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ORIGINAL ARTICLE

Zero Balance versus Conventional Hemofiltration-Impact on Renal Function and Blood Conservation in Adult Valvular Cardiac Surgery

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ABSTRACT

Aim: To compare conventional ultrafiltration (CUF) with zero-balanced ultrafiltration (Z-BUF) in the patients having valvular heart surgery.
Methods: This cross-sectional mono-centered retrospective study was designed. The data of total 471 patients were reviewed during March 2018 to February 2020, only 98 patients fitted in the inclusion criteria and were divided into two groups with 47(47.95%) patients received CUF, while 51 (52.04%) patients were administered with Z-BUF at the Department of Cardiovascular Surgery, King Edward Medical University, Lahore, Pakistan. Statistical analysis was done using SPSS version 25. The early postoperative clinical outcomes included, renal function as primary outcome and hemodynamics stability of the patients as secondary outcome.
Results: Renal functions in terms of serum creatinine (1.1 vs. 1.3mg/dL; P < 0.010) and creatinine clearance ratio (81.51vs. 67.3mL/min; P < 0.01) were improved in the patients having Z-BUF compared with CUF. Urine output was almost double in the Z-BUF cohort compared with the CUF. The hemofiltration technique had no impact on the secondary outcomes as amount of the blood loss and number of patients required blood transfusion were similar (P > 0.05) in our cohort.
Conclusion: Z-BUF appeared to be better hemofiltration method than CUF during CPB when assessed in terms of renal protection without hemodynamic status in patients undergoing valvular heart surgeries in our population.
Keywords: Cardiopulmonary bypass, Ultrafiltration, Renal injury, Hemoglobin, Blood transfusion

INTRODUCTION

Hemofiltration for the treatment of patients having fluid overload and resistant to diuretics was firstly described by Kramer in 1977[1]. The decrease in hematocrit (HCT) during CPB, termed as heamodilution, is most often caused by preoperative fluid infusions, priming the CPB circuit, use of crystalloid part of cardioplegia and surgical blood loss. These factors not only decrease the HCT level and become a cause of volume overload but also result in adverse physiologic effects, increase in cost of operation and haemostatic alternations[2]. Employment of crystalloid priming solutions in CPB circuit is normal practice in adult cardiac surgery[3]. Therefore, hemodilutional impact on hematocrit levels and, thereafter, on kidney function is the subject of much concern[4]. Different techniques including altering the setup of the CPB circuit, decreasing its volume of solution utilized, replacement of prime with blood (autologous or homologous), introducing a negative balance by delivering diuretics and use of hemofiltration have been identified to encounter the heamodilution and its linked effects[5]. Hemofiltration has been shown to decrease total body water and postoperative blood loss and also to improve alveolar to arterial oxygen gradient and pulmonary compliance[6]. The importance of hemofiltration to prevent acute kidney injury (AKI) is due to improvement in HCT[7].

Hemofiltartion during CPB can be achieved either by the Conventional Ultrafiltration (CUF) method or by Zero-Balance Ultrafiltration (Z-BUF) method. The CUF is being used to remove extra fluid from blood during CPB and, thereby, induce hemoconcentration by elevating HCT and less need of blood transfusion[8]. The latter method, Z-BUF, is being employed to filter excess fluid from blood which is, then, replaced with an equal volume of crystalloid solution[9]. The CUF is frequently used to mitigate the effect of heamodilution and anaemia by removing the intravascular plasma water[10-12]. Although earlier evidences suggested that removal of plasma water by CUF reduced intraoperative allogeneic packed red blood cell transfusion and bleeding, but the evidence is not sufficient that CUF can alleviate anaemia and to improving oxygen delivery[13]. It appears that the effects of CUF on various organs remain unclear as more ultrafiltrate volumes may lead to hypovolemia and renal hypoperfusion[10]. It has been found that Z-BUF significantly improves clinical outcomes in patients with preoperative chronic kidney impairment, possibly through the protection of kidneys from CPB-induced acute injury[14]. However a study described that applying Z-BUF versus without use of Z-BUF the urine output was relatively higher and did not influence kidney function markers[14]. It looks that intraopertaive hemofiltration by CUF and Z-BUF has its own benefits and drawbacks and there are insufficient evidences regarding the benefits Z-BUF compared with CUF on the improvement in the renal functions and early clinical outcomes in valvular heart surgeries in our population. To best of our knowledge, there is no study that compared the effects of CUF and Z-BUF methods on early clinical outcomes in valvualr cardiac surgery.

