

# Venoarterial modified ultrafiltration versus conventional arteriovenous modified ultrafiltration during cardiopulmonary bypass surgery

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**BACKGROUND AND OBJECTIVES:** Different types of modified ultrafiltration (MUF) systems evaluated showed that none of the MUF techniques adhered to the normal venous to arterial blood flow dynamics. This study compared a conventional arteriovenous modified ultrafiltration (AVMUF) system to a custom- designed venoarterial modified ultrafiltration (VAMUF) system.

**DESIGN AND SETTINGS:** Randomized, controlled clinical study conducted at the Northwest Armed Forces Military hospital in Tabuk, Saudi Arabia.

**PATIENTS AND METHODS:** Sixty patients who underwent MUF during the years 2007 and 2009 were divided into 2 groups: the AVMUF (n=30) and the VAMUF (n=30) groups. MUF was performed for a mean time of 12 minutes in both groups. In AVMUF, blood was removed from the aorta, hemoconcentrated, and infused into the right atrium (RA). In VAMUF, blood flow was from the RA through a hemoconcentrator and re-infused into the aorta.

**RESULTS:** Results of the study showed that the VAMUF group required a shorter ventilation time ( $P<.001$ ), intensive care unit (ICU) ( $P=.003$ ), and hospital stay ( $P=.007$ ) than the AVMUF group. Results also demonstrated a lower percentage of fluid balance ( $P=.008$ ) in the VAMUF group. The systolic ( $P<.001$ ) and mean blood pressures ( $P<.001$ ) were significantly higher after VAMUF, with a decrease in heart rate ( $P<.001$ ) and central venous pressure ( $P=.002$ ). The VAMUF group showed a significantly greater decrease of creatinine ( $P<.001$ ), serum lactate ( $P<.001$ ), and uric acid ( $P<.027$ ) over time with no significant differences in oximetry.

**CONCLUSION:** Results prove that VAMUF is a more physiological technique than AVMUF.

Numerous advances in cardiopulmonary bypass (CPB) circuits and perfusion techniques have been accomplished over the last 50 years following open heart surgery.<sup>1</sup> Elevated capillary permeability, increased water weight gain, and inflammatory mediators still complicate postsurgical recovery and organ function. Several approaches have been adopted to reduce the accumulation of excess extravascular fluids and complement activation. These include the use of smaller and more biocompatible oxygenators, shorter lines in CPB circuits, use of corticosteroid anti-inflammatory agents and ultrafiltration.<sup>2</sup>

The technique of conventional arteriovenous modi-

fied ultrafiltration (AVMUF) was developed in the early 1990s at the Great Ormond Street Hospital for sick children in London, UK, by Naik et al<sup>3</sup> It is performed after separation of bypass. It entails hemoconcentrating the total circulating blood volume in patient and residual blood volume in the CPB circuit. The concentrated blood is thereafter returned to the patient. Blood is removed from the aorta and passes through a hemoconcentrator (artificial kidney), and is pumped back into the heart via a cannula in the right atrium (RA). The blood flow is retrograde in relation to CPB and the patient's physiological blood flow dynamics.

The implementation of modified ultrafiltration

(MUF) to CPB has shown to decrease postsurgical edema due to hemofiltration, thus reducing the need for blood transfusion and thereby preventing the complications associated with homologous blood transfusion.<sup>4</sup>

The published studies suggest that MUF is an effective tool in reducing inflammatory mediators that cause organ dysfunction and undesirable hemodynamic changes.<sup>5</sup>

This experimental study compared a conventional AVMUF system to a custom-designed venoarterial modified ultrafiltration (VAMUF) system. This technique of VAMUF was designed to mimic the prograde flow pattern of the body and CPB circuit as compared to the conventional retrograde AVMUF systems.

## PATIENTS AND METHODS

### *Preliminary studies*

A survey regarding MUF was carried out in Saudi Arabia using the Arabian Perfusion Web site ([www.sa-sect.sa](http://www.sa-sect.sa)). The Saudi Arabian Society for Extracorporeal Technology was contacted for a member list and relevant emails and contact details together with permission to contact registered members. Once permission was granted and the list was received, a survey was emailed to the respective members. A questionnaire was posted on perfusion Web sites and emailed directly to numerous hospitals within the kingdom. A similar survey was carried out on a larger scale using World Wide Web (WWW) on the Internet, as this was the quickest method of communication considering the large perfusionist population globally. The following perfusion Web sites were consulted: [www.perfusion.com](http://www.perfusion.com), [www.perflist.com](http://www.perflist.com), [www.middleeastperfusion.com](http://www.middleeastperfusion.com) and [www.amsect.com](http://www.amsect.com). The questionnaire was emailed to all the members located across the world. Replies were received from numerous perfusionists from hospitals situated in various countries, e.g., Germany, America, Canada, Europe, India, Australia, and the Netherlands.

Preliminary studies of circuit diagrams were performed to ascertain which of the MUF techniques were the most effective, user friendly, safe, and required the least amount of changes to the CPB circuit.

After analyzing and studying various methods of performing MUF, a circuit was designed that seemed to fulfill all the criteria required for an ideal MUF system. It was unique because blood flow was from the RA to the Aorta after passing through the MUF circuit. This technique was referred to as the venoarterial VAMUF indicative of the direction blood flow. The VAMUF circuit that was designed and finally accepted as the method of choice is depicted in **Figure 1**.

The circuit diagram of the technique together with a detailed PowerPoint presentation was presented to the Department of Cardiac Surgery at the Northwest Armed Forces Hospital (NWAFH) in Tabuk (Saudi Arabia), to obtain permission to carry out “dry” (cardiotomy reservoir circuit without priming fluid) and later “wet” circuit (primed with fluid) assimilation studies.

The study was submitted for ethical approval on animal subjects after all members of the cardiac team were enlightened regarding the technique and agreed that it was safe.

Animal studies commenced on approval from the ethical board of NWAFH. The breed of animal was selected on the basis of the advice from the vet was goats (*Capra hircus*). They were all checked by the vet for abnormalities and were excluded if any was found. The venue allocated for the animal studies was the operating rooms at the department of postgraduate studies at the NWAFH.

Results of animal studies and a proposal to conduct the VAMUF study on human subjects were forwarded to the ethical board for ethical approval. Official permission was obtained from the ethical committee of NWAFH for the study to proceed.

