HHS Public Access

Author manuscript

J Cardiothorac Vasc Anesth. Author manuscript; available in PMC 2022 May 01.

Published in final edited form as:

J Cardiothorac Vasc Anesth. 2021 May ; 35(5): 1310–1318. doi:10.1053/j.jvca.2020.11.036.

Conventional ultrafiltration during elective cardiac surgery and postoperative acute kidney injury

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Abstract

Objective: Conventional ultrafiltration (CUF) during cardiopulmonary bypass (CPB) serves to hemoconcentrate blood volume to avoid allogeneic blood transfusions. Previous studies have determined weight-indexed CUF volumes as a continuous variable are associated with postoperative AKI after cardiac surgery but optimal weight-indexed volumes that predict AKI have not been described.

Design: Retrospective cohort

Setting: Single-center university hospital

Participants: 1,641 consecutive patients that underwent elective cardiac surgery between June 2013-December 2015.

Interventions: CUF volume was removed during CPB in all participants as part of our routine practice. We investigated the association of dichotomized weight indexed CUF volume removal with postoperative AKI development to provide pragmatic guidance for clinical practice at our institution.

Measurements and Main results: Primary outcomes of postoperative AKI was defined by the KDIGO staging criteria and dichotomized, weight indexed CUF volumes (ml/kg) were defined by (i) extreme quartiles (<Q1 vs. >Q3) and by (ii) Youden's criterion that best predicted AKI development. Multivariable logistic regression models were developed to test the association of these dichotomized indices with AKI status. Postoperative AKI occurred in 827 patients (50.4%). Higher CUF volumes were associated with AKI development by quartiles (CUF >Q_3=32.6 vs. CUF <Q_1=10.4 ml/kg; OR=1.68, 95% CI:1.19-2.3) and Youden's criterion (CUF ≥32.9 vs. CUF <32.9 ml/kg; OR=1.60, 95% C:1.21-2.13). Despite similar intraoperative nadir hematocrits

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between groups (P=0.8), higher CUF volumes were associated with more allogeneic blood transfusions (p=0.002) and longer lengths-of-stay (p<0.001).

Conclusions: Removal of weight-indexed CUF volumes >32 mL/kg increased the risk for postoperative AKI development. Importantly, CUF volume removal of any amount did not mitigate allogeneic blood transfusion during elective cardiac surgery. Prospective studies are needed to validate these findings.

Keywords

cardiac surgery; acute kidney injury; cardiopulmonary bypass; ultrafiltration; fluid management

Introduction

Postoperative acute kidney injury (AKI) occurs in up to 50% of patients who undergo cardiac surgery using cardiopulmonary bypass (CPB).[1] AKI is associated with significantly increased risk for morbidity and longer intensive care unit (ICU) and hospital lengths of stay (LOS).[2, 3]

Risk factors for developing postoperative AKI include preoperative anemia, prolonged surgical and CPB duration, and hemodilution during CPB.[4-7] Hemodilution is largely a modifiable risk factor and modern perioperative management of adult cardiac surgical patients has aimed to avoid or correct hemodilution through varying techniques including conventional ultrafiltration (CUF).

CUF is frequently used during CPB to mitigate the effect of hemodilution and anemia on end-organ oxygen delivery[8, 9] by removal of intravascular plasma water, modulation of the systemic inflammatory response,[10] and suppression of post-CPB hyperthermia via pyrogen removal.[11] Although earlier evidence suggested that removal of plasma water by ultrafiltration reduced intraoperative allogeneic packed red blood cell (PRBC) transfusion and bleeding[12], the evidence is not sufficient to support CUF as means of minimizing anemia on CPB and thus improving oxygen delivery through hemoconcentration.[8] The end-organ protective effects of CUF remain unclear in the setting of various volumes removed, whereby higher ultrafiltrate volumes may lead to hypovolemia and renal hypoperfusion.[8]

We hypothesize that removal of higher volumes by CUF, when compared with lower volumes, will be associated with higher risk for postoperative AKI. Futhermore, we theorize that while CUF may raise intraoperative hematocrit, this strategy will not be sufficient to avoid PRBC transfusions during surgery. Therefore, we undertook this study to define the relationship between intraoperative volume removal by CUF, allogeneic (blood-banked) PRBC transfusion, and development of AKI in adult patients undergoing routine, elective cardiac surgery.

Methods

Following Institutional Review Board approval, we performed a retrospective review of 3,539 consecutive patients >18 years who underwent cardiac surgery with CPB from June 1, 2013 to December 9, 2015 at Duke University Hospital. Patient-specific data were queried

from the electronic health record (EHR, Epic Healthcare Solutions, Verona, WI, USA), and entered into a database by trained study personnel. After application of exclusion criteria (Figure 1). 1,641 patients constituted the study cohort. We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines.

Baseline serum creatinine (Cr) was measured within 1-week before surgery per routine presurgical testing. This value was utilized to determine preoperative renal function and creatinine clearance (CrCl). Hemoglobin and hematocrit were concurrently measured by arterial blood gas analysis, every 15-20 minutes during CPB and at timed intervals following separation from CPB. CPB and aortic cross clamp durations were documented. Additionally, we collected transfused allogeneic PRBC volume during surgery and total volume of plasma water filtered by CUF indexed to patient body weight (mL/kg). AKI staging was based on the daily serum Cr maximum fold change from the preoperative serum Cr, across seven postoperative days.