Therefore, we conducted a retrospective cross-sectional study to compare the usefulness of CUF and Z-BUF on renal functions as primary outcomes and blood

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conservation as secondary outcome in patients brought for various elective valvular cardiac surgeries in our institute.

MATERIALS AND METHODS

Study Deign and Patients: We retrospectively reviewed the medical data of patients that were brought to the Department of Cardiovascular Surgery, King Edward Medical University/Mayo Hospital, Lahore, Pakistan after approval from IRB, for various cardiac interventions during March 2018 to February 2020. This study was approved by the Institutional Review Board, King Edward Medical University, Lahore (No. 501/RC/KEMU dated 09-07-2021). The patients having surgeries for coronary artery bypass grafting (CABG), severe pulmonary hypertension, preoperative uncontrolled diabetes, chronic renal failure, depressed left ventricular function (effective fraction ≤30%) and redo valves were excluded from the study. Patients who were preoperatively anaemic, on intra-aortic balloon pump, any ongoing infection or brought to some emergency were also not included in the study. Based on the type of hemofiltration, the patients were divided into two different groups; patients having CUF or having Z-BUF during CPB.

Basal Characteristics of Patients: Baseline information of patients like gender, age, diabetes status, body mass index, ejection fraction, renal function tests including serum creatinine, blood urea and creatinine clearance ratio (CrCl) were extracted from the record. Baseline blood parameters like platelet count, and white blood cell count, blood biochemistry including serum bilirubin, serum glutamic pyruvic transaminase (SGPT) and serum glutamic oxaloacetic transaminase (SGOT) were noted from the medical record. The Society of Thoracic Surgeons National Cardiac Surgery Database definitions were used for the study[15].

Intraoperative and Postoperative Characteristics: The CPB was performed as described earlier under general anesthesia[16]. Hemofiltration either CUF or Z-BUF was carried out using a hemofilter (Sorin/SH14, Arvada, USA) during the rewarming phase of CPB in association to the accessibility of circulating volume and the hematocrit targeted 27-30% at the time of weaning off from CPB. For Z-BUF, an equal amount of isotonic crystalloid fluid (Ringer lactate) was added to keep the fluid balance relatively even. Intraoperative variables comprising CPB time, aortic cross clamp (ACC) time, hemoglobin concentration, volume of filtrate and urine output were recorded. Similarly, activated clotting time (ACT), bilirubin, SGPT, SGOT, leucocytes count and platelet count were also noted from the medical database. Postoperative variables extracted from the medical record were inotropic support (adrenalin infusion rate), weight-indexed filtration volume, ventilation time and length of ICU-stay.

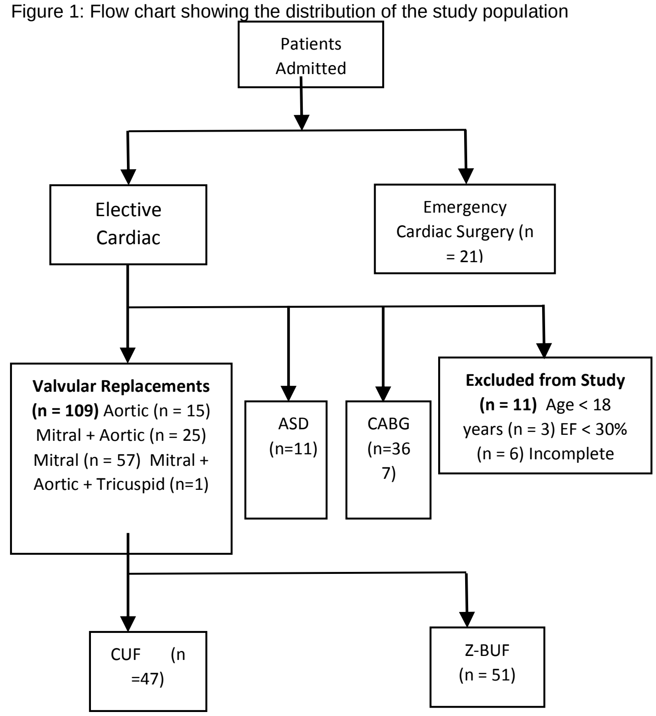
Study Endpoints: Primary outcomes of the study were postoperative renal function status in terms of serum creatinine, CrCl ratio, and intraoperative urine output obtained from the medical record. Acute kidney injury criteria in cardiovascular surgery patients was defined by considering the values of serum creatinine and urine output[17]. The secondary outcome, blood conservation through chest tube drainage (blood loss) and number of patients that required blood transfusion were noted.