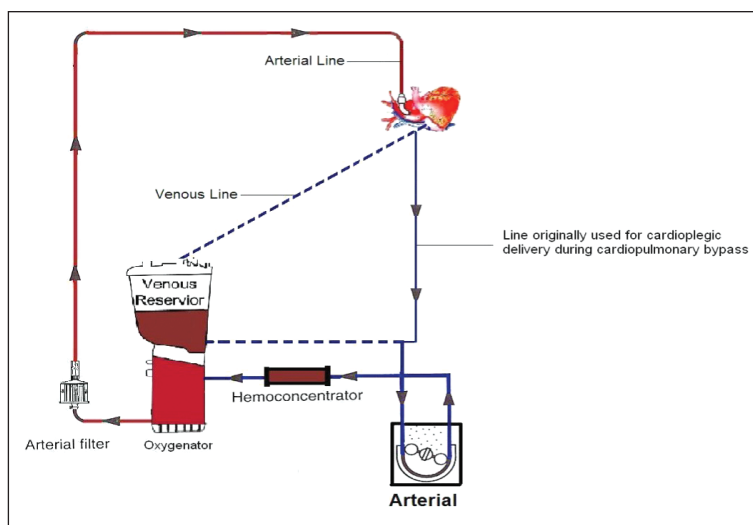
### *Human study*

The location of the study was at the Northwest Armed Forces Military Hospital in Tabuk, Saudi Arabia.

This was a prospective, randomized, clinical controlled study of 60 cardiac surgical patients who required life support by a heart lung machine. A signed informed consent was obtained from every patient. The patients were categorized into 2 groups. Group 1 (AVMUF group) was the control group comprising 30 patients ( $n=30$ ) (**Figure 3**). Group 2 was the experimental group comprising 30 VAMUF patients ( $n=30$ ). For uniformity and consistency, all 60 patients underwent blind randomization on the morning of the procedure by an independent member of staff.

Inclusion criteria included the following: required life support by a heart lung machine, infants/pediatrics congenital cardiac surgical cases that required CPB, adult coronary artery bypass and valve cases on CPB, patients between the ages of 1 week to 75 years, patients with an ejection fraction of 25% and more, patients residing or working in Saudi Arabia, patients operated at the NWAFH.

Exclusion criteria included the following: off-pump coronary artery bypass grafting patients, patients who were hemodynamically unstable after termination of CPB, patients with a low positive fluid balance post-CPB, patients on whom the operating surgeons did not



**Figure 1.** Basic VAMUF circuit diagram.



**Figure 2.** A *Capra Hircus* (goat) being prepared for MUF study at the NWAUF animal lab.

prefer to perform MUF.

Both study groups underwent conventional ultrafiltration (CUF) during CPB and MUF (AVMUF or VAMUF) for 10 to 15 minutes after separation from CPB.

The principal investigator performed the MUF process after termination of CPB. All blood samples were collected at the appropriate times, analyzed, and recorded for final comparison.

Demographic data, length of CPB, length of cardiac surgical unit stay, length of hospital stay, use of hypothermic arrest, complications, hemodynamic support, use of peritoneal dialysis catheters for the relief of abdominal compression, creatinine levels, body weights,

and duration of intubation were also recorded.

The conventional AVMUF technique was performed after the termination of CPB. Blood was removed from the heart retrogradely from the aortic cannula that was originally placed in the aorta during CPB. It was then circulated through a pump head that was dedicated for MUF, where it was hemoconcentrated before being re-infused into the patients via the RA.

Positive fluid balance was calculated, and MUF was terminated when sufficient filtrate was obtained in the ultrafiltrate waste bag. Patients were always left with a reasonable positive fluid balance in both types of MUF to encourage postsurgical urine output.

VAMUF was also performed after the termination of cardiopulmonary bypass. In VAMUF, blood was removed from the RA of the heart from a venous cannula that was originally placed in the RA during CPB. This blood was then circulated through the main pump head where it was hemoconcentrated before being infused into the patients via the arterial cannula that was placed in the aorta during routine CPB (Figure 4). Positive fluid balance was calculated, and VAMUF was terminated when sufficient filtrate was obtained in the ultrafiltrate waste bag. Patient's pressure was observed and controlled at all times in consultation with the anesthetist.

The results of the parameters measured were categorized under 2 major headings, i.e., primary and secondary outcomes.

The primary outcomes measured included the following: (1) postoperative variables including ventilation time, intensive care unit (ICU) stay, hospital stay, and discharge day. (2) Fluid management data including total fluid input, total fluid output, and fluid balance. (3) Hemodynamic variables data analysis including arterial pressure—systolic, as an indication of ventricular function and diastolic, as an indication of pre-load and after-load and mean as an indication of cardiac output—and central venous pressure (CVP) as an indication of blood volume limits and heart rate (beats per min). (4) Blood gas analysis data including partial pressure of oxygen ( $pO_2$ ), partial pressure of carbon dioxide ( $pCO_2$ ), and blood saturation. (5) Hematological data analysis including hematocrit (Hct), hemoglobin (Hb), red blood cell (RBC) count, white blood cell (WBC) count, platelets (PLTs), and albumin (Alb). (6) Electrolyte data analysis including serum concentration of sodium, potassium, calcium, serum phosphate, and magnesium. (7) Renal-related markers data analysis including serum blood urea nitrogen (BUN), creatinine, and uric acid. (8) Cardiac markers data analysis including creatinine kinase (CK), CK myocardial band (CK-MB), and serum lactate.

The secondary outcomes measured included the following: (1) modified ultrafiltration demographic data including patient's mean age, gender, height, weight, body surface area, and type of surgery. (2) CPB data including CPB and cross-clamp time. (3) CUF and MUF data.

The SPSS, version 15.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. A  $P$  value  $<.05$  was considered as statistically significant. All quantitative variables were checked for normality, using the skewness statistic. Quantitative normally distributed data were compared between the 2 arms of the trial using independent  $t$ -tests, whereas non-normal data were compared using Mann-Whitney tests. Pearson chi-square tests were used when the variables were categorical, and Fisher exact test was used in the case of binary variables. Comparison of the difference between pre- and post-values between the treatment arms was achieved by calculating the difference between pre- and post-MUF values in each arm and comparing this difference by means of independent  $t$ -tests. Percentage differences were calculated by dividing the difference by the baseline value and multiplying by 100. Profile plots were generated to visually examine the changes over time by treatment arm.

