THE PREVALENCE AND FACTORS ASSOCIATED WITH POST-OPERATIVE ACUTE KIDNEY INJURY IN PATIENTS UNDERGOING OPEN HEART SURGERY AT KENYATTA NATIONAL HOSPITAL: A RETROSPECTIVE STUDY

By

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Dissertation submitted in partial fulfillment of the requirements for the Master of Medicine Degree (MMed) in Internal Medicine of the University of Nairobi.

STUDENT DECLARATION

I, Dr. **Abdul Onesmas Nakhwanga**, declare that this is my original work and that, to the best of my knowledge, it has not been presented before for a degree or any other academic award at this or any other university.

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DEDICATION

To my parents

To my wife and daughters

ACKNOWLEDGEMENT

I would like to thank my supervisors for their important input, advice and support in the preparation of this dissertation.

I wish to also appreciate my colleagues and family for their encouragement.

I give thanks and praise to the Almighty for sustenance, good health and the gift of life.

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ACRONYMS AND ABBREVIATIONS

ACEI- Angiotensin-converting enzyme inhibitor

ADQI- Acute dialysis quality initiative

AKI- Acute kidney injury

AKIN- Acute kidney injury network

ASD- Atrial septal defect

ARB- Angiotensin receptor blocker

AVR- Aortic valve replacement

AVSD- Atrioventricular septal defect

CABG- Coronary artery bypass graft

CPB(T)- Cardiopulmonary bypass (time)

CCF- Congestive cardiac failure

CIN- Contrast-induced nephropathy

CKD- Chronic kidney disease

COPD- Chronic obstructive pulmonary disease

CPB- Cardiopulmonary bypass

CSA-AKI- Cardiac surgery-associated acute kidney injury

DM- Diabetes mellitus

DVR- Dual valve replacement

eGFR- Estimated glomerular filtration rate

GFR- Glomerular filtration rate

ICU- Intensive care unit

IGFBP7- Insulin-like growth factor binding protein 7

IL-18- Interleukin 18

KDIGO- Kidney Disease: Improving Global Outcome

LCIM- Low- and middle-income countries

LVEF- Left ventricular ejection fraction

MI- Myocardial infarction

MVR- Mitral valve replacement

NGAL- Neutrophil gelatinase-associated lipocalin

NSAID- Non-steroidal anti-inflammatory drug

NYHA- New York heart association

OHS- Open heart surgery

PAD- Peripheral arterial disease

RBC- Red blood cell

RFTs- Renal function tests

RIFLE- Risk-Injury-Failure-Loss-End stage

RRT- Renal replacement therapy

SCr- Serum creatinine

SRI score- Simplified renal index score

TIMP2- Tissue inhibitor of metalloproteinase 2

VSD- Ventricular septal defect

XC(T)- Aortic cross-clamp time

ABSTRACT

Background: Acute kidney injury (AKI) is one of the frequent bad outcomes of heart surgery. It is associated with high levels of morbidity and mortality, higher cost of treatment, and protracted hospital stay. The prevalence of cardiac surgery-associated acute kidney injury (CSA-AKI) ranges from 7.7% to 28.1% depending on the criteria employed to define AKI. Several strategies can be used to reduce the occurrence of AKI in patients undergoing open heart surgery. It is essential to make the diagnosis of CSA-AKI early and initiate interventions promptly. The aim of this study was to determine the prevalence of CSA-AKI and its associations with cardiopulmonary bypass time (CPBT), aortic cross-clamp time (XCT), and comorbidities.

Methods: This is a retrospective observational survey of patients who had open heart surgery at Kenyatta National Hospital between 1st January 2016 and 31st December 2021. We included all patients aged 18 years and above with at least one creatinine level before surgery and one creatinine level after surgery and who had a documented CPBT and XCT. Patients on chronic renal replacement therapy were excluded. AKI was defined using KDIGO criteria. Descriptive statistics were used to profile patient characteristics. The associations between AKI and CPBT and XCT were determined using Student's T-test. The correlation between AKI and the presence of comorbidities was explored using the Chi-square test. In each test $P<0.05$ was considered statistically significant.

Results: Of the 152 eligible patients the majority were male (53.3%). The mean length of hospitalization after surgery was 10.57±7.3 days. The commonest comorbidity was heart failure (86.8%) followed by hypertension (15.1%). AKI developed in 50 (32.8%) patients. The associations between CSA-AKI and CPBT and XCT were found to be statistically significant. However, no statistically significant association was determined between the occurrence of CSA-AKI and any of the preoperative comorbidities.

Conclusions: AKI following open heart surgery (OHS) is common. It is associated with prolonged CPBT and XCT.

CHAPTER ONE

INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

Approximately 2 million cardiac surgeries are performed per year worldwide; 20005 in Africa, 1277 in Sub-Saharan Africa, and 50 in KNH[1]. Indications for cardiac surgery include congenital heart diseases (CHD), valvular heart diseases (VHD), aortic dissections and aneurysms, and coronary artery disease (CAD)[2]. Open heart surgery (OHS) is defined as any surgical procedure on the heart muscle, valves, or major vessels involving the use of a heart-lung machine or cardiopulmonary bypass. Aortic cross-clamping is done during OHS to allow for surgical repairs. Both cardiopulmonary bypass circuit and aortic cross-clamping play an important role in the pathophysiology of CSA-AKI[3].

Cardiac surgery-associated acute kidney injury (CSA-AKI) is defined as a quick worsening in the functioning of the kidneys after heart surgery[2]. The incidence of CSA-AKI ranges from 7.7% to 28.1% depending on the criteria of AKI applied, whether AKIN, RIFLE, or KDIGO[4]. CSA-AKI is associated with increased morbidity and mortality, increased cost of treatment, and prolonged hospitalization. The most severe form of CSA-AKI is that requiring renal replacement therapy (RRT) and its prevalence is approximately 4%[5][6]. It is associated with a high mortality rate of up to 63%[3]. The mortality rate following OHS without AKI ranges from 1% to 8%, it increases more than four times in the background of AKI[7]. CSA-AKI is second to sepsis as a frequent cause of AKI in critical care units[8]. CSA-AKI is associated with increased 10-year mortality.

CSA-AKI results from a complex interplay between several causative entities. These factors include micro-embolisation, nephrotoxins, neurohormonal activation, oxidative stress, inflammation, hemolysis, and ischemic-reperfusion injury[9]. Risk factors for developing CSA-AKI include advanced age, female gender, emergent surgery, reintervention, and comorbidities such as hypertension, heart failure, diabetes mellitus, renal dysfunction, and COPD. Patients with comorbidities are more predisposed to the development of CSA-AKI since they often have a preexisting renal impairment and thus reduced kidney reserve. Moreover, they are more likely to be taking nephrotoxins such as ARBs/ACEIs and NSAIDS and undergo diagnostic tests requiring the use of radiocontrast. Preoperative renal

dysfunction is the most significant predictor of CSA-AKI. Other risk factors are longer CPBT and XCT[3].

A safe cut-off to prevent the occurrence of CSA-AKI has not yet been established as pertains to CPBT and XCT. A CPBT of more than 3 hours was shown in a previous study to be an independent risk factor for developing CSA-AKI[10]. Another study found that aortic cross-clamp times of less than 50 minutes were safe for renal protection during cardiac surgery[11].

Several strategies are recommended by the ADQI to prevent CSA-AKI. These strategies are classified into preoperative, intra-operative, postoperative, and pharmacologic[3]. They include optimization of kidney function before surgery, hemodynamic stabilization using intravenous fluids or inotropes, and limiting RBC transfusion. The use of dexmedetomidine, vasopressin and amino acids has been found to be useful[12].

