperative BUN (mg/dL)	20.91 ± 6.56	9.63 ± 6.56	0.60
BUN a 24 after operation (mg/dL)	21.41 ± 9.98	22.21 ± 7.16	0.73
Preoperative SGOT (IU/dL)	19.31 ± 7.80	25.25 ± 12.88	0.09
Postoperative SGOT (IU/dL)	55.21 ± 80.75	70.64 ± 114.37	0.56
Preoperative SGPT (IU/dL)	23.36 ± 10.73	31.25 ± 20.16	0.13
Postoperative SGPT (IU/dL)	67.07 ± 144.75	91.03 ± 188.05	0.59
Warm-up Hb (mg/dL)	8.58 ± 1.02	8.63 ± 0.97	0.85
Postoperative Hb (mg/dL)	9.55 ± 0.96	8.29 ± 0.57	<0.001
Warm-up HCT (%)	26.96 ± 3.40	25.96 ± 3.20	0.27
Post-operative HCT (%)	29.96 ± 3.23	24.72 ± 1.62	<0.001

Abbreviations: BUN, blood urea nitrogen; Cr, creatinine; Hb, hemoglobin; HCT, hematocrit; ICU, intensive care unit; SGOT, serum glutamic oxaloacetic transaminase or aspartate transaminase or aspartate aminotransferase; SGPT, serum glutamic-pyruvic transaminase or alanine transaminase.
[a] Data are expressed as Mean ± SD.

Table 6. Frequency of ROTERM Parameters at Follow-Up Points Among Study Participants[a]

Variables	MUF	Control	P Value
Preoperative CT (intem)	212.41 ± 93.24	196.86 ± 38.09	0.46
Postoperative CT (intem)	208.47 ± 68.48	194.73 ± 76.47	0.54
Preoperative CFT (intem)	77.54 ± 47.17	65.45 ± 12.99	0.24
Postoperative CFT (intem)	114.48 ± 48.05	98.04 ± 35.69	0.21
Preoperative MCF (intem)	62.75 ± 11.05	63.78 ± 7.68	0.72
Postoperative MCF (intem)	55.68 ± 9.22	60.21 ± 9.24	0.12
Preoperative CT (extem)	60.0 ± 14.09	67.91 ± 54.17	0.56
Postoperative CT (extem)	70.90 ± 15.72	73.43 ± 26.47	0.71
Preoperative CFT (extem)	60.24 ± 30.37	78.73 ± 83.63	0.56
Postoperative CFT (extem)	102.65 ± 34.21	87.01 ± 34.15	0.14
Preoperative MCF (extem)	62.20 ± 8.86	66.86 ± 8.92	0.80
Postoperative MCF (extem)	62.66 ± 22.22	61.82 ± 8.92	0.72

Abbreviations: CFT, clotting firmness time in seconds; CT, clotting time in seconds; MCF, maximum clot firmness in millimeters.
[a] Data are expressed as Mean ± SD.

Mortality and return to the operation room for the control of hemorrhage, and ICU length of stay were similar between the control and MUF groups. These findings are consistent with the findings of Papadopoulos et al. (37) and Weber et al. (43). Amount of postoperative liquid drainage did not significantly differ between the control and MUF groups on the first days after the operation. Postoperative drainage amount was higher in patients of the MUF group. In other studies, such as Papadopoulos (37), Weber (43) and Sever's studies (35), the amount of postoperative drainage among patients of the MUF group was lower than controls.

Rotational Thromboelastography (ROTEG) parameters did not significantly change between the two groups, which is consistent with the findings of Steffens et al. (36); in their study they reported similar outcomes in terms of peri- and post-operative coagulation factors in MUF and

control groups (36). Moreover, Weber et al. demonstrated that plasma level of coagulation factors raise after surgery in patients receiving MUF (43). Evidence suggests that ultrafiltration retains coagulation factors and cellular compartment, which are required for blood clotting while removing pro-inflammatory cytokines. In this situation, it is normal to observe no change in the thromboelastometry test results in the group undergoing MUF, however, it seems to have no direct effects on coagulation factors and ROTEM indices. Mechanical ventilation, ICU stay, and inotrope drug usage in the current study were similar with the study by Sahoo et al. (44) and no significant difference was found between the two study groups. Similar with the Weber study (43), using blood and blood products had no significant differences between the study groups. Contrary to the current study, Torina et al. reported that blood transfusion among patients of the MUF group was decreased and total blood transfusion was lower in patients of the MUF group (45). Moreover, Leyh et al. in their study reported that MUF could cause a decrease in hemorrhage and transfusion rate (46). Most previous studies regarding the use of MUF have low sample sizes. Furthermore, these studies are relatively heterogeneous in case of the mode of filter type and mode of ultrafiltration, and normovolemic or hypovolemic parameters. Therefore, although they provide primary evidence for running larger trials, they could not be a basis for conclusive statements regarding the effectiveness and safety of the MUF. In the current study, the researchers studied a larger sample of adult patients undergoing CPB. This study revealed that MUF usage results in effective hemoconcentration and improves inflammatory response after CPB. However, the results are limited by the follow up for 24 hours in parameters under investigation. To overcome these limitations, the researchers suggest screening of the patients in the long term to identify clinical outcomes after MUF application in CABG patients undergoing CPB.

5.1. Conclusions

MUF reduces the circulatory level of inflammatory cytokines, removes extra fluids, and corrects hemodilution without adversely affecting hemostasis during CPB operations.

Footnotes

Authors' Contribution: Ali Sadeghpour Tabaei and Meysam Mortazian have contributed equally to this work.

Financial Disclosure: Rajaie Cardiovascular Medical and Research Center Research Grant. Trial registry: Iranian Registry of Clinical Trials (www.irct.ir) (IRCTID: IRCT2017042127617N3).

Funding/Support: The present study was funded by the dean of research at Iran University of Medical Sciences, Tehran, Iran.

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