Statistical Analysis: Data were entered and analyzed using the Statistical Package for the Social Sciences program (SPSS Version 26.0. Armonk, NY, USA). Normal distribution of the data was determined using Kolmogorov-Smirnov test. Quantitative variables were presented as a mean ± SD for normally distributed values. Medians (Range) were used to express the data that were not normally distributed. Qualitative variables were presented as frequency, proportion and percentage. Continues data were compared using either independent Student t test or Mann–Whitney U test whichever is applicable. Categorical data were compared using Pearson's π^2 test. Probability value < 0.05 was considered significant. P-values, adjusted for multiple primary and secondary endpoints, were set at p=0.016 and p=0.025, respectively, as already described[18].

RESULTS

Record of 471 patients evaluated during the study period, 450(95.94%) underwent elective cardiac surgery. Within this cohort, 321(71.33%) patients were surgically treated for CABG, while only 109(23.14%) patients underwent valvular surgeries. Only 98(20.80%) patients fulfilled our inclusion criteria (Figure 1). The number of patients operated for aortic valve replacement, double valve replacement (mitral + aortic), mitral valve replacement, triple valve replacement (mitral + aortic + tricuspid) were 15, 25, 57, and 1 respectively. Medical records showed that 47(47.95%) patients received CUF, while 51(52.04%) patients were administered with Z-BUF (Figure 1).

Figure 1: Flow chart showing the distribution of the study population



CABG = Coronary artery bypass grafting; ASD = Atrial septal defect; EF = Ejection fraction.

Table 1 shows that there was similarity with regard to age, weight, body mass index and gender of patients in both groups. The status of diabetes and ejection fraction did not show any difference in both groups. Baseline investigations described that there was no difference in blood urea, hemoglobin, serum creatinine and CrCl in the patients of both groups. Liver function tests (SGPT, bilirubin and SGOT) were also same in both groups. Similarly, we did not find any difference with regard to leukocyte count and platelet count (Table 1).

Study Endpoints: The results of both primary and secondary outcomes are shown in the Table 2. As far as the primary outcomes are concerned, postoperative serum creatinine ($P < 0.05$) were lower with better creatinine clearance ratio ($P < 0.01$) in patients having Z-BUF compared with CUF patients. Urine output was significantly higher ($P < 0.001$) in patients having Z-BUF when compared with the patients treated with CUF. For secondary endpoints, there were no statistical differences with regards to blood loss and number of patients that needed transfusion between groups.

Intra-operative Parameters: As shown in Table 3, the filtrate volume ($P < 0.001$) and weight-indexed filtration volume ($P < 0.01$) were higher in Z-BUF patients when compared to the patients having CUF during CPB. There were no intergroup variations for ACC time, CPB time, blood sugar random, hemoglobin and ACT in both groups (Table 3).

Postoperative parameters: Table 4 showed that the liver enzymes (SGPT and SGOT) were similar in both groups. No intergroup differences were noted for blood urea, adrenalin infusion rate, leukocyte count and platelet count, hemoglobin concentration, ACT, ventilation support and ICU – stay in both groups.

Table 1: Baseline parameters

Parameter	Types of Hemofiltration; Median (Range)		P-Value
	CUF (n = 47)	Z-BUF (n = 51)	
Age (Years)	54 (19 – 71)	55 (20 – 70)	0.795
Weight (Kg)†	67.17 ± 11.57	70.60 ± 13.91	0.179
Body mass index (kg/m^2)†	25.09 ± 3.96	25.92 ± 4.41	0.507
Hemoglobin (g/dL)†	14.60 ± 1.85	14.32 ± 1.85	0.934
Sex (male); n (%)	36 (76.59)	37 (72.54)	0.646
Diabetic (Yes); n (%)	15 (31.91)	21 (41.17)	0.342
Ejection fraction (%)	56 (35 – 77)	55 (30 – 78)	0.717
Blood urea (mg/dL)	28 (15 – 85)	29 (20 – 73)	0.611
Creatinine (mg/dL)	0.90 (0.50 – 1.31)	1.00 (0.60 – 1.60)	0.034
CrCl (mL/min)†	91.79 ± 25.11	87.26 ± 27.71	0.409
Bilirubin (mg/dL)	0.74 (0.40 – 2.60)	0.60 (0.38 – 2.40)	0.606
SGPT (µ/L)	25 (14 – 156)	28 (13 – 163)	0.409
SGOT (µ/L)	37 (17 – 124)	42 (16 – 153)	0.374
White blood cells count (10^3/µL)	9.90 (5.60 – 25.60)	9.25 (4.90 – 26.20)	0.553
Platelets count (10^3/µL)†	252.35 ± 81.34	249.56 ± 98.60	0.192

CUF = Conventional ultrafiltration; Z-BUF = Zero balance ultrafiltration; CrCl = Creatinine clearance ratio; SGPT = Serum glutamic pyruvic transaminase; SGOT = Serum glutamic oxaloacetic transaminase; †Values are expressed as Mean ± SD.