The likelihood of developing CSA-AKI should be assessed preoperatively using tools such as the Cleveland Score and Simplified Renal Index (SRI) score. More caution is taken while operating on those patients at high risk[3]. The diagnosis of CSA-AKI ought to be done early and if need be RRT initiated promptly. Newer biomarkers of AKI such as IGFBP7, TIMP2, NGAL, and cystatin C are useful for early diagnosis of CSA-AKI[13].

This study aimed to determine the prevalence of CSA-AKI among patients who have undergone open heart surgery at KNH between January 2016 and December 2021. It also aimed to establish whether CSA-AKI is associated with CPBT, XCT, and preoperative comorbidities. This information is important in the establishment of measures to aid in the prevention and treatment of CSA-AKI.

1.2 LITERATURE REVIEW

1.2.1 Background

Acute kidney injury is one of the frequently encountered bad outcomes of heart surgery. It is associated with high levels of morbidity and mortality, higher cost of treatment, and protracted hospital stay. The prevalence of AKI following cardiac surgery ranges from 7.7% to 28.1% depending on the criteria used to define AKI[4]. Several strategies can be used to reduce the occurrence of AKI in patients undergoing heart surgery. It is essential to make the diagnosis of CSA-AKI early and initiate interventions promptly.

Numerous definitions, more than 30, of AKI have been in use previously. They include the risk-injury-failure-loss-end stage kidney disease (RIFLE) criteria[14], the Acute Kidney Injury Network (AKIN)[15] and Kidney Disease: Improving Global Outcomes (KDIGO). According to KDIGO, AKI is defined as as a quick reduction (within 48 hours) of kidney functioning with an absolute rise in sCr (>0.3mg/ dL or >26 mmol/L) or >50% (1.5 times compared to baseline), or a reduction in urine output <0.5ml kg/hr for >6 consecutive hours. Even minute elevations in sCr levels (>0.3mg/dL or >26 mmol/L) have a big impact on mortality[8]. The KDIGO definition of AKI is more sensitive compared to the AKIN and RIFLE definitions. SCr is affected by other non-GFR related factors such as nutrition, gender, comorbidities, drugs, and biochemical analysis. As such the above 3 definitions which rely on changes in sCr may not be 100% accurate. Changes in sCr do not indicate whether the kidney injury is of glomerular or tubular origin.

Figure 1: RIFLE, AKIN and KDIGO criteria for the definition of Acute Kidney Injury

Stage	RIFLE	AKIN	KDIGO
Stage 1/ Risk	SCr 1.5x baseline (within 7 days) **or** GFR decrease >25%	SCr 1.5–2.0x baseline (within 7 days) **or** ≥0.3 mg/dl increase (within 48 h)	SCr 1.5–1.9x baseline (within 7 days) **or** ≥0.3 mg/dl increase (within 48 h)
		Urine Output <0.5 ml/kg/h x 6 h	
Stage 2/ Injury	SCr 2x baseline **or** GFR decrease >50%	SCr 2–3x baseline	SCr 2.0–2.9x baseline
		Urine Output <0.5 ml/kg/h x 12 h	
Stage 3/ Failure	SCr 3x baseline **or** GFR decrease 75% **or** Cr ≥4 (*with acute rise ≥0.5 mg/dl*)	SCr >3x baseline **or** SCr ≥4 (*with acute rise ≥0.5 mg/dl*) **or** initiation of KRT	SCr 3x baseline **or** increase in Cr ≥4 *(with ≥0.3 mg/dl increase within 48 h or 1.5x baseline)* **or** initiation of KRT
		Urine Output <0.3 ml/kg/h x 24 h **or** anuria x 12 h	
Loss	Complete loss of kidney function >4 weeks		
ESRD	End-stage kidney disease (>3 months)		

RIFLE, AKIN and KDIGO criteria for the definition of Acute Kidney Injury, adapted from the Clinical Journal of American Society of Nephrology[17]

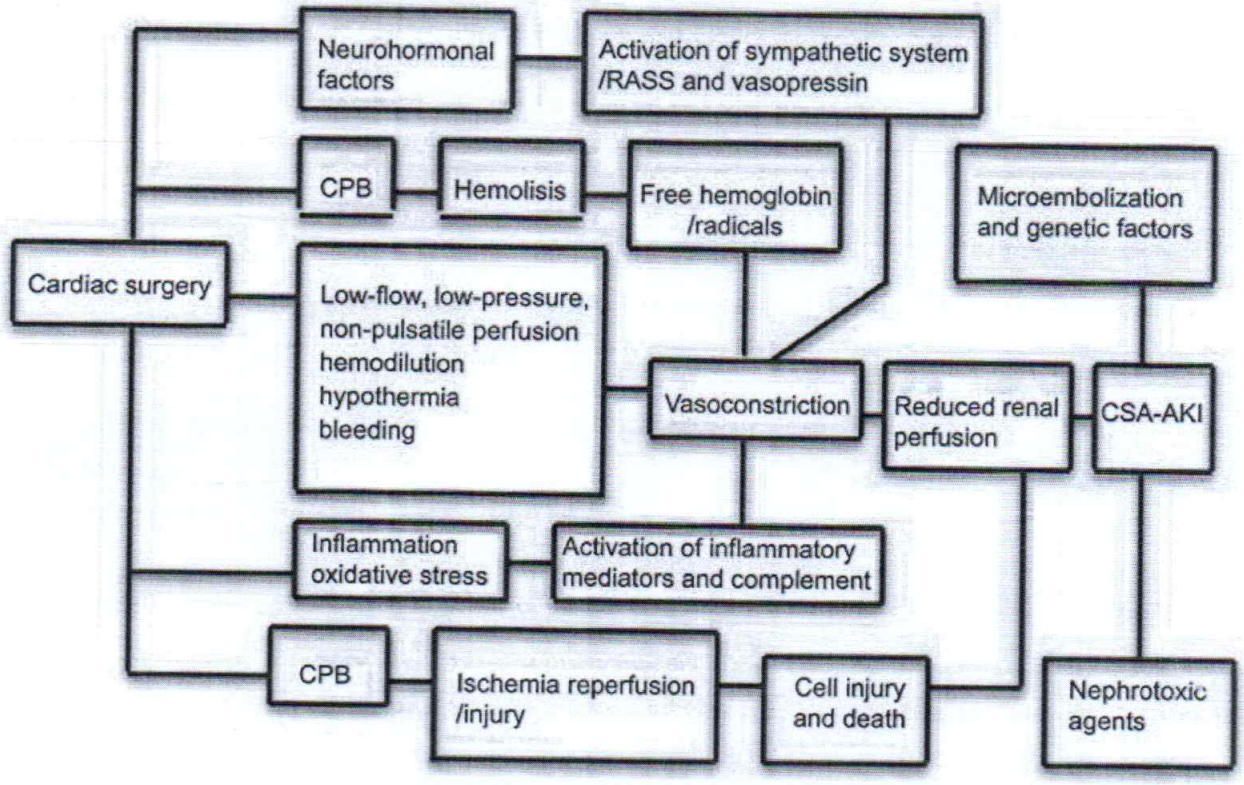
The prevalence of CSA-AKI varies according to the geographical setting of cardiac surgery and the definition of AKI used[18]. Several studies have been done to determine the prevalence of CSA-AKI as shown in table 1:

Table 1: Prevalence's of CSA-AKI in different Studies done in different Countries