Intraoperative vasoactive medication use including epinephrine, norepinephrine, dopamine, dobutamine, milrinone, and vasopressin were collected to compute vasoactive-inotropic score (VIS)[13]. The VIS reflects the amount of vasoactive and inotropic medications a patient is on at the end of the case and has been shown to predict poor outcomes after cardiac surgery.

Hypotension during CPB was evaluated using the Time-MAP integral (TM_{50}) which was determined by calculating the area under a MAP of 50 mmHg each minute for the duration of CPB. Thus, the greater the TM_{50}, the longer the patient spent below a MAP of 50 mm Hg while on CPB. We tabulated demographic, patient and procedural characteristics, preoperative renal biomarkers, and comorbidities. A detailed description of our anesthetic care, CPB management and diagram of our circuit configuration has been provided in the supplement.

Postoperative AKI status was determined based on Kidney Disease: Improving Global Outcomes (KDIGO) staging criteria,[14] which uses preoperative serum Cr as baseline and compares this value with postoperative daily serum Cr for seven days after surgery. Diagnosis of AKI requires an increase in serum Cr (≥0.3mg/dL) within 48 hours following surgery, increase in serum Cr concentration ≥1.5-fold baseline *or* urine volume <0.5mL/kg/hour for 6 consecutive hours. AKI stages were defined by the ratio of the maximum serum Cr during 1-week after surgery to the baseline preoperative serum Cr according to the following: stage 0 if ratio <1.5; stage 1 if ratio is 1.5 - 2; stage 2 if ratio is 2.0 – 3.0; and stage 3 if (i) ratio is >3.0. (ii) maximum Cr difference from baseline is >4, or (iii) initiation of renal replacement therapy. The KDIGO criteria for diagnosing and staging postoperative AKI have been validated in cardiac surgery patients[15] and display greater sensitivity to detect AKI and predict in-hospital mortality than other established AKI criteria.[16] For our analysis, we used the highest KDIGO stage of injury determined during the first 7 days after surgery.

To evaluate CUF volume as an independent factor in the development of postoperative AKI, *a priori* definitions of dichotomized CUF volume-indices were generated for comparison.

The first definition *($CUF_{Quartile}$)* was based on comparing AKI patients according to weight-indexed CUF volume removal below 1st-quartile with those that underwent CUF volume removal higher than the 3rd-quartile values. The second definition *(CUF_{Youden})* was based on the optimal weight-indexed CUF volume cutoff of CUF for predicting AKI as determined by the receiver operating characteristic (ROC) curve and the Youden index J-statistic (sensitivity+specificity-1). The CUF value that corresponded to the maximum Youden index was chosen as this optimal cutoff (CUF_{Youden}) and AKI patients were compared according to those ≥ CUF_{Youden} vs. < CUF_{Youden}. In addition, the chi-square statistic was used to determine the relationship between postoperative AKI stage (0, 1, 2, or 3) and CUF volume separated by weight-indexed ranges around the median and interquartile range (IQR).

Patient demographics and characteristic variables were summarized by frequency (percentage) for categorical variables and mean (±SD) for continuous variables by AKI status. Chi-square, Fisher exact test, two-sample *t*-test, and Wilcoxon Rank-Sum test were used as appropriate to evaluate differences in each variable between patients according to AKI status. The variables with $p<0.15$ were considered candidate covariates to construct an initial multivariable regression model. Backward elimination was conducted with Akaike Information Criterion (AIC) to determine the final set of variables for inclusion in the multivariable regression model. In each iteration, the least significant covariate was excluded, and its corresponding AIC was tracked for model fitness. The model that reached the minimum AIC was chosen as the final multivariable model to test the effect of CUF volume on AKI using both $CUF_{Quartile}$ or CUF_{Youden} definitions. This statisitical approach was applied to secondary outcomes such as hospital and ICU LOS.

As a secondary outcome to explore the relationship between AKI, CUF volume, and survival, data was obtained from the Social Security Administration's Death Master File and the National Death Index. Survival data was collected upto 1-year after the index operation for each patient. The Kaplan-Meier method was then used to assess the extent to which AKI status and the combination of CUF and AKI could differentiate patient survival. In order to capture all deaths within 30-days, 60- days, 90-days, 180-days and 1-year after surgery, CUF_{Youden} was used as the dichotomous volume-index to maximize mortality events within this population. Patients were classified into three clusters: 1) No AKI, 2) AKI and CUF <CUF_{Youden}, and 3) AKI and CUF ≥CUF_{Youden}. The Kaplan-Meier survival curves for these three groups were compared using the log-rank test. The Cox proportional hazard model was used to estimate and test hazard ratios (HR) for each comparison. R-version 3.3.3 was utilized for analysis and the programming code was preserved for quality control.

Results

Of the 1,641 patients, 687 (41.9%) underwent coronary artery bypass grafting (CABG), 677 (41.3%) had only valve surgery, and 277 (16.9%) had CABG/valve operations (Figure 1). Postoperative AKI occurred in 827 patients (50.4%), which is similar to the 54% rate previously reported in adult cardiac surgery using the KDIGO criteria.[1] Table 1 summarizes patient demographics, procedural and renal characteristics according to AKI status (AKI No [stage 0] vs. AKI Yes [stages 1, 2, or 3]).