## RESULTS

In **Tables 1 and 2**, the data suggest that there were no significant difference in any of the demographic variables or type of procedure by treatment arm.

In **Table 3**, the results reflect that neither CPB time nor cross-clamping time showed any difference between the 2 treatment arms of the study, whereas **Table 4** shows a statistically significant difference in the mean percentage of fluid output between the 2 arms ( $P=.044$ ), with the VAMUF arm having a greater percentage output than the AVMUF arm. A statistically significant difference was also observed in fluid balance between the 2 arms ( $P=.008$ ), with the VAMUF arm having a lower percentage fluid balance than the AVMUF arm. The VAMUF group had a remaining fluid balance of 15.1% of the total fluid input, whereas the AVMUF group had a higher remaining fluid balance of 20.8% of the total fluid input.

**Table 5** demonstrates that there were no significant differences in the changes in any of the electrolyte variables between pre-MUF and post-MUF values between the treatment arms.

In **Table 6**, creatinine and uric acid showed a significantly greater decrease over time in the VAMUF group than the AVMUF group ( $P<.001$  and  $P<.027$ , respectively).

The results in **Table 7** confirm that there was a sta-

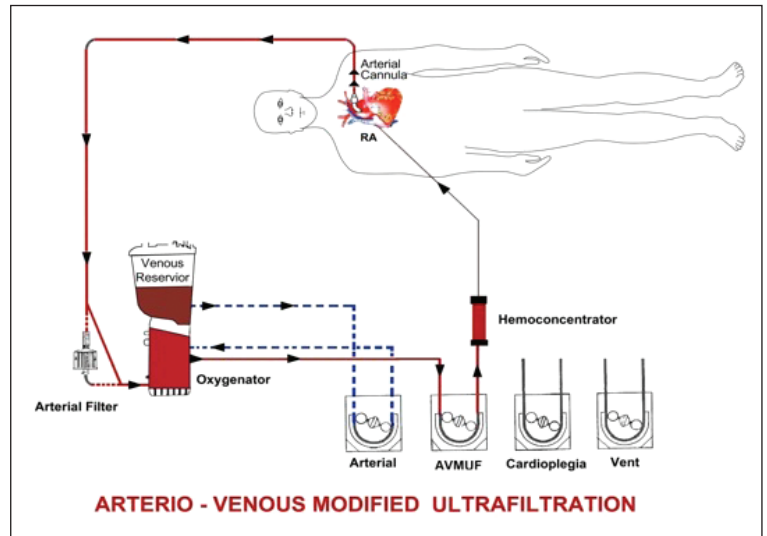


Figure 3. AVMUF technique.

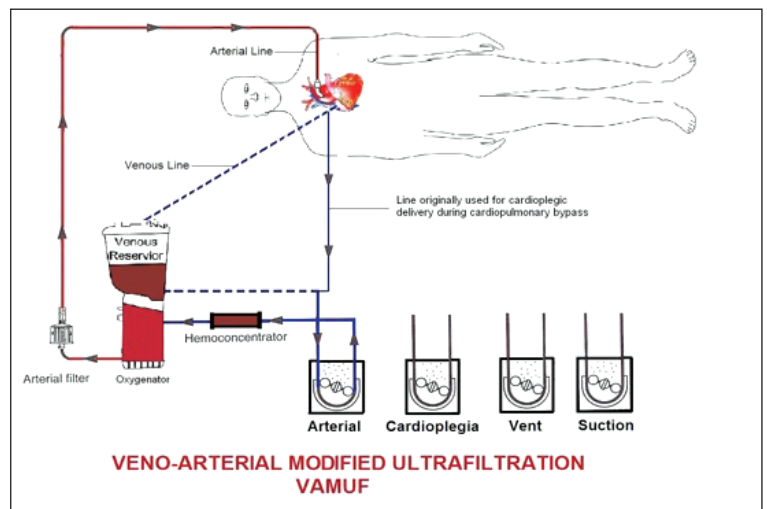


Figure 4. VAMUF technique.

tistically significant difference in the ventilation time between the 2 arms of the study ( $P<.001$ ). The VAMUF group showed a much lower ventilation time than the AVMUF group. ICU stay, hospital stay, and discharge days were significantly lower in the VAMUF group as well ( $P=.003$ ,  $P=.007$ , and  $P=.007$ , respectively).

**Table 8** demonstrates that there was a borderline statistically significant difference in the median CUF volume between the 2 arms ( $P=.043$ ), with the VAMUF arm having the greater volume. There was no difference between the arms with regard to MUF volume ( $P=.275$ ).

In **Table 9**, the results of all the hemodynamic variables showed that the changes between pre- and post-

**Table 1.** Modified ultrafiltration demographic data.

Variables	AVMUF (n=30) Mean (SD)	VAMUF (n=30) Mean (SD)	P value
Age (y)*	37.0 (28.8)	43.3 (26.7)	.382
Gender (M:F)	19:11	23:7	.260
Height (cm)*	132.9 (38.8)	144.0 (34.9)	.253
Weight (kg)*	50.6 (33.1)	53.6 (26.9)	.706
BSA (m <sup>2</sup> )*	1.2 (0.7)	1.3 (0.6)	.419
BMI (kg/m <sup>2</sup> )*	23.3 (8.0)	22.7 (6.5)	.763

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, M:F: male-to-female ratio, BSA: body surface area, BMI: body mass index.

**Table 2.** Types of operation performed.

Type of operation	AVMUF (n=30) Mean (%)	VAMUF (n=30) Mean (%)	P value
CABG	16 (53.3%)	16 (53.3%)	.791
Valve	3 (10.0%)	6 (20.0%)	
ASD	3 (10.0%)	3 (10%)	
VSD	4 (13.3%)	3 (10%)	
ASD+VSD	1 (3.3%)	0 (0%)	
Rastelli operation	1 (3.3%)	0 (0%)	
Other congenital	2 (6.7%)	2 (6.7%)	

CABG: Coronary artery bypass grafting, ASD: atrial septal defect, VSD: ventricular septal defect, AVMUF: arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration.

**Table 3.** CPB and cross-clamp time in the AVMUF and VAMUF group.

Variables	AVMUF (n=30) Mean (SD)	VAMUF (n=30) Mean (SD)	P value
CPB time (min)	106.0 (41.6)	107.07 (43.8)	.928
Cross-clamp time (min)	79.2 (33.2)	76.70 (33.6)	.770

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, CPB: cardiopulmonary bypass.