Study	Setting	Prevalence of CSA-AKI	CSA-AKI requiring RRT
Andujar *et al*[19]	Spain	30%	2-5%
Karkouti *et al*[7]	Canada	34%	1-2%
Machado *et al*[20]	Brazil	43%	3.8%
Ali *et al* [21]	Egypt	3-50%	5-20%
Rodriguez *et al*[22]	Brazil	10%	2.4%
Mangano *et al*[10]	USA	7.7%	1.4%
Antunes *et al* [23]	Portugal	5.6%	0.6%
Arnaoutakis *et al*[24]	USA	28%	8%
Sampaio *et al*[25]	Brazil	19.3%	8%
Ho *et al*[26]	Canada	14%	-
Al-Githmi *et al*[27]	Saudi Arabia	34%	-
Lee *et al*[28]	Taiwan	41%	-
Savita *et al*[29]	India	23.8%	-

The pathogenesis of CSA-AKI is complex and multifactorial. Several mechanisms are postulated to be involved: micro-embolisation, exogenous and endogenous toxins, neuro-hormonal activation, oxidative stress, ischemia-reperfusion injury, metabolic and hemodynamic and inflammation factors. These mechanisms are interrelated and synergistic and lead to reflex changes in the kidneys resulting in reduced renal function, persistent renal vasoconstriction, and renal cells death[30]. Use of nephrotoxins such as aminoglycosides, glycopeptides, non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin receptor blockers (ARBs) during the peri-operative period may cause or worsen the AKI[31]. The heart-lung machine causes changes in the flow of blood and the tone of blood vessels in the kidney. It reduces renal blood flow by 30%[31]. Interaction of blood with the CPB circuit causes activation of systemic inflammation leading to the formation of micro-emboli which damage kidney capillaries directly. Renal tubular damage may also come about as a result of the discharge of free hemoglobin secondary to hemolysis[32].

Figure 2: Pathophysiology of cardiac surgery-associated acute kidney injury[3]



Pathophysiology of cardiac surgery-associated acute kidney injury, adapted from Acute kidney injury after cardiac surgery: prevalence, impact and management challenges by Vives et al[3]

Risk factors of CSA-AKI include the following:[3]

- Advanced age
- Female
- Heart failure (NYHA IV, cardiogenic shock, reduced LVEF, CCF)
- Emergency surgery
- Repeat surgical intervention
- Diabetes mellitus
- Renal dysfunction (eGFR<60ml/min, creatinine > 2.1mg/dL)
- COPD

The risk factors for developing CSA-AKI can be classified as preoperative, intraoperative, and postoperative. Some risk factors are modifiable while others are non-modifiable. Patient's demographics such as advanced age, race and gender are non-modifiable preoperative risk factors for developing CSA-AKI. The relative risk of developing CSA-AKI

increases with advanced age. In a study by Mangano et al, the relative risk of developing post-cardiac surgery AKI was 1.6 in the age group 70-79 years compared to 3.5 in the 80-95 years group[33]. Females are more predisposed to developing CSA-AKI than males. Better outcomes have been reported in Afro-Caribbeans who developed CSA-AKI as compared to Caucasians[34]. A study by Lee et al in Taiwan showed no significant differences in age and sex between the CSA-AKI group and non-CSA-AKI group[28]

A retrospective study involving 159 patients conducted by Al-Githmi et al at King Abdullah University Hospital in Jeddah Saudi Arabia revealed a prevalence of CSA-AKI of 34%. In this study, the commonest risk factor for CSA-AKI was diabetes mellitus (61%), followed by angina pectoris (58.5%), hypertension (53.5%), acute myocardial infarction (51.6%) and COPD (1.3%) in that order[27].

Reduced kidney function prior to surgery is the most important risk factor for developing CSA-AKI. Other factors that confer a higher risk are the type of surgical procedure (valvular surgery+/- CABG> CABG alone), longer XCT, longer CPBT(23.18 minutes 95% CI 16.7-29.66 $p<0.0001$), intraoperative RBC transfusion, hemodilution during CPB, and preoperative anemia (HB<12.5 g/dL)[3].

A safe cutoff to prevent the occurrence of CSA-AKI has not yet been established as pertains to CPB time and aortic cross-clamping time. Several studies have been done in this regard. CPB time lasting 3 or more hours was shown to be an independent risk factor that exacerbates the odds of having CSA-AKI in a study by Mangano et al[33]. Findings by Rodrigues et al showed that a CPB time of more than 120 minutes was an independent risk factor for the development of CSA-AKI ($p=0.001$, OR 7.040)[22]. According to Suen et al a CPB time of more than 140 minutes was strongly associated with CSA-AKI requiring RRT ($p=0.005$), more in patients undergoing valve surgery ($p<0.0001$) than in patients who underwent CABG ($p<0.05$)[35]. The mean CPBT was longest in patients who developed CSA-AKI requiring RRT (166+/-77), followed by those that developed CSA-AKI not requiring RRT (115+/-41 minutes, $p<0.001$) then the group that did not develop CSA-AKI (107+/-40 minutes, $p<0.001$). Sirvinskas et al also confirmed the strong association between a longer duration of CPB and incidence of CSA-AKI, 134+/-62.02 minutes in the CSA-AKI group versus 100.59+/-43.99 minutes in the non-AKI group ($p=0.003$)[36]. Ali et al in a study done in Egypt showed that the CPB time was prolonged in the AKI group (155 minutes) than in the non-AKI group (129 minutes)[21]. A retrospective study by Xu et al on

115 patients undergoing emergency thoracic aortic surgery established that CPB time is an independent risk factor for CSA-AKI and that an increase in CPB time by 10 minutes raised the risk of CSA-AKI approximately 17.1%[37].

Karim et al analyzed the relation between aortic cross-clamp time and the occurrence of CSA-AKI. It was shown that aortic cross-clamp times of 61-120 minutes and >120 minutes increased the CSA-AKI risk by odds ratios of 2.84 and 3.64 respectively as compared to cross-clamp time <60 minutes[38]. Iqbal et al in a study conducted at the Punjab Institute of Cardiology showed that aortic cross-clamp times of less than 50 minutes were safe for renal protection during cardiac surgery[11]. De Wolf et al found no statistically significant variance in the incidence of AKI between the short XCT and long XCT groups (p=0.373)[39].

Comorbidities such as high blood pressure, chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), diabetes mellitus (DM), congestive cardiac failure (CCF), and preexisting chronic kidney disease (CKD) confer a patient a higher risk of developing CSA-AKI. These patients usually have preexisting impairment in renal perfusion and reduced kidney reserve. Furthermore, they are more likely to be on nephrotoxins such as ARBs, ACEIs, NSAIDs and, antibiotics (aminoglycosides) which increases their susceptibility[2][40]. The use of radiocontrast for diagnostic purposes may lead to contrast-induced nephropathy (CIN). Mangano et al established that CCF, DM and previous myocardial revascularization are independent risk factors for the occurrence of CSA-AKI[10]. Preoperative presence of hypertension is predictive of the development of CSA-AKI according to Leballo et al[41]. Rodrigues et al determined that CCF, COPD, MI within the prior 30 days, and PAD are independently associated with CSA-AKI[22].

It is important to classify patients according to the likelihood of developing CSA-AKI before cardiac surgery as this helps in taking therapeutic and preventive measures[3]. A number of tools for predicting the odds of developing CSA-AKI do exist but there is no consensus on which one is preferable[3]. They include the Cleveland Clinic Score, the Mehta Score and the Simplified Renal Index (SRI) score[42]. They are useful in predicting the need for initiation of dialysis but their utility in the prediction of AKI not requiring RRT is quite poor[43]. In clinical practice, the Cleveland and SRI are the most commonly utilized owing to their simplicity as compared to the Mehta Score[44]. The modified Cleveland score has a huge number of variables thus rendering it difficult to calculate the score[6].

Several measures can be put in place to prevent the development of CSA-AKI. The measures can be classified as preoperative, intraoperative, postoperative, and pharmacologic. Due to the multifactorial and complex pathophysiology of CSA-AKI, there is currently no pharmacologic agent that is consistently associated with renal protection.