Patients with postoperative AKI were only slightly older (64.3 vs 61.8yr; p<0.001), had higher body mass index (BMI, 29.5 vs 28.8 kg/m^2; p<0.001), significantly higher incidence of T2DM, CAD, and preoperative pulmonary hypertension, and had a higher vasoactive-inotropic score (Table 1). AKI patients had a slightly lower preoperative creatinine clearance (71.7 mL/min vs 74.7; p=0.001) (Table 1). Patients with postoperative AKI had longer aortic cross-clamp (106.8 vs 98.7 min; p=0.013) and CPB durations (211.7 vs. 193.4min; p<0.001). Importantly, there was no significant differences in sex, incidence of depressed left ventricular ejection fraction (LVEF ≤40%), congestive heart failure, preoperative or perioperative diagnosis of atrial fibrillation, essential hypertension, peripheral vascular disease or previous history of MI when compared to patients without AKI. Hypotension during CPB as measured by the TM_{50} was not significantly longer in AKI patients (386.2 vs 359.1 mmHgmin; p=0.115).

Median (IQR) weight-indexed CUF volume in all patients was 19.1 mL/kg (Q_1=10.4, Q_3=32.6) and CUF_{Youden} at or above which predicted AKI was 32.9 mL/kg. In fact, higher weight-indexed CUF volume was significantly associated with postoperative AKI stage (p<0.001, Figure 2). Furthermore, patients with CUF ≥32.6 mL/kg displayed higher daily serum Cr each day for seven consecutive days after surgery compared with those that experience CUF volumes <10.4 mL/kg (Figure 3A). Remarkably, patients with postoperative AKI were more likely to receive allogeneic PRBC transfusions of any amount (n=197 AKI patients [23.8%] vs n=134 non-AKI patients [16.5%]; p<0.001) and on average, received more allogeneic PRBC volume compared to non-AKI patients (780.0 vs. 653.9 ml; p=0.01).

Our initial and final multivariable regression models, based on our two dichotomized CUF indices (CUF_{youden} and $CUF_{quartile}$), are displayed in the online supplement. The CUF volume ≥CUF_{Youden} (32.9 mL/kg) volume removed was significantly associated with increases in the risk of postoperative AKI (OR=1.6, 95% CI:1.2, 2.1; p<0.001) after adjusting for age, BMI, last hematocrit prior to surgery, CPB duration, TM_{50}, and vasoactive-inotropic score. Similarly, the CUF volumes ≥$CUF_{quartile3}$(32.0 mL/kg) also signficantly increased AKI risk comparing to CUF volume <$CUF_{quartile1}$(10.4 mL/kg) (OR=1.68, 95% CI:1.19, 2.37; p=0.003) after adjusting for age, BMI, pulmonary hypertension, CPB duration and vasoactive-inotropic score. Overall, both models showed that larger CUF volume removal is associated with postoperative AKI.

Next, we determined the relationship of AKI status and dichotomized CUF volume-indices by Youden (<32.9 ml/kg vs. ≥32.9 ml/kg) with secondary outcomes, including allogeneic PRBC transfusion volume and lengths-of-stay (Table 2). Interstingly, patients with both AKI and CUF volume removal ≥32.9 ml/kg displayed the longest hospital and ICU lengths-of-stay (both p<0.001), and were transfused with the largest volume of allogeneic blood (p=0.002). Notably, while higher CUF volume removal was linked to higher VIS (Table 2b), higher CUF volume predicted AKI development after adjusting for VIS between the groups.

The effect of AKI on mortality remained significant through 30 days and hazard ratios were not statisitically important beyond this interval up to 1-year after surgery. There was significant separation of Kaplan-Meier survival curves between patients with and without postoperative AKI at 30 days (HR=3.43, 95% CI,1.18-9.95; p=0.023). To explore the

relationship between CUF, AKI status, and survival, we stratified the AKI group (n=22 deaths at 30-days) by patients with CUF ≥32.9 mL/kg (n=7) and those with CUF <32.9 mL/kg (n=15). Interestingly, while HR for patients with AKI and CUF <32.9 mL/kg reached significance (HR=3.83, 95% CI,1.27-11.55; p=0.017) and HR for patients with AKI and CUF ≥32.9 mL/kg was not significant during this period (HR=2.80, 95% CI, 0.82-9.56; p=0.10), survival curves violated assumptions of the Cox PH model by displaying multiple crossing timepoints (Figure 3B). Given the small numbers of events within 30 days, we opted not to pursue log-rank alternatives to evaluate nonproportional crossing hazard interactions.

Discussion

This single center, retrospective study investigated the relationship between the volume of fluid removed by CUF and development of AKI after adult cardiac surgery. After excluding patients with preexisting renal insufficiency and risk adjustment, we found that volumes of >32.6mL/kg,(2.2L for a 70kg adult) independently associated with higher incidence of postoperative AKI, severity by staging, and LOS. We also tested weight-indexed CUF volume as a continuous variable and did not observe an effect, confirming the findings in Paugh et al. that suggested an association between CUF and postoperative AKI, but similarly did not find an association with AKI when weight-indexed CUF volume was modeled as a continuous variable.[8] The likely reason for these findings is that a single-unit increase in weight-indexed CUF volume will be insufficient to impact risk. In our analysis, we divided weight-indexed CUF volume into quartiles, and when values reached Youden's cutoff or 3rd quartile values, the impact on AKI risk became apparent. Additionally, we felt that by using weight-indexed quartiles, application to clinical practice would be more relevant.