CPB time (min): Total time a patient was supported by the heart lung machine.

Cross-clamp time (min): Total anoxic time when there is no blood flow to heart muscles.

MUF were significantly different between the 2 study arms. In **Table 10**, the results demonstrate that there were no significant differences between the 2 treatment arms with regard to the change in blood gas variables.

In **Table 11**, Hct, HB, RBC (%), and Alb concentrations showed significant differences from pre- to post-treatment between the 2 treatment arms. All values increased over time, to a greater extent in the VAMUF arm ( $P=.006$ ,  $P=.001$ ,  $P=.030$ , and  $P<.001$ , respectively).

The mean (SD) Hct in the AVMUF group increased from 26.2% (2.9) to 31.7% (5.7), with an increase of 5.5%. In **Figure 5** the VAMUF group had a more significant increase in the mean (SD) Hct, i.e., from 25.2% (3.5) to 33.8% (4.0), with an increase of 8.6%.

In the AVMUF group, mean (SD) Hb levels increased from 8.8 (0.9) g/dL to 10.8 (1.4) g/dL, with a difference of 1.9 g/dL. In the VAMUF group, mean (SD) Hb increased from 8.4 (1.1) g/dL to 11.3 (1.3) g/dL, with an increase of 2.8 g/dL (**Table 11**). **Figure 6** illustrates that the VAMUF study group had a more significant rise in Hb, with an increase of 34.6%, when compared to the AVMUF group, which had a 22.5% increase in Hb.

In the AVMUF group, the mean (SD) RBC count increased from 3.3 (1.1) M/ $\mu$ L to 3.7 (0.6) M/ $\mu$ L, with a mean difference of 0.3 M/ $\mu$ L. The VAMUF group had a more significant increase of the RBC count from 3.1 M/ $\mu$ L to 3.8 (0.7) M/ $\mu$ L, with a difference of 0.7 M/ $\mu$ L (**Table 11**). **Figure 7** illustrates that the RBC count in the VAMUF study group increased by 24.3%, whereas the RBC count in the AVMUF group increased by 14.6%.

In **Table 11**, the mean (SD) WBC in the AVMUF group increased from 15.1 (7.3) K/ $\mu$ L to 16.1 (9.6) K/ $\mu$ L, with a difference of 1.06 K/ $\mu$ L. The VAMUF group had a less rise in WBC from 16.3 (6.3) K/ $\mu$ L to 16.9 (6.2) K/ $\mu$ L, with a difference of 0.65 K/ $\mu$ L. **Figure 8** shows that WBC in the AVMUF group increased by 9.5%, whereas in the VAMUF group it increased by 4.0%.

The mean (SD) PLT count in the AVMUF group increased from 165.2 (37.1) K/ $\mu$ L to 172.2 (47.9) K/ $\mu$ L, with a difference of 5.9 K/ $\mu$ L (**Table 12**). In the VAMUF group, it rose from 193.7 (56.5) K/ $\mu$ L to 198.7 (54.5) K/ $\mu$ L, with a difference of 4.97 K/ $\mu$ L. Both the AVMUF group (4.6%) and the VAMUF group (4.5%) showed a positive increase in the PLT count (**Figure 9**), thereby improving clotting factors that assist in reducing postsurgical bleeding.

The mean (SD) serum Alb in the AVMUF group increased from 22.9 (5.4) g/L to 29.2 (6.6) g/L, with

**Table 4.** Fluid management data.

Group	Total fluid input (mL)	Standard deviation	Total fluid output (mL)	Standard deviation	Fluid balance (mL)	Standard deviation
AVMUF (n=30)	2702.67	1282.02	2118.67	1028.11	598.33	410.41
AVMUF (%)	100 %	0	79.5%	9.1%	20.8%	9.1%
VAMUF (n=30)	2947.33	1362.89	2481.17	1187.50	449.17	280.59
VAMUF (%)	100 %	0	84.2%	8.8%	15.1%	6.9%

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, CPB: cardiopulmonary bypass. Total Fluid Input=Preoperative fluid input + CPB fluid prime + Cardioplegia + Fluid added on CPB. Total Urine Output=Urine output pre-CPB + urine output during-CPB + urine output post-CPB. Total Fluid Output = Total CUF + Total MUF + Total Urine output + Total in drains. Total Fluid Balance = Total fluid input - (Total CUF + Total MUF + Total urine output)

**Table 5.** Electrolyte concentrations in the AVMUF and VAMUF groups.

Variables	AVMUF (n=30)		VAMUF (n=30)		P value
	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	
Na+ (mmol/L)	136.7 (3.0)	138.2 (3.2)	137.1 (3.5)	139.6 (4.9)	.271
K+ (mmol/L)	4.0 (0.6)	3.8 (0.5)	4.0 (0.6)	3.8 (0.6)	.590
Ca <sup>2+</sup> (mmol/L)	1.3 (0.4)	1.2 (0.3)	1.3 (0.3)	1.2 (0.3)	.990
PO <sub>4</sub> <sup>-</sup> (mmol/L)	0.9 (0.4)	0.9 (0.4)	1.0 (0.3)	1.0 (0.4)	.640
Mg <sup>2+</sup> (mmol/L)	1.2 (0.3)	1.1 (0.3)	1.1 (0.3)	1.0 (0.2)	.388

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration.

**Table 6.** Renal related markers in the AVMUF and VAMUF groups.

Variables	AVMUF (n=30)		VAMUF (n=30)		P value
	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	
BUN (mmol/L)	4.9 (2.3)	4.8 (2.1)	5.7(3.5)	5.6 (3.4)	.520
BUN (%)	100	102.6 (15.6)	100	98.3 (10.5)	.221
S-Creat (mmol/L)	67.9 (37.2)	67.1(38.1)	71.1 (25.1)	59.8 (26.0)	.001
S-Creat-(%)	100	98.7 (17.4)	100	82.8 (18.7)	.001
Uric acid (mmol/L)	272.2 (85.2)	268.9(77.8)	276.5 (±76.9)	258.1(65.8)	.027
S – Uric acid (%)	100	99.9 (10.4)	100	94.1 (9.2)	.025

BUN: Blood urea nitrogen, S-Creat: S-creatinine, MUF: modified ultrafiltration.