Diagnosis of CSA-AKI based on the rise in serum creatinine may delay diagnosis by 24-72 hours. This is because about half of the renal function ought to be lost before there is a rise in sCr. Moreover, sCr level is affected by other factors other than the reduction in GFR. The new biomarkers of AKI such as plasma neutrophil gelatinase-associated lipocalin (NGAL), tissue inhibitor of metalloproteinases-2 (TIMP-2), cystatin C, insulin-like growth factor – binding protein 7 (IGFBP7) , and urinary IL-18 can be used to mitigate this diagnostic issue. The utility of multiple biomarkers is recommended for better accuracy in diagnosis. Biomarkers may be used in predicting the worsening of CSA-AKI[45].

1.3 STUDY JUSTIFICATION AND SIGNIFICANCE

CSA-AKI is associated with high morbidity, mortality, high cost of treatment, prolonged hospitalization, and poor quality of life. In cases of CSA-AKI requiring RRT mortality could be as high as 63%. As of now, we do not have local data. Reliable and comprehensive data concerning the prevalence, risk factors, diagnosis, and renal protective strategies is needed to aid in the prevention and treatment of CSA-AKI. Early detection, diagnosis and treatment of CSA-AKI is especially important in our setup due to the inadequacy of RRT services including kidney transplantation.

Our study reports the prevalence and factors associated with AKI in patients who have undergone OHS at KNH. Our findings provide meaningful insights to help inform practice and policy. We will seek to publish our study results and also disseminate our results to the relevant departments.

1.4 STUDY QUESTION

What is the burden of AKI in patients undergoing open heart surgery at KNH between 1st January 2016 and 31st December 2021?

1.5 OBJECTIVES

1.5.1 Broad objective

To determine the prevalence of AKI and factors associated with AKI in patients undergoing open heart surgery at KNH

1.5.2 Specific objectives

1. To determine the prevalence of AKI in patients who have undergone open heart surgery at KNH between 1st January 2016 and 31st December 2021
2. To determine the association between the duration of cardiopulmonary bypass and CSA-AKI in patients who have undergone open heart surgery at KNH between 1st January 2016 and 31st December 2021
3. To determine the association between aortic cross-clamp time and CSA-AKI in patients who have undergone open heart surgery at KNH between 1st January 2016 and 31st December 2021

1.5.3 Secondary objective

1. To determine the association between the presence of preoperative comorbidity and CSA-AKI in patients who have undergone open heart surgery at KNH between 1st January 2016 and 31st December 2021

CHAPTER TWO

METHODS

2.1 STUDY DESIGN

A retrospective observational study of patients undergoing open heart surgery at KNH

2.2 STUDY SETTING

The study was done at Kenyatta National Hospital (KNH). KNH was chosen as the centre of the study due to the large number of persons undergoing open heart surgery per year, approximately 60 OHS per year. KNH is a level 6 national referral hospital.

2.3 STUDY POPULATION

Medical records of patients who underwent OHS at KNH between 1st January 2016 and 31st December 2021

2.4 PATIENT SELECTION CRITERIA

2.4.1 INCLUSION CRITERIA

1. Medical records of patients ≥18 years who underwent open heart surgery at KNH between 1st January 2016 and 31st December 2021
2. Sufficient documentation on variables of interest (at least 2 measured creatinine levels 1 before OHS and 1 after, CPBT, XCT)

2.4.2 EXCLUSION CRITERIA

1. Incomplete essential data such as SCr levels during the study period, cardiopulmonary bypass time, and aortic cross-clamp time.
2. Medical records of patients on RRT before surgery.

2.5 SAMPLE SIZE DETERMINATION

The estimated prevalence of CSA-AKI defined using KDIGO criteria in a study conducted in South Africa is 28%[41]. Using a finite population of 300 patients who underwent OHS at KNH between 2016 and 2021, the sample size was calculated based on the Daniel formula:

$n` = NZ^2P(1-P)/d^2(N-1)+Z^2P(1-P)$, where:

n`= sample size with finite population

N= population size (300)

Z= abscissa of the normal curve (1.96)

P = expected proportion (0.28)

d= precision (0.05)

$n`=(300x1.96^2x0.28x0.72)/(0.05^2x299+1.96^2x1.96^2x0.28x0.72)$

n`= **150**

To calculate the sample size for comparing means using a T-test between patients with CSA-AKI and those without, we used the formula below:

$n= (z\alpha/2+z\beta)^2x(\sigma1^2+\sigma2^2)/(\mu1-\mu2)^2$, where:

n= the required sample size for each group

$z\alpha/2$= the critical value for a two-tailed test at a significance level (α) of 0.05, 1.96

$z\beta$= the critical value for the desired power ($1-\beta$), 0.84

$\sigma1$ and $\sigma2$ = the standard deviations of the two groups (with and without CSA-AKI, respectively)

$\mu1$ and $\mu2$= the means of the two groups (with and without CSA-AKI, respectively)

A study by Sirvinkas et al that established the association between longer CPBT and CSA-AKI had mean CPBTs and SDs of 134±62.02 minutes and 100.59±43.99 minutes in the CSA-AKI and non-CSA-AKI groups respectively. Thus,

$n= (1.96+0.84)^2 x(62.02^2+43.99^2)/ (134-100.59)^2$

n= 29

A study by Karim et al, in which CSA-AKI was significantly associated with longer XCT, the mean XCTs and SDs for the AKI group and the non-AKI group were 81.44±30.99 minutes and 64.49±40.24 minutes respectively. Applying the above formula, the sample size for determining the association between longer XCT and CSA-AKI would be:

$n = (1.96+0.84)^2 \times (30.99^2 + 40.24^2) / (81.44-30.99)^2$

$n = 48$

A sample size of **152** was used in this study as it adequately met all primary objectives.

2.6 SAMPLING TECHNIQUE

Consecutive sampling method was done sequentially from the hospital records using the study eligibility criteria. This was due to the limited number of records available of patients who have undergone OHS. A study number was allocated sequentially to the records of subjects who met the inclusion criteria.

2.7 STUDY PROCEDURES

All medical records for patients who underwent open heart surgery patients in KNH between 1st 2016 and 31st 2021 were retrieved by the study personnel. The records were then evaluated for eligibility. Records for patients meeting the inclusion criteria were included. Patient parameters such as [Age (years), gender, race, comorbidity present, admission serum creatinine, CPBT, XCT, current medications, ICU admission, length of stay, disposition (discharged, dead or currently admitted), and need for nephrologist review, need for RRT(hemodialysis, peritoneal dialysis), duration of dialysis, outcome]; were retrieved from the patients' files and captured using a standard case report form.

2.8 DEFINITIONS OF STUDY VARIABLES

- AKI was defined using KDIGO criteria as:

✓ SCr rise 1.5 times or more above the baseline in less than 7 days or

✓ SCr ≥ 26.5μmol/L in less than 48 hours

- Baseline SCr refers to the previous best SCr level within the last 3 months if available or the minimum SCr level during admission.
- Urine output (UO) will not be used to define AKI as it may be erroneous owing to intraoperative administration of intravenous fluids and diuretics. Urine output is relatively nonspecific as a marker of AKI[42] and may even be paradoxically increased in AKI secondary to tubular damage[46].
- AKI severity was defined according to KDIGO severity as:

✓ Stage 1: SCr rise by 1.5 to 1.9 times above the baseline SCr or ≥ 26.5micromole/L within 48 hours

✓ Stage 2: SCr rise by 2 to 2.9 times above the baseline SCr

✓ Stage 3: SCr rise ≥ 3 times above the baseline SCr or ≥ 354μmol/L or the initiation of RRT.