CUF has been part of our standard institutional practice in all adult cardiac surgical cases using CPB and we believe this uniform approach served to reduce selection bias in patients with higher disease severity (i.e., heart failure) who often present with some baseline renal dysfunction. Therefore, we excluded those patients with a diagnosis of or preexisting renal disease, heart failure, and other potential effect modifers to avoid conflating our analysis. Moreover, the strict exclusion criteria established *a priori*, applied to define our study cohort were intended to ensure the best assessment of a relationship between CUF and AKI. While our selection criteria eliminated important confounders, it limited ability to characterized the relationship between CUF and survival. This occurred in the presence of a clear association between weight-indexed CUF volume and postoperative AKI as well as postoperative AKI and 30-day survival after surgery.

An important limitation of our study is that CUF may not be standard practice at other insitutions. However, our results may be widely applicable. Specifically, we applied strict exclusion criteria so that the study cohort would be representative of patients with low cardiac disease severity that undergo elective, routine cardiac surgery at our institution. Our selection criteria is also indicative of similar patient groups that undergo similar procedures at other insitutions, making our findings broadly applicable. Our universal use of hemofiltration allowed us to remove the selection bias of using in-line filters in only select

patients (usually of higher disease-severity), which resulted in a more powered analysis of treatment effects on clinical outcomes.

The application of CUF during CPB gained popularity as a technique for correcting hemodilution, potentially avoiding early renal stress from acutely worsening anemia, and by maintaining hemoglobin levels above a set transfusion trigger, and by reducing transfusions and their associated complications. Hemodilution has been identified as a modifiable factor contributing to postoperative AKI during initation of CPB.[7, 12]

While mitigation of hemodilution by CUF should reduce the incidence of AKI,[5] both preoperative and nadir hematocrits during CPB were equivalent between the AKI and non-AKI groups, suggesting that hemodilution did not contribute to AKI development in our study. Additionally, we found that weight-indexed CUF volume removal in general did not reduce allogeneic blood transfusions. In fact, we found that patients with more CUF volume removed that developed AKI were transfuse with higher volumes of allogeneic blood. Although this observation may represent an epiphenomemon unrelated to CUF and may suggest additional modifiers which were not accounted for, the evidence does not support use of CUF as a blood conservation strategy. The etiology of the paradoxical finding that *higher* volumes of CUF were associated with *higher* transfusion volumes requires further investigation. Both groups had similar nadir hematocrits on CPB and similar transfusion threshold triggers. However, the retrospective nature our investigation can only suggest that CUF volume removal can not prevent allogeneic blood transfusion in anemic patients.

Lannemyr *et al*. proposed an additive renal injury model, where hemodilution and the non-pulsatile CPB flow worsened renal oxygen deficits by an additional 20%, despite best attempts to improve perfusion through substantial increases in CPB flows.[17] Indexed flow during CPB at our institution was maintained at or above 2.4 L/min/m^2 and monitoring flow-probes were placed after the CUF/hemofiltration shunt line. Intential pump flow drops led to drops in MAP that were incorporated in the TM_{50} parameter, which was not associated with postoperative AKI development.

The incidence of AKI is only partly explained by CUF volume, and may involve intrinsic and extrinsic causes related to tissue oxygen delivery, vasoconstriction and corticomedullary blood flow, which would predispose to AKI[17], all of which were not directly measured in our study and remain important limitations.[17] Additionally, we did not capture the duration of preoperative anemia or the duration of hypotension outside of the operating room, which may have contributed to postoperative AKI development.[18] Of note, evaluation of postoperative serum creatinine levels can illustrate important changes within 24-hours after kidney stress/injury and this likely explained the serum creatinine peak on postoperative day-1 (Figure 3A).[18]

Urine output on CPB was not reliably documented in the EMR. While urine output may have provided insight into the relationship between CUF, GFR during CPB and the development of AKI, adequate output does not assure normal renal function during CPB as a result of cold diuresis and centrally-shunted non-pulsatile blood flow.[17, 19]

Recently published guidelines have highlighted the importance of *early* detection of modifiable risks factors for renal stress and AKI, and goal directed fluid therapy for adequate tissue oxygen delivery.[20] Goal-directed volume resuscitation in non-cardiac surgery has been shown to reduce postoperative AKI and early evidence supports a similar strategy in adult cardiac surgery patients.[21, 22] These studies focused on the postoperative period where our study is the first investigations to identify the importance of fluid management during cardiac surgery with CPB to potentially reduce the *early* occurance of renal stress.

We evaluated the association between postoperative AKI and survival up through 1-year after surgery using the death master file and the national death index, however, only 30-day survival demonstrated significicant hazard ratios and was influenced by postoperative AKI. Yet, due to the few number of deaths in our population-based cohort, we were unable to derive reasonable conclusions regarding the relationship between CUF volume removed during CPB, postoperative AKI and mortality at 60, 90, 180 days or 1-year after surgery. Despite the robust volume of data, the acquisition of decendent data derived from the Death Master file and National Death Index databases has several limitations. Among these are improper classficiation of death status in women due to changes in surnames that may not be affiliated with a social security number or lower reporting of deaths associated with social security numbers due to the incorrect spelling of ethnic names belonging to deceased naturalized citizens or resident aliens.[23]

Finally, while we did not find any obvious benefit to lower volumes of CUF, we did not aim to demonstrate that lower volumes were linked with less incidence of AKI. To investigate this aim, we would have to include similar patients that did not receive CUF and determine outcomes across three patient groups (i.e., no CUF volume removal, low CUF volume removal, high CUF volume removal). Unfortunately, during this period, all patients received CUF during cardiopulmonary bypass at our institution.