Table 2: Primary and secondary outcomes

Parameter	Types of Hemofiltration; Median (Range)		P-Value
	CUF (n = 47)	Z-BUF (n = 51)	
Primary Outcomes			
Post-operative creatinine (mg/dL)	1.3 (1.0 – 1.7)	1.1 (0.6 – 1.9)	0.010
Post-operative CrCl (mL/min) †	67.33 ± 14.76	81.51 ± 26.73	0.003
Urine output (mL)	550 (380 – 750)	1050 (440 – 1050)	0.000
Secondary Outcomes			
Blood loss (mL)	500 (40 – 1560)	470 (170 – 1550)	0.898
Blood transfusion; n (%)	6 (12.76)	5 (9.80)	0.643

CUF = Conventional ultrafiltration; Z-BUF = Zero balance ultrafiltration

Table 3: Intra-operative parameters

Parameter	Types of Hemofiltration; Median (Range)		P-Value
	CUF (n = 51)	Z-BUF (n = 51)	
Aortic cross clamp time (minutes)	50 (22 – 163)	60 (27 – 171)	0.063
CPB time (minutes)	100 (38 – 197)	101 (63 – 218)	0.553
Blood sugar (g/dl)†	208.72 ± 61.14	220.96 ± 74.01	0.302
Filtrate volume (mL)	1600 (1200 – 1800)	1800 (1700 – 2000)	<0.001
weight-indexed filtration (mL/kg)	22.66 (16.67 – 37.50)	25.64 (18.75 – 46.34)	0.005
Hemoglobin (g/dL)	8.8 (5.5 – 12.5)	8.3 (5.5 – 12.9)	0.614
Activated clotting time (seconds)	660 (400 – 1141)	609 (363 – 1473)	0.787

CUF = Conventional ultrafiltration; Z-BUF = Zero balance ultrafiltration; CPB = Cardiopulmonary bypass; †Values are expressed as Mean ± SD.

Table 4: Post-operative investigations

Parameter	Types of Hemofiltration; Median (Range)		P-Value
	CUF (n = 51)	Z-BUF (n = 51)	
Blood Urea (mg/dL)	39 (18 – 81)	35 (18 – 95)	0.297
Hemoglobin (g/dL)†	10.84 ± 1.70	10.77 ± 1.67	0.616
Adrenalin infusion rate (µg/kg/minute)	0.05 (0.0 – 0.14)	0.05 (0.0 – 0.20)	0.565
SGPT(µ/L)	37 (15 – 359)	28 (15 – 106)	0.079
SGOT (µ/L)	62 (21 – 384)	61 (19 – 327)	0.977

White blood cells count (10^3/ μL)†	20.34 ± 6.49	18.47 ± 5.24	0.701
Platelets count (10^3/ μL)†	169.53 ± 57.48	176.94 ± 70.15	0.603
Activated clotting time (seconds)	109 (90 – 154)	111 (92 – 160)	0.504
Ventilation time (minutes)	120 (30 – 900)	121 (60 – 960)	0.297
ICU – stay (days)	5 (4 – 8)	5 (3 – 18)	0.272

CUF = Conventional ultrafiltration; Z-BUF = Zero balance ultrafiltration; SGPT = Serum glutamic pyruvic transaminase; SGOT = Serum glutamic oxaloacetic transaminase; ICU = Intensive care unit; †Values are expressed as Mean ± SD.

DISCUSSION

Cardiac surgery using CPB for valvular heart diseases is linked with volume overload in the patients which translates into tissue edema and subsequently organ dysfunction[6,19]. The use of hemofiltration during CPB to overcome hemodilutional affects for adult cardiac surgical procedures is still not clear[8]. A few studies described that CUF is beneficial in terms of improving renal function, acidosis, mortality as well as heamodilution in cardiac surgery[20,21]. On contrary to earlier statement, others claimed that Z-BUF is advantageous considering improved renal function without reduction in blood transfusions[22,23]. Therefore, it was necessary to compare both CUF and Z-BUF techniques considering primary outcome as renal function after CPB in valvular heart surgeries.