- Stratification of AKI in-patients based on the AKI stage attained. This was done by comparing the highest to the baseline creatinine level.
- eGFR was computed using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI 2009) equation based on serum creatinine
- CKD definition was based on KDIGO guidelines as renal dysfunction or decreased eGFR (<60ml/min/1.73m^2) for more than 3 months or patients on RRT.
- Data on patient demographics, comorbidities, medications, SCr levels, ICU admission, outcomes, and length of stay were collected.
- Comorbidities were defined as diseases documented in the file.
- CKD was not included as a comorbidity because ascertaining its diagnosis will be difficult as few patients have prehospitalization eGFR.
- An acceptable recorded case was a file with data on demographics and inclusion criteria
- **Open heart surgery (OHS)** refers to any surgical procedure performed on the heart and/or any of its major vessels involving the use of a heart-lung machine. Indications for OHS include:
    - ✓ Correction of congenital heart defects
    - ✓ Valve repair or replacement
    - ✓ Repair of aneurysms and aortic dissections
- **Cardiopulmonary bypass(CPB)**-diversion of the flow of blood to the aorta via a pump and oxygenator avoiding both the heart and lungs
- **Aortic cross-clamping(XC)**-interruption of blood flow through the aorta by application of a clamp during OHS to allow for surgical repairs
- **Cardiopulmonary bypass time(CPBT)**-time spent by the patient on the heart-lung machine expressed in minutes
- **Aortic cross-clamp time(XCT)**-time during which blood flow from the heart to the aorta is restricted expressed in minutes

2.9 DATA COLLECTION

An electronic data collection tool was used to collect data from patient records/charts. Logical checks and range checks were inbuilt into the digitized form to reduce major data entry errors. Records of each study subject were assigned a unique serial number to avoid data duplication.

2.10 QUALITY ASSURANCE

To assist in the collection of data, the research assistant was taught how to obtain the needed variables from the files with strict adherence to the study protocol. The principal investigator worked alongside the assistant during the data collection procedure. Data verification was done by the principle investigator at the completion of each data collection day so as to minimize errors. Collected data were screened for duplicate records, missing data, and erroneous data. Duplicate records were removed. Logical errors, missing data and erroneously entered/transcribed data points were corrected with confirmation from the source patient document.

2.10 DATA ANALYSIS

Data from Kobo Toolbox was downloaded as an Excel file and then transferred to STATA software version 13.1 for analysis. Collected data were screened for duplicate records, missing data, and erroneous data. Duplicate records were removed. Logical errors, missing data and erroneously entered/transcribed data points were corrected with confirmation from the source patient document. For completely unavailable data, this was coded in the database to reflect that data was unavailable.

Descriptive statistics of means, medians, interquartile ranges (IQR), SD, and frequency/proportion for categorical variables were used for analyzing patients' socio-demographics and clinical parameters. Means for patients with AKI and those without AKI were compared using the student T test for continuous variables (age, length of stay and SCr) and chi-square for categorical variables (race, sex, comorbidities, AKI stages, ICU admission, disposition, and nephrology consult)

2.11 ETHICAL CONSIDERATION

Approval from KNH-UON ERC and the Department of Clinical Medicine was sought before the commencement of the study, approval number **P764/10/2022**. This included permission to access and utilize patients' medical records in KNH main records department. Data of only those who met our inclusion criteria were extracted.

Medical records were handled with confidentiality by using coded identification numbers and names were not indicated in data collection forms. Soft copy data was securely stored using a password. Data was accessed by the study staff only. One assistant was trained on the study protocol by the Principal Investigator to assist with data collection.

CHAPTER 3

RESULTS

3.1 RECRUITMENT PROCESS

Out of 300 patients who underwent OHS between 1st January 2016 and 31st December 2021, 152 met the study inclusion criteria. The most common reason for exclusion was lack of documented CPBT, XCT or both. Figure 3 shows the study flowchart:

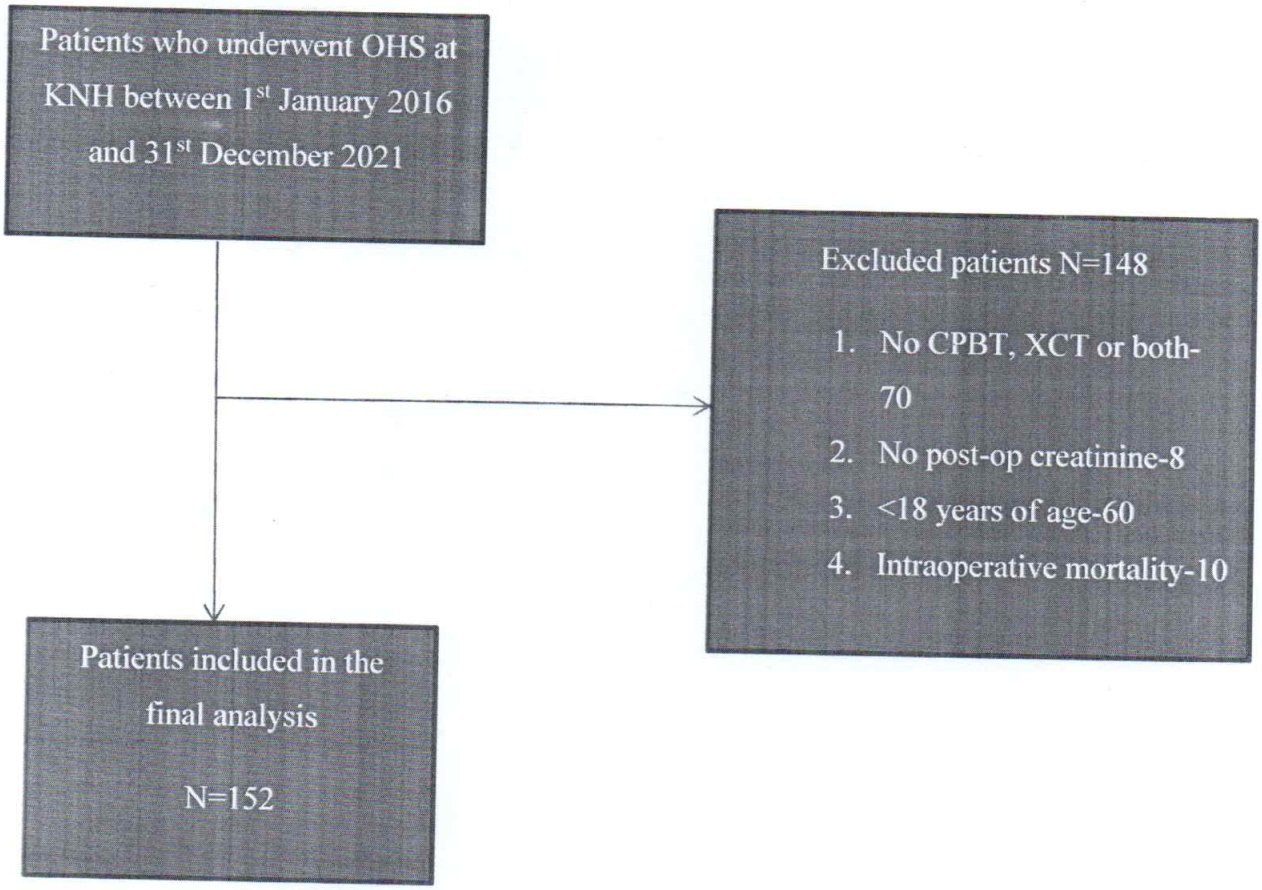


Figure 3: Study flowchart

3.2 Patients Baseline Characteristics

Table 2 shows baseline patient characteristics. The mean age of eligible patients was 38.17±13.69 years with the majority of patients being ≤30 years (38.2%). All patients were Africans. The comorbidities documented in the patients' records were heart failure (86.8%), hypertension (15.1%), HIV (1.97%), DM (1.3%), and COPD (0.66%).