Conclusion

Our study shows that a weight-indexed CUF volume of more than 32 mL/kg removed during CPB for elective adult cardiac surgery increases both the incidence of postoperative AKI and AKI severity at the time of diagnosis. The routine practice of conventional ultrafiltration did not reduce allogeneic blood transfusions during surgery and our study does not support CUF volume removal as a blood conservation strategy. Based on these findings, we cannot recommend the routine use of CUF as a technique to reduce or prevent allogeneic blood transfusion during cardiac surgery using cardiopulmonary bypass. While our institution's cardiac surgical practice has changed to align with our findings, further prospective investigation is needed to fully realize the contribution CUF on the development of postoperative AKI. Moreover, prospective studies in adult cohorts with higher disease severities and lower survival rates are needed to determine the relationship between CUF volume removal and death after adult cardiac surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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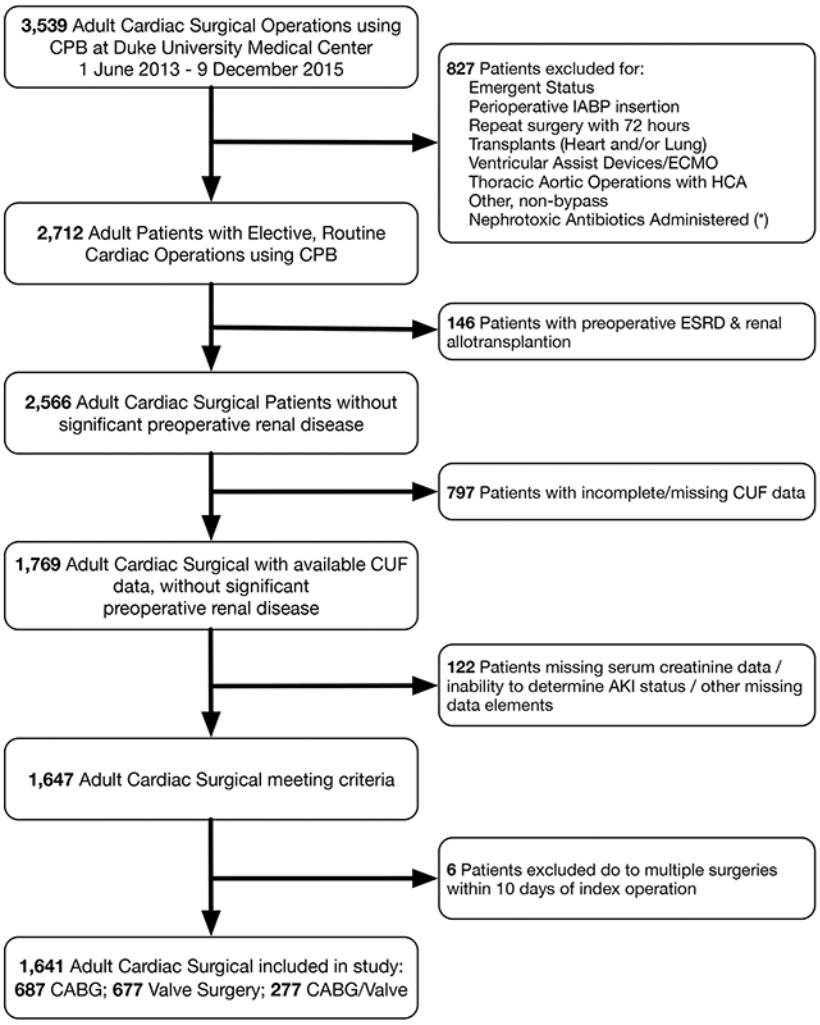


Figure 1: Selection of the Study Population.

*Nephrotoxic antibiotics administered during hospital stay include: Imipenem/Cilastatin, Tigacycline, Piperacillin/Tazobactam, Aminoglycosides, Nafcillin, Acyclovir. AKI=acute kidney injury; CABG=coronary artery bypass grafting surgery; CPB=cardiopulmonary bypass; CUF=conventional ultrafiltration; ECMO=extracorporeal membrane oxygenation; ESRD=end-stage renal disease; HCA=hypothermic circulatory arrest; IABP=intra-aortic balloon pump.