**Table 7.** Anesthetic, perfusion, and clinical data.

Variables	AVMUF (n=29) Mean (SD)	VAMUF (n=29) Mean (SD)	P value
Ventilation time (h)	15.1 (5.1)	10.2 (2.6)	<.001
ICU stay (h)	46.3 (25.7)	30.1 (11.0)	.003
Hospital stay (d)	8.7 (1.9)	7.4 (1.8)	.007
Discharge days (POD)	7.8 (1.9)	6.4 (1.8)	.007

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, ICU: intensive care unit, POD: post-operative days. Ventilation time (h): The total time the patient is on the ventilator postoperatively in ICU. ICU stay (h): Reflects the total time patient was brought to ICU post-bypass until they leave the unit. Hospital stay (d):- Reflects the total number of days the patient spends in the hospital until discharge. Discharge days (POD): Includes days from the date of surgery until the day of discharge.

**Table 8.** CUF and MUF data in the AVMUF and VAMUF groups.

Variables	AVMUF (n=30) Mean (SD)	VAMUF (n=30) Mean (SD)	P value
CUF volume (mL)	150 (363)	325 (700)	.043
MUF volume (mL)	900 (438)	825 (613)	.275

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, CUF: conventional ultrafiltration, MUF: modified ultrafiltration, CPB: cardiopulmonary bypass. Total CUF = Ultrafiltrate removed from the circuit during CPB. Total MUF= Ultrafiltrate removed from the patient and circuit post-CPB.

**Table 9.** Hemodynamic variables in the AVMUF and VAMUF groups.

Variables	AVMUF (n=30)		VAMUF (n=30)		P value
	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	
HR (bpm)	109.7 (19.1)	106.5 (19.2)	106.03 (17.3)	92.57 (17.1)	<.001
HR (%)	100	97.0 (6.4)	100	87.4 (8.6)	<.001
SP (mm Hg)	99 (13.4)	108.3 (10.8)	93.07 (12.6)	114.6 (12.5)	<.001
SP (%)	100	110.1 (8.3)	100	124.07 (11.1)	<.001
DP (mm Hg)	51.3 (10.4)	59.0 (10.2)	50.0 (7.1)	56.57 (7.0)	.533
DP (%)	100	116.9 (18.0)	100	113.8 (11.9)	.447
MP (mm Hg)	65.8 (8.7)	71.7 (6.6)	61.6 (±7.9)	74.9 (7.5)	<.001
MP (%)	100	109.7 (10.4)	100	122.9 (16.4)	<.001
CVP (cmH <sub>2</sub> O)	12.1 (3.8)	10.4 (3.2)	12.3 (3.4)	9.53 (±3.7)	.002
CVP (%)	100	86.5 (8.8)	100	76.1 (13.2)	.001

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, MUF: modified ultrafiltration, CVP: central venous pressure, HR: heart rate. The VAMUF group showed the largest decrease in heart rate (HR) and CVP. The mean pressure also increased more in the VAMUF group than in the AVMUF group.

**Table 10.** Blood gas analysis data.

Variables	AVMUF (n=30)		VAMUF (n=30)		P value
	Pre- MUF Mean (SD)	Post- MUF Mean (SD)	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	
pO <sub>2</sub> (mm Hg)	218.8 (102.0)	194.9 (72.1)	202.8 (89.6)	199.47 (81.9)	.287
pO <sub>2</sub> (%)	100	96.6 (27)	100	105.8 (42.2)	.322
pCO <sub>2</sub> (mm Hg)	36.7 (4.9)	37.1 (5.9)	35.3 (5.7)	34.6 (2.5)	.488
pCO <sub>2</sub> (%)	100	103.0 (26.6)	100	100.1 (14.1)	.590
SaO <sub>2</sub> (%)	99.0 (1.6)	99.3 (1.1)	99.0 (2.4)	99.8 (0.7)	.191

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, MUF: modified ultrafiltration.

a difference of 6.2 g/L. In the VAMUF group, serum Alb increased from 22.3 (4.5) g/L to 32.2 (4.7) g/L, with a difference of 11.9 g/L (Table 11). Serum Alb in the AVMUF group increased by 28.3%, whereas the VAMUF study group demonstrated a more significant increase of 56.2%. The results in Figure 10 suggests that the VAMUF group had a more significant impact

on increasing the serum proteins like Alb ( $P < .001$ ), thereby increasing blood viscosity and oncotic pressures that could possibly encourage tissue perfusion post-surgery.

Table 12 represents the analysis of cardiac markers expressed as mean (SD). Only serum lactate showed a significant difference over time between the treatment

**Table 11.** Haematological data analysis.

Variables	AVMUF (n=30)		VAMUF (n=30)		P value
	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	Pre-MUF Mean (SD)	Post-MUF Mean (SD)	
Hct (%)	26.2 (2.9)	31.7 (5.7)	25.2 (3.5)	33.8 (4.0)	.006
Hb (g/dL)	8.8 (0.9)	10.8 (1.4)	8.4 (1.1)	11.3 (1.3)	.001
Hb (%)	100	122.5 (15.3)	100	134.5 (12.4)	.001
RBC (M/ $\mu$ L)	3.3 (1.1)	3.7 (0.6)	3.1 (1.4)	3.8 (0.7)	.056
RBC (%)	100	114.5 (15.9)	100	124.3 (18.0)	.030
WBC (K/ $\mu$ L)	15.0 (7.3)	16.1 (9.6)	16.2 (6.3)	16.9 (6.2)	.781
WBC (%)	100	109.4 (51.0)	100	103.9 (31.0)	.927
PLT (K/ $\mu$ L)	165.2 (37.1)	172.2 (47.9)	193.7 (56.5)	198.6 (54.5)	.919
PLT (%)	100	104.5 (23.7)	100	104.5 (21.2)	.999
Alb (g/L)	22.9 (5.4)	29.2 (6.6)	22.3 (4.5)	32.2 (4.7)	<.001
Alb (%)	100	128.2 (15.5)	100	156.1 (19.8)	<.001

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, MUF: modified ultrafiltration, Hct: hematocrit, Hb: haemoglobin, RBC: red blood cell, WBC: white blood cell, PLT: platelet, Alb: albumin.