The findings of our study in which data of 98 patients were retrospectively retrieved revealed that Z-BUF in comparison with CUF is an effective hemofiltration technique which can improve renal function postoperatively without affecting the blood loss, transfusion requirements and ICU – stay of the patients undergoing valvular heart surgeries.

The present study, for the first time, is describing the effects of two methods of hemofiltrations (CUF vs. Z-BUF) on renal injury and blood conservation in patients underwent elective valvular cardiac surgery. Presently, we demonstrated that postoperative serum creatinine was higher in CUF patients compared with Z-BUF patients. The results of a multicenter study by Paugh and his colleagues support our findings that patients having CUF had an increased risk of AKI and further suggested about a small volume of CUF for those patients having lower CrCl to reduce the risk of developing AKI (10). Similarly a recent study proved our findings that renal injury, higher volumes of blood transfusions and longer ICU-stay were linked with higher volumes of CUF[24]. Another study revealed that routine use of CUF during cardiac surgery had no advantages in renal protection[7]. While a recent study described that higher ultrafiltration volumes using CUF are associated with increase in postoperative CrCl values without any change in blood transfusions in cardiac surgery[24]. On the other hand Joseph et al. using their hospital protocol for kidney preservation described in their study that Z-BUF along with optimal blood volume, haemoglobin and high mean arterial pressure during CPB can prevent the increase in serum creatinine level after cardiac surgery[25]. Similarly a single centered randomized trial in which patients received Z-BUF compared with those had not treated with Z-BUF showed significant reduction in renal injury markers like CrCl, serum creatinine and urea soon after weaning off CPB[14]. The decrease in postoperative serum creatinine and CrCl in our study might be due to reduction in the volume shift from kidneys using Z-BUF compared with CUF which is appeared to produce hypovolemia[10].

Urine output during CPB provides insight into relationships among CUF, glomerular filtration rate during CPB, and development of AKI, but adequate urine output does not necessarily means normal renal function that may be due to cold diuresis or centrally shunted nonpulsatile blood flow[5,26]. Our study showed that the Z-BUF group patients had about twice the urine output compared with CUF patients (550 vs. 1050 mL). Mongero and co-workers demonstrated that there was decreased urine volume with the higher volumes of filtrate being removed[5]. The decrease in urine volume in CUF cohort may be due to shifting of intravascular fluid in the filtrate and less extracellular fluid volume is available for urine formation that is not true for Z-BUF where equal quantity of fluid was substitute with Ringer lactate to make the extracellular fluid volume balanced.

Intraoperative hemofiltration (CUF and Z-BUF) techniques are not well established for blood conservation and for reducing postoperative blood loss in adult cardiac surgery. Regular utilization of CUF in CPB for the patients having lower bodyweight considered to be a suitable technique as it may results to improve hematocrit value without requiring extra transfusion of allogenic blood[27]. In our cohort, we could not find any differences in blood loss and number of patients that required blood transfusions in both the groups. Our study supported the findings of Golab and his colleagues showing that use of CUF during cardiac surgery affect neither blood transfusions nor clinical endpoints. Different studies conflicting with our report have shown various advantages of CUF after CPB with improved heamodynamics and decreases transfusion requirements[8,28,29]. Choi found that there was no significant difference in blood loss, ICU-stay and mechanical ventilation in patients having hemofiltration during CPB and those having no hemofiltration[30]. On the other hand, a recent study explained that patients treated with Z-BUF had an impact on decreasing postoperative blood loss; blood transfusion; time to extubation; length of ICU stay and blood urea[31]. A randomized control trial conducted by Khalili et al. showed that the use of Z-BUF can improve the incidence of clinical complications by improving arterial blood gasses in patients undergoing CPB[32].

Though the filtration volume and weight-indexed filtration volume are not our required outcomes, but our study showed that Z-BUF patients had greater volume of filtration along with weight index compared with CUF patients. This was justified by randomized control trial by Zhu et al. that greater volume of filtrate during CPB was linked with Z-BUF[33].

CONCLUSIONS

Our study demonstrates that Z-BUF is better than CUF during CPB in terms of renal protection without affecting blood loss and blood transfusions. However, further clinical trials are warranted to support these findings.

Conflict of interest: Nil

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