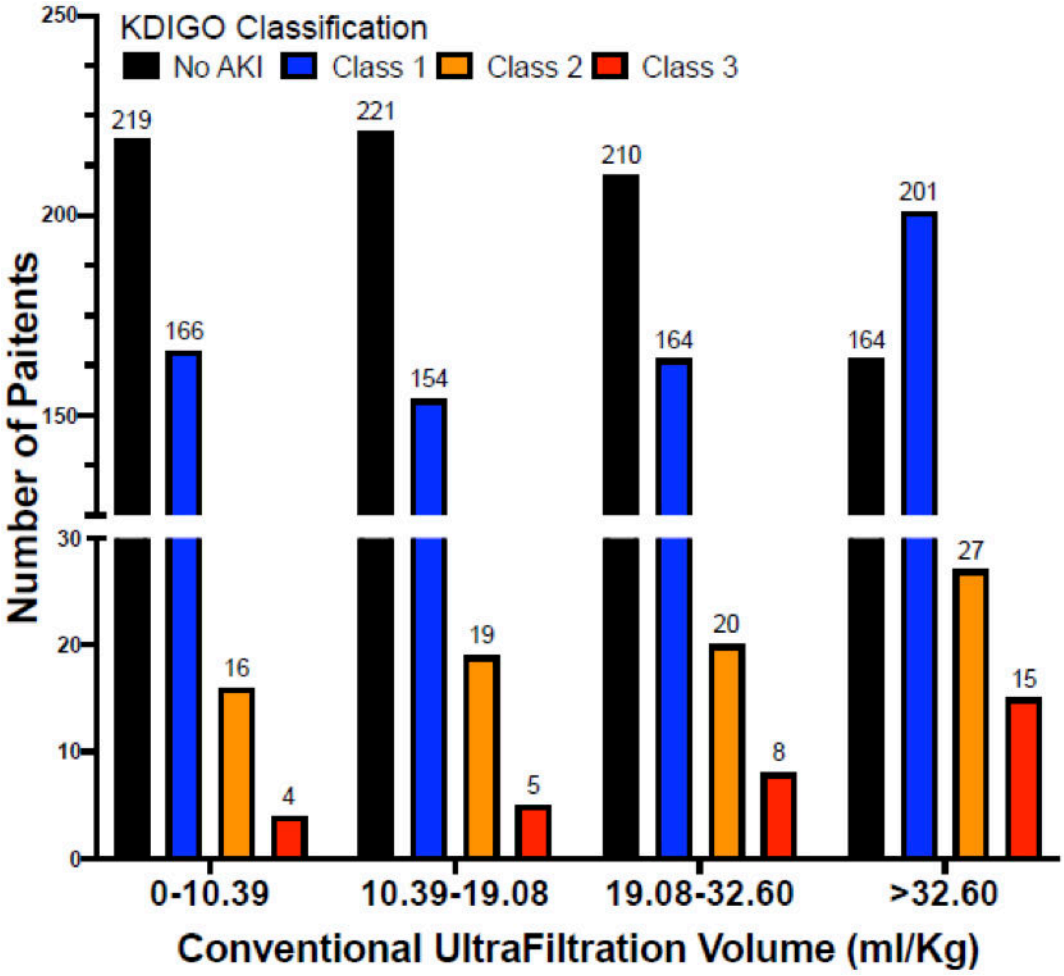
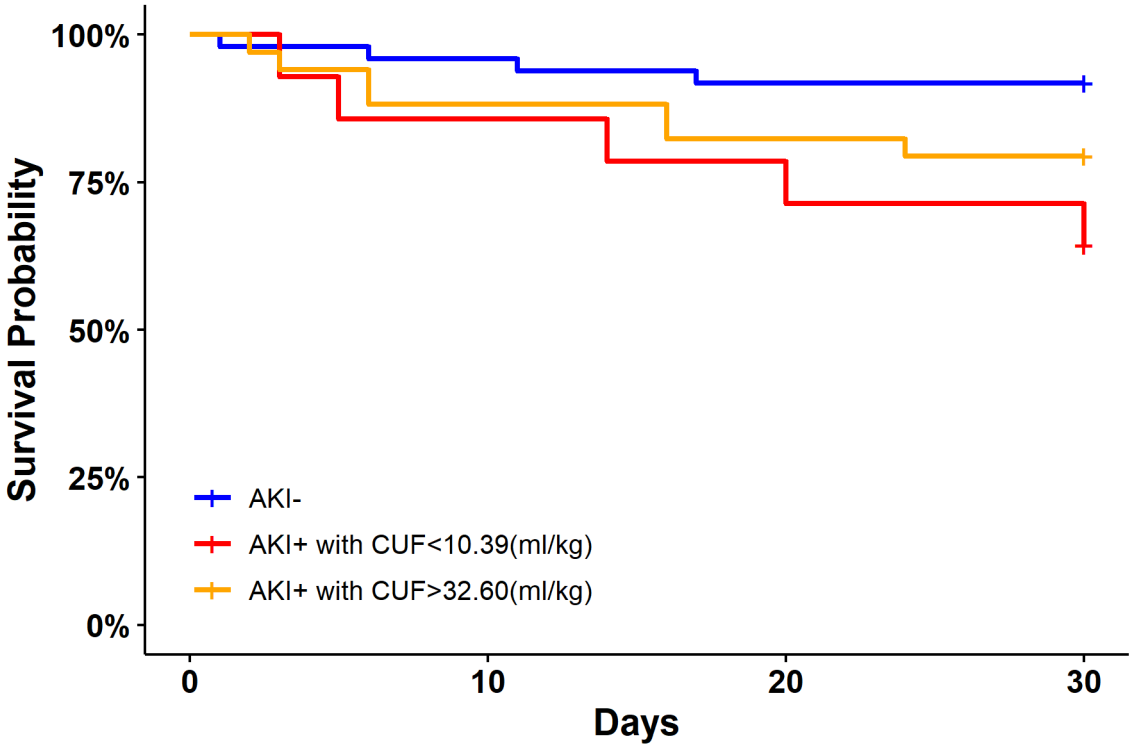


Figure 2: Weight-indexed CUF volume (ml/kg) is associated with AKI status (No AKI vs. AKI) and KDIGO AKI staging after elective cardiac surgery (P=0.00027).

CUF volumes that exceed 32.60ml/kg (Q3) display higher incidence of AKI and higher KDIGO stages-2 and-3 compared with CUF volumes below this value. AKI=Acute kidney injury; CUF=Conventional ultrafiltration; KDIGO=Kidney Disease Improving Global Outcomes criteria for AKI; Q3=Third/upper quartile.



