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Impact of Intraoperative Ultrafiltration on the Development of Acute Kidney Injury in Chronic Kidney Disease Patients Undergoing Cardiac Surgery

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ABSTRACT

OBJECTIVE To evaluate the incidence and effectiveness of using ultrafiltration in chronic kidney disease (CKD) patients during cardiac surgery.

METHODS A retrospective record review of all chronic kidney disease patients who underwent cardiac surgery at a university hospital medical center in Thailand from January 2013 to December 2018.

RESULTS Data from 306 eligible CKD patients were analyzed. The average age of patients was 63.89 ± 10.05 years. Two-hundred and twenty-two patients were male (72.2%). More than half of the patients (162/306 or 52.9%) underwent ultrafiltration (UF) during cardiopulmonary bypass (CPB). During the postoperative period, CKD patients who had received the UF were more likely to have higher postoperative serum creatinine after surgery and on postoperation day 1 ($p < 0.01$). However, there was no statistically significant difference in the occurrence of acute kidney injury (AKI) among CKD patients who received ultrafiltration and those who did not.

CONCLUSIONS In this study, the ultrafiltration intervention did not reduce the incidence of AKI among patients with CKD who underwent cardiac surgery during CPB. However, further prospective investigation is needed to fully evaluate the contribution of ultrafiltration in reducing the risk of developing postoperative AKI among patients with preexisting renal failure.

KEYWORDS ultrafiltration, chronic kidney disease, acute kidney injury, cardiac surgery

INTRODUCTION

Individuals with chronic kidney disease (CKD) undergoing cardiac surgery are placed in the high-risk category for acute kidney injury (AKI) (1). AKI is a renal function deterioration complication which can develop within 48 hours after cardiac surgery and can significantly increase the risk of postoperative morbidity and mortality. AKI can also increase the length of hospital stays and the cost of medical care. The incidence of cardiac surgery-associated AKI varies from 5 to 45% depending on the patient's preoperative diagnostic AKI criteria and the type of cardiac surgery (2). According to the previous studies, the occurrence of AKI has a complex pathophysiology with many risk factors such as perioperative hemodynamic alterations, comorbid condition, predisposing renal injury, reperfusion injury, hemolysis, inflammation, and pharmacological toxicity associated with cardiac surgery (3, 4).

Early recognition of patients at high-risk of developing postoperative AKI is essential to provide appropriate support and care. Creatinine clearance has been viewed as an important preoperative predictor of cardiac surgery outcome. Since the level of serum creatinine is dependent on body size and the state of dehy-

dration, it can indicate possible renal impartment in CKD patients (5, 6). Moreover, CKD patients of advanced age and those who have other comorbid conditions such as diabetes mellitus, hypertension, dyslipidemia, and chronic obstructive pulmonary disease are at a high risk of developing AKI (7, 8).

Cardiac surgery is commonly accompanied by a cardiopulmonary bypass (CPB) to temporarily support the heart and respiratory functions necessary to maintain the patient's blood circulation and oxygenation (9, 10). Inflammatory mediators are secreted into the CPB circulation due to the contact of blood with a non-epithelial foreign surface (11). These mediators may increase the total amount of fluid from the intravascular area passing through tissue, preventing organs and tissues from functioning normally (8). Excess fluid load during cardiac surgery is a leading cause of the higher incidence of death in CKD patients compare to patients without excessive fluid. AKI complication following cardiac surgery can be reduced by the application of preventive intervention by healthcare professionals during perioperative and intraoperative stages.

Ultrafiltration is the most practical technique for reducing hemodilution and preventing major organ dysfunction associated with CPB as it eliminates excessive prime volume, reduces fluid accumulation and systemic inflammatory response syndrome (12-15). Using this method, inflammatory cytokines and plasma-free water are eliminated by passing blood through a hemofilter containing a semipermeable membrane during ultrafiltration. Currently, conventional ultrafiltration (CUF) and modified ultrafiltration (MUF) are the two main techniques used in cardiac surgery. CUF can be performed during CPB to avoid hemodilution by removing volume of filtrate through a venous reservoir (16),while MUF is usually performed after separation from CPB and before decannulation (17). The MUF technique has been established as standard-of-care in the pediatric population (17). However, the benefit and risk of using ultrafiltration (either CUF or MUF) in adult cardiac surgical populations remains controversial.

According to the American Society of Extracorporeal Technology and the Society of Cardiovascular Anesthesiologists, fluid management and mechanical circulatory support using ultrafiltration should be monitored continually during CPB (18, 19). Recently, ultrafiltration has been implemented in a cardiovascular surgery center in Thailand. However, few studies have reported on the benefit of using ultrafiltration in CKD patients undergoing cardiac surgery. This retrospective study aimed to contribute to the ongoing research on kidney disease prevention among patients undergoing cardiac surgery.

OBJECTIVES

The objectives of this retrospective study were to evaluate the frequency of AKI and the effectiveness of ultrafiltration in reducing the incidence of AKI in CKD patients following cardiac surgery.