**Table 12.** Cardiac markers in the AVMUF and VAMUF group.

Variables	AVMUF (n=30)		VAMUF (n=30)		P value
	Pre -MUF Mean (SD)	Post-MUF Mean (SD)	Pre- MUF Mean (SD)	Post-MUF Mean (SD)	
CK (U/L)	541.0 (334.9)	719.6 (436.1)	435.3 (219.9)	551.1 (242.1)	.140
CK-MB (IU/L)	16.8 (12.2)	16.8 (5.9)	16.9 (6.9)	22.6 (13.8)	.062
CK-MB (%)	4.2 (3.6)	3.9 (3.6)	5.0 (3.4)	4.7 (2.9)	.825
S-Lact (mmol/L)	3.6 (1.4)	3.2 (1.3)	3.9 (1.0)	2.5 (0.9)	<.001
S-Lact (%)	100	88.7 (12.9)	100	62.1(14.7)	<.001

AVMUF: Arteriovenous modified ultrafiltration, VAMUF: venoarterial modified ultrafiltration, MUF: modified ultrafiltration, CK-MB: creatinine kinase myocardial band.

arms ( $P < .001$ ). The VAMUF arm showed a larger decrease between pre- and post-MUF than the AVMUF arm. The change in the other variables did not differ significantly between the treatment arms.

**Table 12** demonstrates that mean (SD) CK values in the AVMUF group increased from 541.0 (334.9) U/L to 719.6 (436.1) U/L, with a mean difference 189.6 U/L. In the VAMUF group, CK increased from 435.3 (219.9) U/L to 551.1 (242.1) U/L, with a mean difference of 115.8 U/L. **Figure 11** illustrates that there was a more significant increase in CK in the AVMUF group compared to the VAMUF study group.

**Figure 12** demonstrates that there was no significant difference in the 2 groups. In the AVMUF group,

the mean (SD) CK-MB decreased from 4.2% (3.6) to 3.97% (3.6), with a difference of 0.4%, and in the VAMUF group it decreased from 5.03% (3.4) to 4.79% (2.9), with a mean difference of 0.24%.

**Table 12** demonstrates that mean (SD) serum lactate levels decreased in the AVMUF group from 3.6 (1.4) mmol/L to 3.2 (1.3) mmol/L, with a mean difference of 0.42. In the VAMUF group, it decreased from 3.9 (1.0) mmol/L to 2.5 (0.9) mmol/L, with a mean difference of 1.46 mmol/L. A more significant decrease was observed in serum lactate in the VAMUF study group (37.9%) than in the AVMUF control group, which had a decrease (11.2%) after MUF post-CPB (**Figure 13**).



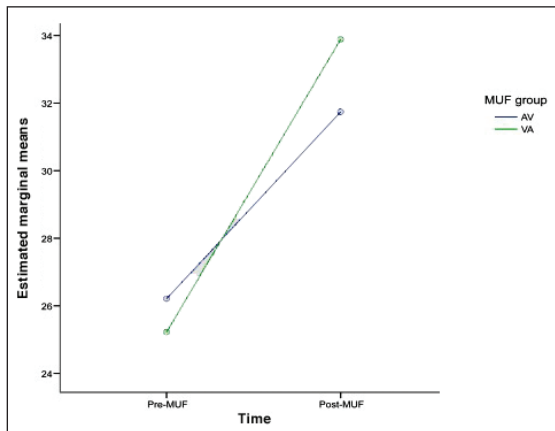


Figure 5. Profile plot of mean Hct over time by treatment arm ( $P=.006$ )

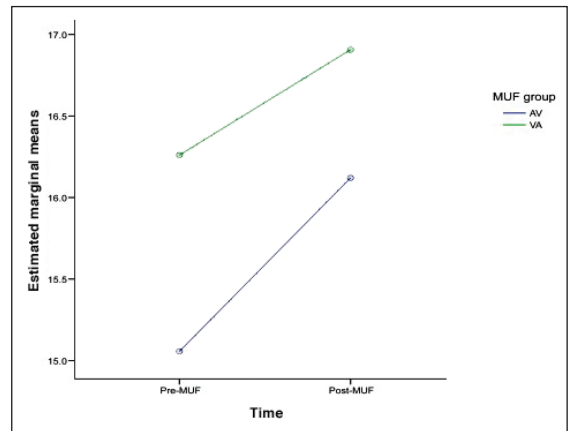


Figure 8. Profile plot of mean WBC over time by treatment arm.

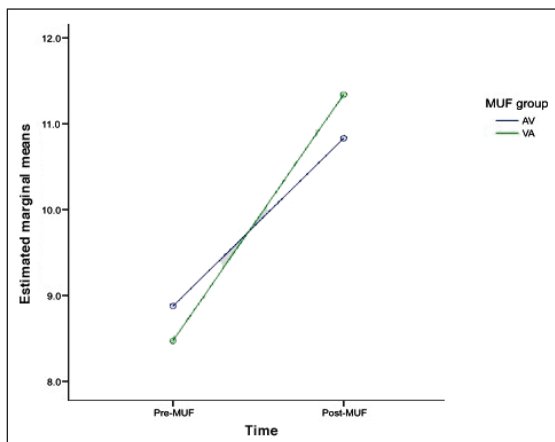


Figure 6. Profile plot of mean Hb over time by treatment arm ( $P=.001$ ).

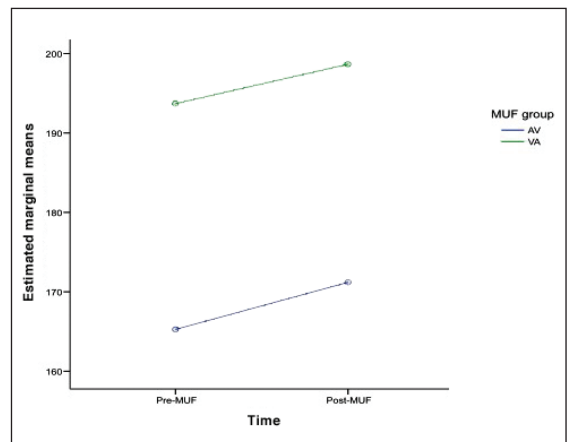


Figure 9. Profile plot of mean platelets over time by treatment arm.