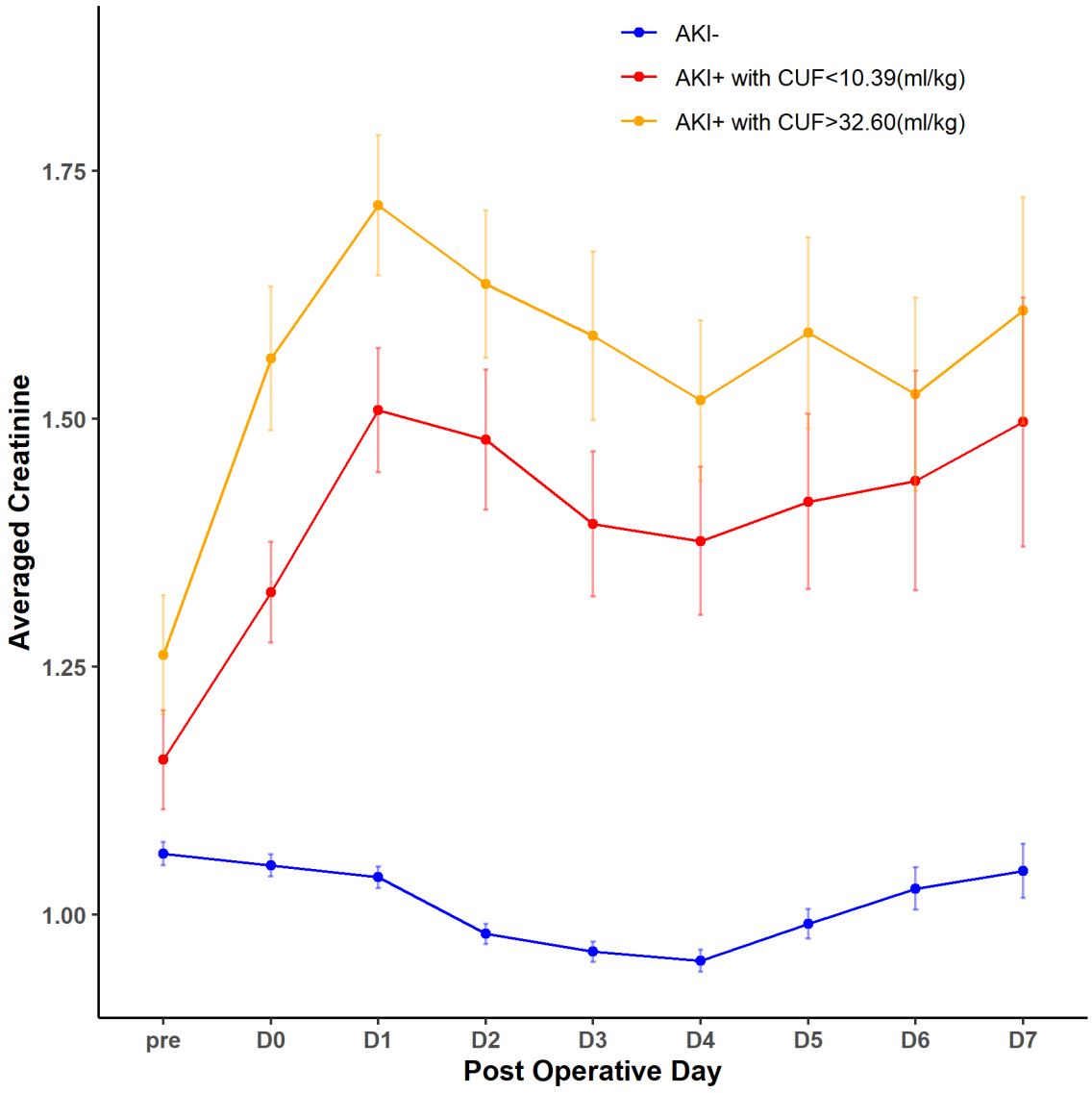


Figure 3A/B:

(**A**) Average daily serum creatinine values (mg/dL) are displayed from preoperative measurements through postoperative day-10, with AKI defined according to KDIGO criteria. Blue line represents average creatinine values for non-AKI patients. Red line represents AKI group with <10.4mL/kg removed using CUF (1st Quartile,Q_1), and orange line represents AKI group with >32.6mL/kg removed using CUF (3rd Quartile,Q_3). Higher volume removed by CUF was associated with worsening AKI. (**B**) Kaplan-Meier curve of 30-day survival, stratifying AKI patients that died by Youden criterion CUF volume (orange line, ≥32.9mL/kg removed, n=7; red line, <32.9ml/kg, n=15). Four patients died in the non-AKI group (blue line). Although patients with AKI had increased 30-day mortality, the relationship between mortality and CUF volume was unclear based on our results.

Abbreviations:AKI=acute kidney injury; CUF=conventional ultrafiltration; KDIGO=Kidney Disease: Improving Global Outcomes.

Table 1.

Descriptive Characteristics.