MATERIALS AND METHODS

Study design and patient selection

This retrospective study was conducted in accordance with the guidelines of the Helsinki Declaration after obtaining approval from the Chiang Mai University Faculty of Medicine Research Ethics Committee. The study utilized data from 306 CKD patients (stage 3-5) who had undergone cardiac surgery between January 2013 and December 2018.

Patient demographic data, co-morbidities, CPB, operation times, laboratory values, cross-clamp times, hospital stay duration, and complications were investigated retrospectively using patient medical records. In the perioperative period, the following parameters were examined: serum creatinine (Cr) (at admission then every 24 hours for a minimum of 48 hours), duration of CPB and cross-clamping, as well as the need for the renal replacement therapy (RRT) during the intensive care unit (ICU) stay, and AKI staging (see Table 1). In this study, AKI staging was classified according to Acute Kidney Injury Network (AKIN) criteria using changes in serum Cr alone (20).

Inclusion criteria

CKD patient inclusion criteria were:

1. Aged 18 years or older;
2. CKD at stage 3 or greater who underwent elective cardiac surgery;
3. Serum Cr levels > 1.5 mg/dL; and

Table 1. AKI staging by AKIN criteria

Stage	Serum creatinine (Cr) criteria	Urine output criteria
1	Increase in serum Cr of > 0.3 mg/dL or an increase to > 150 to 200% (1.5 to 2 fold) from baseline	< 0.5 mL/kg/hr > 6 hrs
2	Increase in serum Cr of > 200 to 300% (> 2 fold to 3 fold) from baseline	< 0.5 mL/kg/hr > 12 hrs
3	Increase in serum Cr of > 300% (> 3 fold) from baseline or serum Cr > 4 mg/dL with an acute increase of at least 0.5 mg/dL	< 0.3 mL/kg/hr for 24 hrs and least 0.5 mg/dL auria for 12 hrs

AKI, acute kidney injury; AKIN, Acute Kidney Injury Network; Cr, creatinine

4. Glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2

Exclusion criteria

CKD patients who met any of the following criteria were excluded from the study:

1. Under 18 years of age;
2. CKD patients at stage 1 and 2; or
3. Undergoing emergency surgery

Statistical analysis

Statistical analysis was performed using the SPSS for Windows, version 16.0 (Statistic Inc. version Chicago, IL, U.S.A.). Descriptive statistics are shown as mean ± standard deviation (SD) for continuous variables, and number plus percent for nominal variables. Chi-square test, Fisher's exact test, and ANOVA were used for comparing preoperative, intraoperative, and post-operative patient characteristics between patients who received ultrafiltration and those who did not. The results were considered statistically significant when $p < 0.05$, a 95% confidence interval.

RESULTS

The demographic data and preoperative features of the patients are summarized in Table 2. This retrospective study included 306 patients with CKD stage 3-5 who had undergone cardiac surgery. More than half of the patients (162/306 or 52.9%) also underwent ultrafiltration during CPB. The average age of the patient was 63.89 ± 10.05 years. Two-hundred and twenty-two patients were male (72.2%). Younger male patients with a history of CKD stage 3-5 were more likely to have received ultrafiltration during cardiac surgery than older patients and females ($p < 0.05$).

The incidence of AKI among CKD patients (stage 3-5) who underwent cardiac surgery is shown in Table 3. The number of patients with AKI associated cardiac surgery was 67 (20.9%). However, there was no statistically significant difference in the incidence of AKI between CKD patients who received ultrafiltration and those who did not (19.1%; 95% CI: 0.89–1.57 vs. 25.0%, 95% CI: 0.65–1.09, respectively; $p = 0.22$).

During the postoperative period (Table 4), CKD patients who received ultrafiltration were more likely to have higher postoperative serum Cr after surgery, post-operation day 1 and day 2 ($p < 0.01$). The average length of hospital stays among CKD patients who received ultrafiltration during cardiac surgery was 23.52 ± 24.42 days vs. 16.35 ± 12.87 days for those who did not receive ultrafiltration.

DISCUSSION

The ultrafiltration technique is one strategy for preventing major organ dysfunction associated with CPB by minimizing hemodilution effects, reducing fluid accumulation and reducing mediators that can initiate a systemic inflammatory response syndrome (15, 18).

This study found no statistically significant difference in the prevalence of AKI among CKD patients who received ultrafiltration and those who did not. This result is similar to a study by Boodhwani et al. (21) which similarly reported no significant benefit of the CUF technique after CPB. Additionally, Paugh et al. (18) reported that there was an increased risk of developing AKI after CPB among adult patients with baseline CKD. The present study found no difference in patient preoperative risk profiles between the two groups. As our study samples were cardiac patients with CKD stage 3 and 4, there was obvious selection bias because the average serum Cr level and CKD stage in the ultrafiltration group were higher than the

Table 2. Preoperative and intraoperative demographic characteristics among CKD patients