The mean preoperative serum creatinine and eGFR were 81.82±27.78 µmol/l and 111.23±36.87 ml/min/1.73m^2, respectively. 13 patients (8.6%) had e-GFR <60ml/min/1.73m^2. The mean preoperative hemoglobin level was 13.19±1.64 g/dL. The mean total hospital stay was 27.33±18.61 days, while the mean number of days in hospital postoperatively was 10.7±8.1 days.

The majority of patients underwent valve replacement surgeries (50.6%). The other surgeries done included septal defects repair (21.7%), Bentall procedure (21.1%), subaortic membrane excision (3.3%), left atrial myxoma excision (1.97%), and left ventricle aneurysm repair (1.3%)

Table 2: Patient Characteristic

Variables	Overall (n=152)
Age (years) mean ± SD	38.17±13.69
Age categories (years)	
≤30	58 (38.2%)
31-40	35 (23.0%)
41-50	28 (18.4%)
51-60	20 (13.2%)
61-70	10 (6.6%)
>70	1 (0.7%)
Sex	
Male n (%)	81 (53.3%)
Female	
Race	
Africans n (%)	152 (100%)
Hospital stay	
Total hospital stay (days) mean ± SD	26.9±18
Hospital stay after surgery (days)	10.9±8.1
Baseline preoperative	
Preoperative creatinine (µmol/l) mean ± SD	81.82±27.78
Preoperative hemoglobin (g/dl) mean ± SD	13.19±1.64
Preoperative eGFR (ml/min/1.73m^2 mean ± SD	111.23±36.87
CKD (e GFR<60ml/min/1.73m^2) n (%)	13 (8.6%)
Comorbid Conditions	
Hypertension n (%)	23 (15.1%)
Heart failure n (%)	132 (86.8%)
Diabetes mellitus n (%)	2 (1.3%)
HIV n (%)	3 (1.97%)
COPD n (%)	1 (0.66%)
Types of OHS	
Mitral valve replacement +TA n (%)	43 (28.2%)
Aortic valve replacement n (%)	21 (13.8%)
Dual valve replacement n (%)	13 (8.6%)
Bentall procedure n (%)	32 (21.1%)
Septal defect repair n (%)	33 (21.7%)
Subaortic membrane excision n (%)	5 (3.3%)
Myxoma excision n (%)	3 (1.97%)
Left ventricle aneurysm repair n (%)	2 (1.3%)
Intraoperative characteristics	
Cardiopulmonary bypass time (minutes) mean ± SD	138.4±60.4
Aortic cross-clamp time (minutes) mean ± SD	87.8±49.5

3.3 Patient Characteristics by AKI Status

Table 3 shows the patients' baseline characteristics by AKI status. The patients who developed AKI were younger compared with the ones who did not (36.9±13 vs 40.5±14). However, age was not statistically significant for the diagnosis of AKI (p=0.127). The total hospital stay was longer in the non-AKI group (27.5±18.6 days) than in the AKI group (25.6±16.7 days), though this had no statistical significance (p=0.551). On the other hand, hospital stay after surgery was longer in the AKI group (12.8±11.4 days) than the non-AKI group (10.0±5.7), and this was statistically significant (p=0.044). The preoperative e-GFR was higher in the AKI group (114±39.2 ml/min/1.73m^2) compared with the non-AKI group, but this was statistically insignificant (p=0.394). The hemoglobin levels before surgery were comparable between the two groups of patients and this had no statistical significance. Four out of the thirteen patients with a baseline e-GFR <60ml/min/1.73m^2 developed CSA-AKI. Eight out of the thirteen patients who underwent DVR had CSA-AKI.

Table 3: Patient Characteristics by AKI Status

Variables	Overall (n=152)	AKI (N=50)	NO AKI (N=102)	P VALUE
Age (years) mean ± SD	38.17±13.69	40.5±14	36.9±13	0.127
Age categories (years) ≤30 31-40 41-50 51-60 61-70 >70	 58 (38.2%) 34 (22.4%) 29 (19.1%) 20 (13.2%) 10 (6.6%) 1 (0.7%)	 16(27.6%) 9(26.5%) 12(41.4%) 8(40%) 4(40%) 1(100%)	 42(72.4) 25(73.5) 17(58.6) 12(60) 6(60) 0(0)	 0.981 0.171 0.573 0.141 0.082 -
Sex Male n (%) Female	 81 (53.3%) 71 (46.7%)	 31(38.3) 19(26.8)	 50(61.7) 52(73.2)	 0.132
Race Africans n (%)	 152 (100%)	 50(32.9)	 102(67.1)	 -
Hospital stay Total hospital stay (days) mean ± SD Hospital stay after surgery (days)	 26.9±18 10.9±8.1	 25.6±16.7 12.8±11.4	 27.5±18.6 10.0±5.7	 0.551 **0.044**
Baseline preoperative (mean ± SD) Preoperative creatinine (µmol/l) Preoperative hemoglobin (g/dl) Preoperative e GFR (ml/min/1.73m^2)	 81.82±27.78 13.2+-1.64 111.23±36.87	 79.6+-32.3 13.4+-1.6 114.9+-39.2	 82.9+-25.4 13.1+-1.6 109.4+-35.8	 0.494 0.392 0.394
CKD (e GFR<60ml/min/1.73m^2) n (%)	13 (8.6%)	4(30.8)	9(69.2)	0.566
Comorbid Conditions Hypertension n (%) Heart failure n (%) Diabetes mellitus n (%) HIV n (%) COPD n (%)	 23 (15.1%) 132 (86.8%) 2 (1.3%) 3 (1.97%) 1 (0.66%)	 8(34.8) 41(31.1) 1(50) 0(0) 0(0)	 15(65.2) 91(68.9) 1(50) 3(100) 1(100)	 0.834 0.216 - - -
Types of OHS Mitral valve replacement +TA n (%) Aortic valve replacement n (%) Dual valve replacement n (%) Bentall procedure n (%) Septal defect repair n (%) Subaortic membrane excision n (%) Myxoma excision n (%) Left ventricle aneurysm repair n (%)	 45(29.6) 19(12.5) 13(8.6) 32(21.1) 33(21.7) 5(3.3) 3(2) 2(1.3)	 17(34) 5(10) 8(16) 11(22) 9(18) (0) 0(0) 0(0)	 28(27.5) 14(13.7) 5(4.9) 21(20.6) 24(3.5) 5(4.9) 3(2.9) 2(2)	 0.406 0.514 **0.022** 0.841 0.437 0.132 0.296 0.449
Intraoperative characteristics Cardiopulmonary bypass time (min) mean ± SD Aortic cross-clamp time (min) mean ± SD	 138.4±60.4 87.8±49.5	 148.3±55.6 96.5±7.3	 126±5.0 79.2±4.0	 **0.0198** **0.027**

3.4 Prevalence of CSA-AKI

The patients who were diagnosed with Acute Kidney Injury were 50 (32.9%) and those who did not have the AKI were 102 (67.1%).