Parameter	AKI Status		P-value
	No, n=814 (49.6%) KDIGO 0	Yes, n=827 (50.4%) KDIGO 1, 2, 3	
Patient Demographics			
Age (years)	61.8±12.8	64.3±11.9	0.001[b]
BMI (kg/m^2)	28.8±8.1	29.5±6.3	0.001[b]
Female	271(33.3%)	266(32.2%)	0.626[a]
Male	543(66.7%)	561(67.8%)	
DM Type 1	5(0.61%)	4(0.48%)	0.751[d]
DM Type 2	157(19.3%)	215(26%)	0.001[a]
Essential hypertension	400(49.1%)	448(54.2%)	0.041[a]
Pulmonary hypertension	24(3%)	52(6.3%)	0.001[a]
Hyperlipidemia	276(33.9%)	287(34.7%)	0.734[a]
CAD	358(44%)	423(51.1%)	0.004[a]
STEMI	42(5.7%)	52(7%)	0.299[a]
NSTEMI	64(8.4%)	74(9.7%)	0.390[a]
PVD	34(4.2%)	35(4.2%)	0.956[a]
Atrial fibrillation	115(14.1%)	137(16.6%)	0.171[a]
Atrial flutter	15(1.8%)	20(2.4%)	0.420[a]
History of atrial fibrillation	35(4.3%)	38(4.6%)	0.772[a]
Angina pectoris	82(10%)	70(8.4%)	0.261[a]
CHF	221(27.2%)	232(28%)	0.682[a]
LVEF≤40%	25(3.1%)	33(4%)	0.313[a]
COPD	55(6.8%)	60(7.3%)	0.693
Procedural Parameters			
CUF (mL/kg)-Median (IQR)	17.6(9.9, 30.0)	20.8 (11.1, 35.4)	<0.001[b]
Last Hct Prior to Surgery	39±5	38±5	<0.001[b]
AoX-Clamp (min)	98.7±46.4	106.8±53.7	0.013[b]
CPB (min)	193.4±75.2	211.7±88.1	<0.001[b]
TM_{50} (mmHg•min)	359.1±277.2	386.2±321.4	0.115[a]
Lowest Intraoperative Hct (%)	31.0±4.0	31.0±4.0	0.778[b]

Parameter	AKI Status		P-value
	No, n=814 (49.6%) KDIGO 0	Yes, n=827 (50.4%) KDIGO 1, 2, 3	
Lowest Hgb on CPB (g/dL)	10.5±1.4	10.4±1.3	0.387[b]
Patients with PRBC Transfusion	137(16.5%)	197(23.8%)	<0.001[a]
PRBC Transfusion Volume (mL)	653±466.7	782±586.78	0.010[b]
Vasoactive Infusion Score	3.4(6.4)	6.13(13.7)	<0.001
Renal Function			
Preoperative CrCl (mL/min)	74.7±21.6	71.7±26.7	0.001[b]
Postoperative CrCl (mL/min)	68.7±18.8	45.9±18.6	<0.001[b]
Baseline Serum Cr (mg/dL)	1.06±0.33	1.19±0.73	0.006[a]
Peak Postoperative Serum Cr (mg/dL)	1.13±0.32	1.83±1.20	<0.001[a]
Baseline to Peak Creatinine (ΔCr,%)	7.0±15.0	65.0±79.0	<0.001[a]

a=Chi-Square

b=Wilcoxon

c=Equal Variance T-Test

d=Fisher Exact

Values are n (%) or standard deviation

AKI “No”=KDIGO Stage-0; AKI “Yes”=KDIGO Stages-1,-2, or-3; AoX-Clamp=aortic cross-clamp; CAD=coronary artery disease; CHF=congestive heart failure; COPD=chronic obstructive pulmonary disease; CPB=cardiopulmonary bypass; Cr=creatinine; CrCl=creatinine clearance; CUF=conventional ultrafiltration; DM=diabetes mellitus; Hct=hematocrit; Hgb=hemoglobin; LVEF=left ventricular ejection fraction; NSTEMI=non-ST-elevation myocardial infarction; PRBC=packed red blood cells; PVD=peripheral vascular disease; STEMI=ST-elevation myocardial infarction; TM_{50}=time-mean arterial pressure integral <50mmHg on CPB.

g CUF (3^{rd} Quartile,Q_3). Higher volume removed by CUF was associated with worsening AKI. (**B**) Kaplan-Meier curve of 30-day survival, stratifying AKI patients that died by Youden criterion CUF volume (orange line, ≥32.9mL/kg removed, n=7; red line, <32.9ml/kg, n=15). Four patients died in the non-AKI group (blue line). Although patients with AKI had increased 30-day mortality, the relationship between mortality and CUF volume was unclear based on our results. Abbreviations:AKI=acute kidney injury; CUF=conventional ultrafiltration; KDIGO=Kidney Disease: Improving Global Outcomes.

Table 2a.

Secondary Outcomes according to AKI and CUF status

	No AKI		AKI		
Outcome	**CUF < CUF_{Youden}**	**CUF ≥ CUF_{Youden}**	**CUF < CUF_{Youden}**	**CUF ≥ CUF_{Youden}**	**P-Value***
Hospital LOS (days)	6.9±3	7.8±4.8	10.6±9.5	11.4±8.8	<0.001
ICU LOS (days)	1.3±1.5	1.5±1.4	2.9±6.4	3.4±5.3	<0.001
PRBC Transfusion (mL)	601.1±445.9	759±494.9	726.92±488	877.7±720.9	0.002

CUF_{Youden}=32.6ml/kg volume removal during CPB

Values are n ± standard deviation

* p-values were from Kruskal-Wallis tests; AKI=acute kidney injury; CUF=conventional ultrafiltration; LOS=length of stay; PRBC=packed red blood cells

Table 2b.

Blood Transfusions and Vasoactive Inotropic Score

	Quartiles				
	0 – 10.39 ml	**10.39-19.08 ml**	**19.08-32.60 ml**	**>32.60 ml**	**P-Value***
Transfusion (ml)	648.4 (564.6)	598.3 (260.1)	746.1 (483.0)	835.9 (659.6)	0.0065
VIS	4.4 (8.8)	3.7 (5.5)	5.4 (16.0)	5.4 (7.4)	<0.0001

Values are mean (standard deviation)

* (ANOVA)