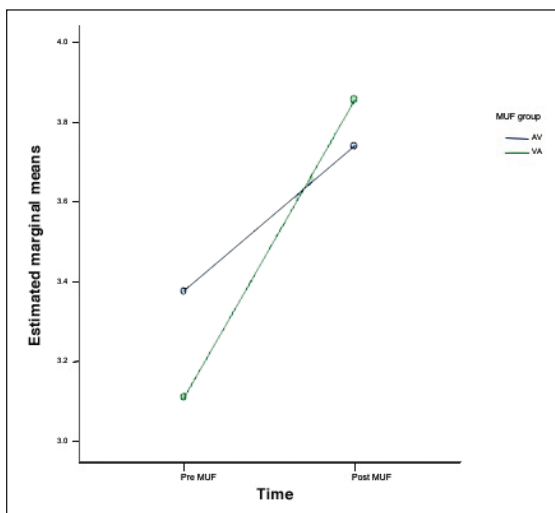


Figure 7. Profile plot of mean RBC over time by treatment arm ( $P=.030$ ).

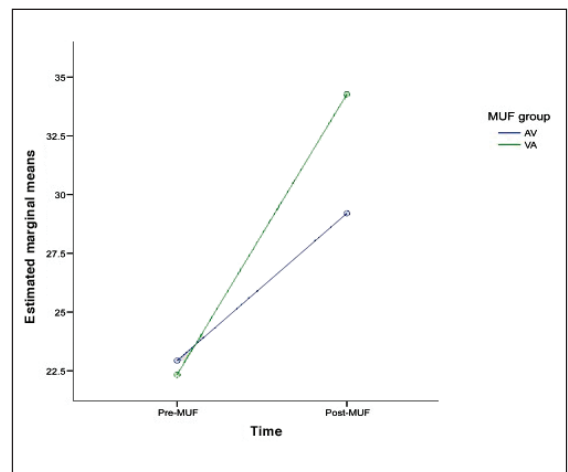


Figure 10. Profile plot of mean albumin over time by treatment arm ( $P<.001$ )

## DISCUSSION

Numerous types of MUF were investigated during the preliminary studies of this research. One of them included the conventional AVMUF used by Naik et al.<sup>3</sup>

Some were circuits taken from publications, whereas a few were selected from the feedback acquired from other hospitals. All these various techniques of MUF were compared to the VAMUF circuit that was designed uniquely in this study.

No published studies had suggested that VAMUF had been attempted or published at other centers worldwide. During the VAMUF, the blood that was removed from the RA via the venous cannula flowed through the hemoconcentrator. The filtrated blood was then returned to the aorta through the aortic cannula. This method followed the same physiology as CPB and the body's normal blood flow pattern.

To terminate MUF, different centers used different criteria. Some terminated MUF when the CPB circuit contents were completely salvaged,<sup>6</sup> some used a time-based criterion,<sup>3</sup> others used an Hct end point,<sup>7</sup> and a few used an ultrafiltrate volume end point.<sup>8</sup> Although the use of varying techniques and end-point criteria made the interpretation of published results difficult, the beneficial effects of MUF have still been independently reproduced at many institutions. The VAMUF system incorporated all of these criteria documented in the above-mentioned publication while taking into consideration optimal Hct, volume constraints, calculated excess fluid volume, and blood flow dynamics.

This experimental study explored the difference in the method of performing MUF on a total of 60 patients (30 VAMUF and 30 AVMUF) to establish which technique was more physiological and followed the normal physiological blood flow pathway of the body and the CPB circuit.

No significant differences were observed in any of the demographic variables or type of procedures included in this study.

Electrolyte variables in this study demonstrated that there were no significant differences in the changes in any electrolyte between pre-MUF and post-MUF in both groups. The changes on serum sodium (Na<sup>+</sup>), serum potassium (K<sup>+</sup>), serum calcium (Ca<sup>2+</sup>), serum phosphate (PO<sub>4</sub><sup>-</sup>), serum Magnesium (Mg<sup>2+</sup>), after MUF were insignificant. However, although there were no significant difference in change between electrolytes in pre-MUF and post-MUF, both groups demonstrated that they did not have a negative impact on electrolyte balance.

Fluid management data revealed that there was a statistically significant difference in the fluid output be-

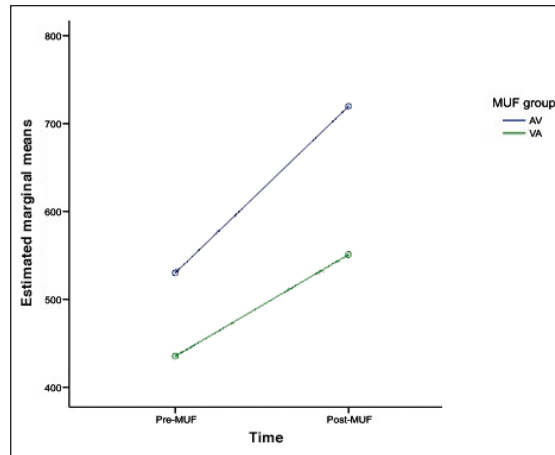


Figure 11. Profile plot of mean creatinine kinase (CK).

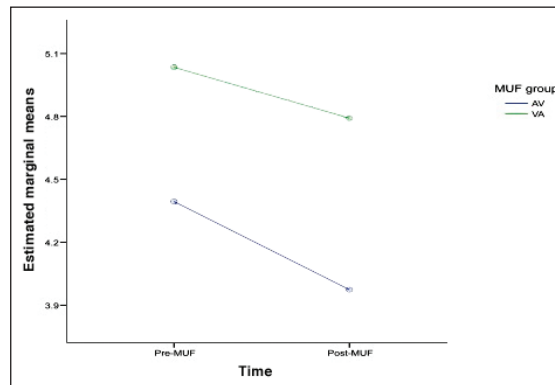


Figure 12. Profile plot of mean CK-MB percent by treatment arm.

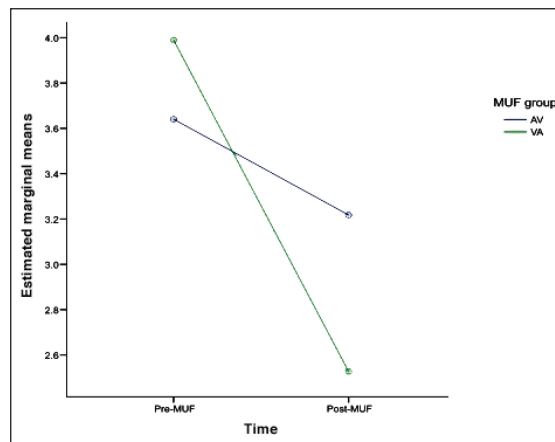


Figure 13. Mean serum lactate (s-lact) ( $P < .001$ ).

tween the 2 groups ( $P=.044$ ) with the VAMUF arm having a greater percentage output than the AVMUF. There was also a statistically significant difference in the fluid balance between the 2 arms ( $P=.008$ ) with the VAMUF arm having a lower percentage fluid balance than the AVMUF arm. After MUF, the VAMUF patients had a remaining fluid balance of 15.11% of the total fluid input, whereas the AVMUF patients had a higher remaining fluid balance of 20.81% of the total fluid input. This decrease in decreased remaining fluid balance after MUF was also documented in other studies.<sup>3,7</sup>

The effects of MUF on metabolites and renal-related markers showed that creatinine and uric acid had a significantly greater decrease over time in the VAMUF group ( $P<.001$  and  $P<.027$ , respectively). The ratio of urea to creatinine also showed significant differences between the treatment arms, but the VAMUF group showed a greater increase over time than the AVMUF group. However, it is not clear if the removal of these markers actually signify end-organ improvement after MUF. More studies will have to be carried out to prove their relationship in the future.