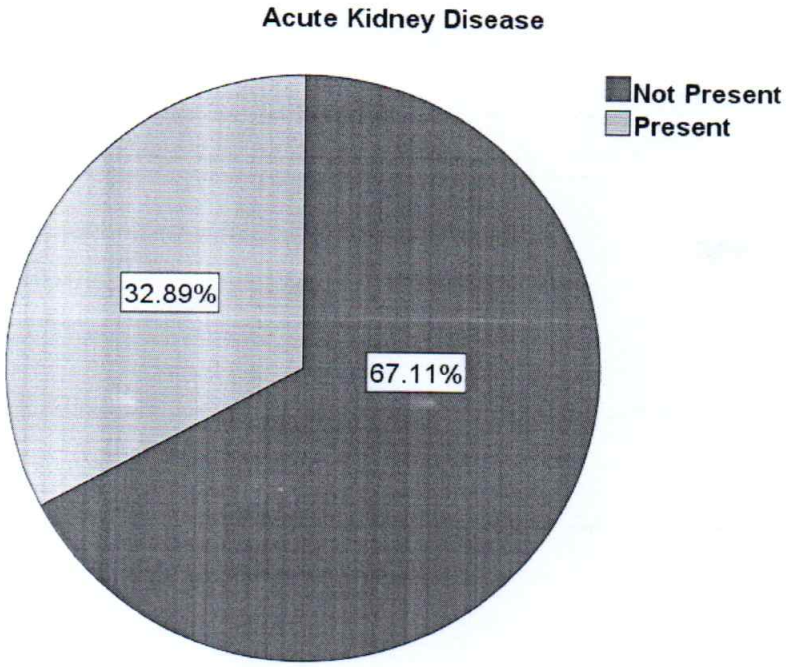


Figure 4: Prevalence of CSA-AKI pie chart

All the patients (152) in the dataset underwent open heart surgery; therefore, the prevalence of AKI among patients undergoing open heart surgery at KNH was (32.9%) as shown below.

$$\text{Prevalence} = \frac{Number\ of\ patients\ with\ CSA-AKI}{total\ number\ of\ patients\ who\ underwent\ open\ heart\ surgery\ (n)} * 100$$

Prevalence=50/152*100=32.9% ,95% CI (21.1-41.1)

3.5 Association between CSA-AKI and Cardiopulmonary bypass time

A Student's T-test was used to demonstrate the association between cardiopulmonary bypass time (CPBT) and the occurrence of AKI as shown in table 4:

Table 4: Table for the association of CPBT and AKI

	Mean CPBT time	T-test p-value
AKI Present	148.3±55.6	0.0198
AKI Absent	126.9±5.0	

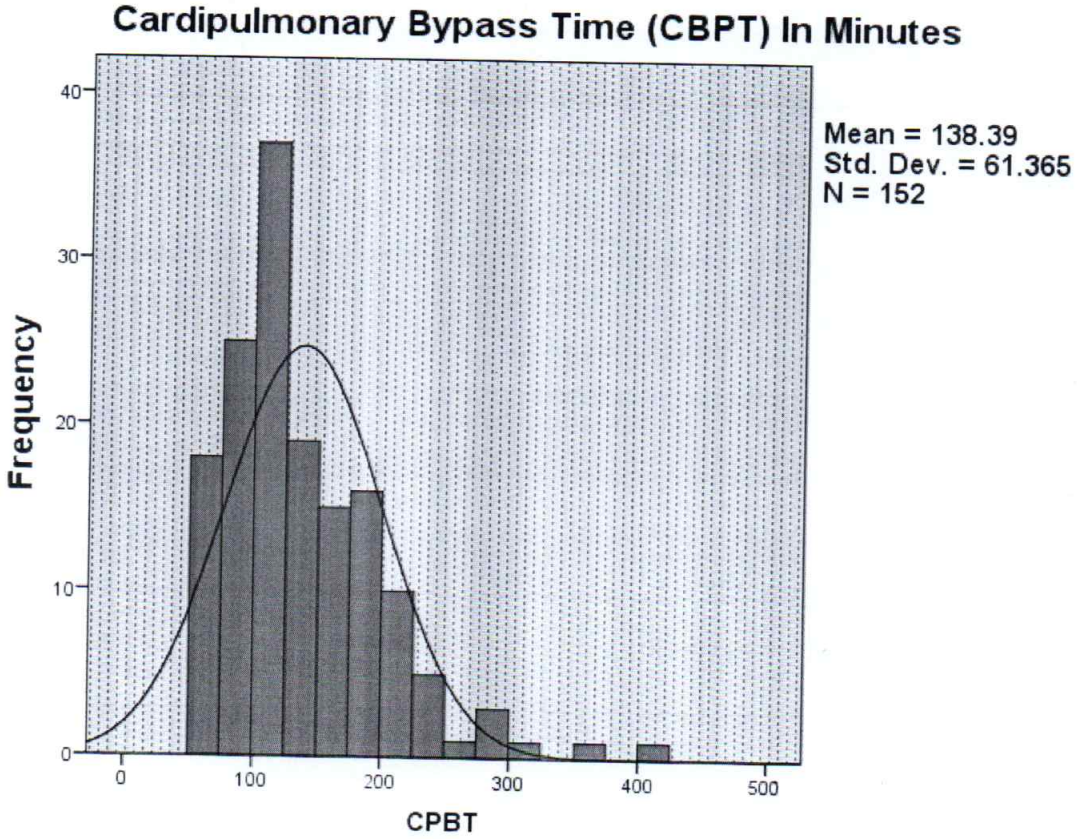


Figure 5: Cardiopulmonary bypass time histogram

When the independent t-test was performed the results were as follows: 50 participants were diagnosed with Acute kidney injury (M=148.3, SD=55.6), while the 95% confidence interval was (132.3, 164.2). The 102 participants who did not have acute kidney injury had a

(M=126.9, SD=5.0), the 95% confidence interval was (116.9, 136.8). The P-value was Pr (|T| > |t|) = 0.0198 for equal variances. The p-value is less than α=0.05 therefore this shows that the difference in average CPBT was statistically significant.

3.6 Association between CSA-AKI and aortic cross-clamp duration

A student's T-test was used to explore the association between aortic cross-clamp time (XCT) and the occurrence of CSA-AKI as shown in table 5:

Table 5: Table for the association of XCT and CSA-AKI

	Mean XCT	T-test P-value
AKI present	96.5±7.3	0.027
AKI absent	79.2±4	

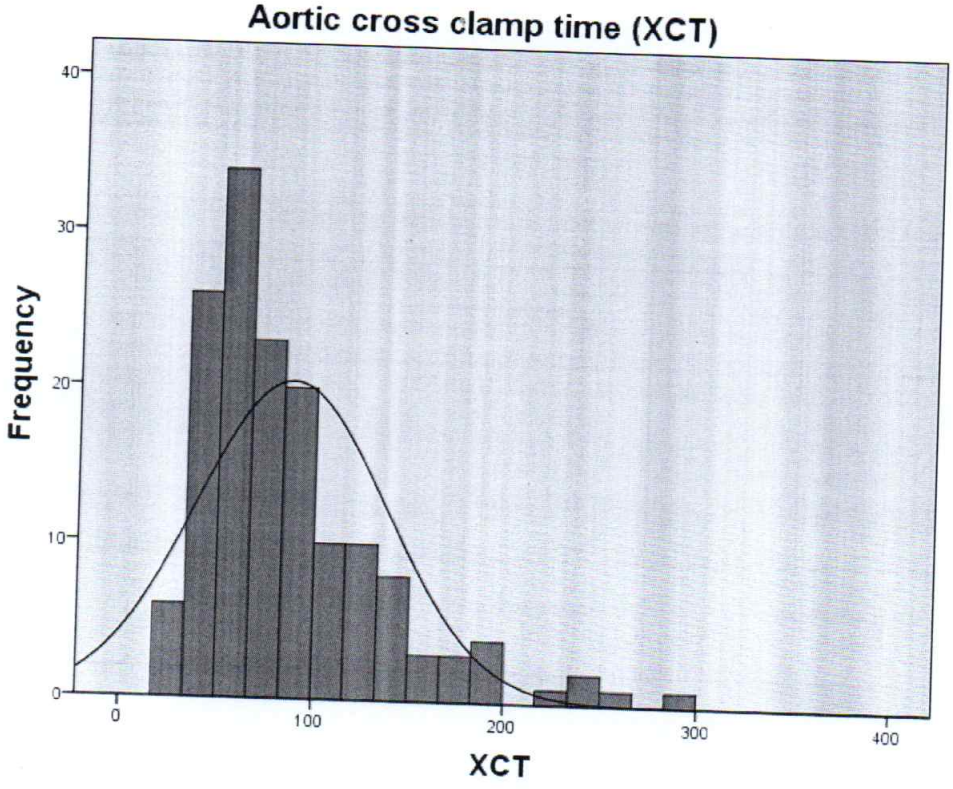


Figure 6: Aortic cross-clamp time histogram

The 50 participants who had AKI had a mean XCT of 96.5±7.3 (95% confidence interval 81.7-111.2) while the non-AKI group had a mean XCT of 79.2±4.0 (95% confidence interval 71.2-87.3). Independent T-test gave a P-value =0.0271 meaning that the difference in XCT was statistically significant.