Variables	Ultrafiltration		*p*-value
	No	Yes	
Number of procedures	144 (47.1%)	162 (52.9%)	
Perioperative			
Age	65.26±9.63	62.66±10.28	0.02
Sex			
Male	105 (72.9%)	116 (71.6%)	0.79
Female	39 (27.1%)	46 (28.4%)	
BSA	1.60±0.18	1.59±0.17	0.66
Serum Cr level	1.80±0.28	3.91±2.82	< 0.001
Comorbid condition			
Diabetes Mellitus	50	71	0.10
Hypertension	92	108	0.61
Dyslipidemia	59	67	0.94
COPD	4	4	0.87
Pre-hemodialysis			
Yes	0 (0%)	32 (19.8%)	< 0.001
No	144 (100.0%)	130 (80.2%)	
CKD staging			
Stage 3 (n=169)	119 (82.6%)	50 (30.9%)	< 0.001
Stage 4 (n=74)	25 (17.4%)	49 (30.2%)	
Stage 5 (n=63)	0 (0%)	63 (38.9%)	
Intraoperative			
CPB time (min)	129.90±56.84	130.81±62.90	0.89
Cross-clamp time (min)	86.80±55.40	77.61±59.89	0.17

CKD, chronic kidney disease; BSA, body surface area; Cr, creatinine; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass

Table 3. Incidences of AKI among CKD patients after cardiac surgery

	No. of AKI cases	AKI incidences (%)	95% CI		*p*-value
			Upper	Lower	
Ultrafiltration	31	19.1	0.89	1.57	0.22
No-ultrafiltration	36	25.0	0.65	1.09	

AKI, acute kidney injury; CKD, chronic kidney disease

Table 4. Postoperative data for CKD patients

Variables	Ultrafiltration		*p*-value
	No (n=144)	Yes (n=162)	
RRT at ICU			
Yes	3 (2.1%)	11 (6.8%)	0.05
No	141 (97.9%)	151 (93.2%)	
Creatinine level			
Post-op day 0	1.64±0.43	2.99±1.95	< 0.001
Post-op day 1	2.03±0.52	3.76±2.29	< 0.001
Post-op day 2	2.27±0.77	3.98±2.17	< 0.001
Hospital stay (days)	16.35±12.87	23.52±24.42	< 0.01

CKD, chronic kidney disease; RRT, renal replacement therapy; ICU, Intensive Care Unit

non-ultrafiltration group. Fluid overload from CPB and excessive fluid removal during ultrafiltration intervention can negatively impact renal function. Using ultrafiltration in patients with CKD might increase the risk of developing AKI due to the greater infiltration volume as

well as to other baseline conditions of this group (22). The ultrafiltration group also have had acute kidney injury due to their cardiac condition which could have resulted in serum Cr and postoperative serum Cr being higher at every point in time. Changes in serum Cr show that the non-ultrafiltration group had elevated serum Cr until postoperative day 2, while serum Cr in the ultrafiltration group remained at baseline without elevation. The intermediate interoperative serum Cr level in the ultrafiltration group was lower than baseline but rose in postoperative day 2. The incidence of postoperative RRT in the ultrafiltration group was only 6.8% even though they had RRT preoperatively, while in non-ultrafiltration group there was no postoperative RRT despite no preoperative RRT. This might indicate that ultrafiltration can lessen or delay the impact of CPB which can contribute to renal dysfunction after cardiac surgery.

Ultrafiltration, however, might not have affected the overall clinical cost because the patients in ultrafiltration group on average had a longer hospital stay. Duration of surgery in our study could be a limitation because the mean CPB times of the non-ultrafiltration group and ultrafiltration group were 129.90 ± 56.84 min and 130.81 ± 62.90 min, respectively. The mean cross-clamp time of the non-ultrafiltration group and the ultrafiltration group were 86.80 ± 55.40 min and 77.61 ± 59.89 min, respectively. According to empirical studies, longer CPB time or cross-clamp time might impact the effectiveness of ultrafiltration. Previous studies have suggested that the risk of AKI can increase from 10-to 15-fold after 60 min of CPB (23, 24). Prolonged cross clamp time might increase the risk of low cardiac output, unfortunately, the definitive safe period of time for clamping remains undefined (25).

LIMITATIONS

First, it is acknowledged that this study was limited, as any retrospective study is, by the low number of patients and thus also less data on urine output and mortality rate as well. Nevertheless, there are some questions that cannot be answered based on the available data: are there risk factors associated with postoperative AKI such as nadir oxygen delivery, hematocrit level during and after operation, and the amount of transfusion during ultrafiltration. These and other associated potential risk factors should be a focus of future study. Secondly, the majority of CKD patients were males and living in Northern Thailand, which limits generalization of finding to CKD patients to females and to individuals living in other areas of Thailand and in other countries. Lastly, this study presents the unique experience in one cardiovascular center, further large, multicenter observational study are needed.

CONCLUSIONS

Ultrafiltration intervention does not reduce the risk of AKI among patients with CKD who undergo cardiac surgery during CPB. Further prospective investigation is needed to more fully evaluate the contribution of ultrafiltration to reducing the risk of postoperative AKI among patients with preexisting renal failure. Prospective studies in adult cohorts with higher disease severities are needed to determine the relationship between the ultrafiltration technique and other potential risk factors for developing AKI following cardiac surgery.

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CONFLICTS OF INTEREST

The authors have no conflict of interest to disclose.

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