The VAMUF patients had a significant decrease of 1.61% on their serum BUN after CPB, whereas the patients who underwent AVMUF demonstrated an increase of 2.64%. This suggested that VAMUF was more effective in removing BUN than AVMUF. However, a study performed by Williams and team in 2006 noted that urea measurement 48 hours postsurgically showed no signs of any difference between DUF and MUF.<sup>9</sup>

When compared to the AVMUF group, the VAMUF group demonstrated significant improvement in immediate postsurgical arterial oxygenation in patients. The VAMUF also resulted in higher arterial pressures. Moreover, the VAMUF patients required less homologous blood transfusion and had shorter ventilatory support time than the AVMUF. Shorter ventilation time as a result of MUF was documented by Meliones et al., which may have been due to the removal of free water and the use of fewer transfusions that may have contributed to improved pulmonary mechanics after CPB.<sup>10</sup> This is probably what caused earlier extubation in the VAMUF patient group. The removal of small molecule inflammatory agents, including endothelin-1 (a potent pulmonary vasoconstrictor)<sup>11</sup> and other cytokines, may have also played a significant role in lowering postsurgical pulmonary arterial pressure and reducing lung injury after reperfusion.<sup>8</sup>

The results of the study also confirmed that there was a statistically significant difference in the ventilation time between the two arms of the study ( $P<.001$ ).

The VAMUF group showed a much lower ventilation time than the AVMUF group. Previous MUF studies also showed a decrease in ventilation time in patients who underwent MUF as was demonstrated in this study.<sup>12-14</sup> ICU stay, hospital stay, and discharge days were reduced in both groups as noted by other studies.<sup>1,9,10</sup> However, these values were significantly lower in the VAMUF group.

Hemodynamic data showed that the change between pre-MUF and post-MUF was significantly different between the 2 groups in terms of heart rate and CVP. The VAMUF group showed a larger decrease. This group also demonstrated a greater increase in terms of systolic and mean pressure as compared to the AVMUF group. There was a more significant drop in heart rate in the VAMUF group as compared to the AVMUF group ( $P=.001$ ) with an increase in the mean blood pressure (BP). The advantages of a decrease in heart rate with an increase in the mean BP post-MUF was also documented.<sup>15</sup>

The VAMUF group showed a more significant rise of 24.07% in the mean systolic BP in comparison to the AVMUF group that had a 10.18% rise in the mean systolic BP (post-surgery 0.001). The rise in systolic BP was published in previous studies.<sup>15-18</sup>

The VAMUF group displayed a more significant rise in the mean BP with a 22.93% elevation in the mean arterial BP, whereas the AVMUF group displayed an increase of 9.78% in the mean BP. The AVMUF group demonstrated a CVP decrease of 13.5%, whereas the VAMUF group demonstrated a more significant reduction of 23.88% of the pre-MUF CVP, with an increase in the mean pressure.

The VAMUF group had more control over the post-bypass serum oxygen transition rate with an increase of +5.8%, whereas the AVMUF had a  $pO_2$  drop of  $\approx 3.3\%$ . This increase in  $pO_2$  post-MUF was documented by Aeba et al.<sup>19</sup> No significant changes were noted in the  $pCO_2$  levels from pre-MUF to post-MUF in both the groups, although as related to other studies both groups showed an improvement in  $pCO_2$  levels after MUF.<sup>19,20</sup> No significant changes were observed in pre-MUF and post-MUF arterial oxygen saturation that remained stable and within normal ranges, thus making these procedures safe with regard to oximetry parameters.

Hematological data that included Hct, HB, RBC, and Alb showed significant differences in change from pre-MUF to post-MUF between the 2 groups. The VAMUF group had a more significant increase in the mean Hct from 25.2% (3.5) to 33.9% (4.0) with an increase of 8.66%. This increase in Hct was documented in previous trials.<sup>21</sup> The VAMUF group had a more

significant rise of 34.6% in Hb as compared to the AVMUF group that had a 22.5% increase in Hb. This rise in Hb was in keeping with previous studies.<sup>22,23</sup>

Hematological results indicated that the RBC count in the VAMUF group increased by 24.3%, whereas it only increased by 14.6% in the AVMUF group. Fujita et al. also published a study that documented that the RBC count increased post-MUF. White blood cells increased by 4.0% in the VAMUF group, whereas it increased by 9.5% in the AVMUF group.<sup>25</sup> This significant difference ( $P=.781$ ) suggested that VAMUF caused less WBC activation.

The effects of MUF on the patient's PLT count was first documented by Ootaki et al and Fujita et al.<sup>24,25</sup> Both the AVMUF group and the VAMUF group showed a positive increase of 4.6% and 4.5%, respectively in the PLT count. Hence, this improved clotting factors that assisted in reducing postoperative bleeding.

The VAMUF group demonstrated a more significant increase of 56.2% in serum Alb, whereas the AVMUF group only achieved a 28.3% increase in serum Alb. These results suggested that the VAMUF group had a more significant impact on increasing the

serum proteins like Alb (post-surgery 0.001), thereby increasing blood viscosity and oncotic pressures that could have possibly encouraged tissue perfusion post-cardiac surgery.<sup>24,25</sup>

A limitation with the VAMUF circuit was that it required a greater volume of blood to remain in the CPB/MUF circuit, whereas the AVMUF circuit used smaller size tubing from the hemoconcentrator to the patient. Nevertheless, this did not pose as a serious problem because all the blood from the circuit volume was returned to the patient at the end of MUF in both groups.

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