3.7 Association between CSA-AKI and preoperative comorbidities

A chi-square test was used to explore the correlation between various comorbidities among patients undergoing OHS at KNH with the occurrence of AKI as shown in table 6.

Comorbidities were defined as the diseases documented in the patients' records.

Table 6: Association of preoperative comorbidity and CSA-AKI

	Total	**AKI**	**No AKI**	**P-value**
Hypertension	23(15.1%)	8(34.8%)	15(65.2%)	0.834
Heart failure	132(86.8%)	41(31.1%)	91(68.9%)	0.216
DM	2(1.3%)	1(50%)	1(50%)	-
HIV	3(1.97%)	0(0%)	3(100%)	-
COPD	1(0.66%)	0(0%)	1(100%)	-

The P-values obtained for the correlation between the various comorbidities and the development of CSA-AKI were all >0.05 meaning that our study did not show any statistical significance in the association between the presence of comorbidities and the occurrence of AKI after OHS. Our study was not powered enough to show these associations due to the small sample size.

CHAPTER FOUR

4.1 DISCUSSION

The aim of this retrospective cohort study was to determine the prevalence of AKI and factors associated with AKI in patients who have undergone OHS. To the best of our knowledge, there is limited data on AKI following OHS, especially in East Africa. To date, no study has been published locally on this subject.

The majority of the patients were male 81 (53.3%). The mean age of the patients in this study was 38.17±13.69 years. Our mean age was comparable to the mean age in a study done in India (37.01±12.28 years) by Karim et al [38] but markedly lower compared to a study done in Italy (51.2±9.7 years) by Serraino et al[47]. The difference in mean age comes about as a result of differences in indications for OHS in developed countries as compared to low- and middle-income countries (LMICS)[47][38][48][49]. In India and locally, the main indication for OHS is rheumatic heart disease (RHD) while in Italy it is coronary artery disease (CAD)[47]. The age group of ≤30 years had the largest number of patients (58) followed by 31-40 years. The difference in the mean age in the group that developed AKI (40.48±14.6) and the non-AKI group (36.75±13.4) was not statistically significant, p=0.127. Al Githmi et al found no correlation between age and the occurrence of CSA-AKI[27]. Lee et al also did not find any significant differences in age and sex between the CSA-AKI group and non-CSA-AKI group[28]

The total hospital stay was longer in the non-AKI group than in the AKI group but this had no statistical significance (p=0.551). The postoperative hospital stay was, however, statistically significantly longer in the AKI group (p=0.044), corroborating findings by Leballo et al and Vives et al[41][3]. The total hospital stay is influenced by many factors, including lack of theatre space, lack of blood for transfusion, low hemoglobin level, raised INR, deranged renal function, absence of personnel, and lack of funds to clear hospital bills. Some of these factors such as lack of theatre space and lack of funds are more likely to delay an elective case as opposed to an emergency. Emergency cardiac surgeries have a higher risk of CSA-AKI than elective ones[50]. This could explain the longer total hospital stay in the non-AKI group.

The majority of the patients had heart failure (86.8%) while 15.1% had hypertension. The incidences of DM (1.31%), COPD (0.7%), and human immunodeficiency virus (HIV) (1.97%) were much lower. Owing to the huge RHD and unmet CHD burden among our

patients and other LMICs, the average age of our patients was lower compared to other studies, and this could explain the lower prevalences of DM and COPD in our study population[51][52][53]. Our surgical interventions, as also seen in other LMIC setups, were done late when patients had already developed advanced or irreversible stages of heart failure compared to Western countries. The underlying reasons for this scenario are inadequate cardiac surgery centres and personnel, loss of follow-up after diagnosis, refusal of surgery earlier in life, and late diagnosis[54].

The commonest indication for OHS in our study was RHD (50%), followed by septal defects (21.7%) and ascending aortic aneurysm (21.1%). Other indications were subaortic membrane (3.3%), left atrium myxoma (1.97%), and left ventricle aneurysm (1.3%). The commonest valvular lesion was aortic regurgitation (AR), followed by mitral regurgitation (MR) and mitral stenosis (MS). Overall, the mitral valve lesions exceeded the aortic valve lesions, in keeping with other studies in LMIC[55][48][49]. The most frequent surgical operation was valve replacement, accounting for 50% (MVR plus TA [28.3%], AVR [13.8%], DVR [8.6%]). This was followed by septal defects (ASD and AVSD) repair (21.7%), Bentall procedure (21.1%), subaortic membrane excision (3.3%), myxoma excision (1.97%), and ventricular aneurysm repair (1.31%) in that order. The proportions of indications for OHS and the specific surgical procedures were similar to other studies done in other LMICs such as India, Nigeria and Pakistan[49][51][48]. This differed from studies done in developed countries. For instance, in a multinational European survey done by Roques et al, the majority of patients underwent isolated CABG (65%) followed by valve surgery (29.4% [AVR -16.8%, MVR-8.5%, DVR-4.1%]), thoracic aortic surgery (2.6%), ASD repair (1.2%), and heart transplant (0.71%)[56]. The number of uncorrected CHD in adults was high in our study as in other studies in LMIC due to inadequate cardiac surgery facilities, late diagnosis, loss to follow-up or reluctance to undergo surgery at an earlier age[55][54][57]. The patients had similar optimized hemoglobin levels (mean 13.19±1.64 g/dl, median 12.9g/dl) and baseline renal function (mean e GFR 111.23±36.87) before surgery.

CSA-AKI developed in 50 patients out of the 152 sampled giving a prevalence of 32.9%. This is comparable to a study by Al Githmi et al with a prevalence of CSA-AKI of 34% in a cohort of 159 patients. The prevalence could be attributed to the careful selection of patients for OHS and preoperative optimization of patients in terms of renal function, coagulation profile, and hemoglobin levels. Machado et al found a higher prevalence of 43% [20]while Sampaio et al found a lower prevalence of 19.3%[25]. All the patients in the study by

Machado et al had elevated baseline serum creatinine levels, while Sampaio et al excluded patients over 80 years of age, correction of CHDs and repair aortic aneurysms. This could explain the disparity in the prevalence of CSA-AKI[20][25]. AKI in SSA is a public health concern due to disease burden, late presentation and diagnosis, and inadequate resources[58]. In ICU, sepsis cause the biggest proportion of AKI followed by cardiac surgery[30].

The mean CPBT was 138.4±60.4 minutes. The AKI group had a higher mean CPBT (148.37±55.6, 95% CI 132.3-164.2) compared to the non-AKI group (126.9±5.0, 95% CI 116.9-136.8). A P-value of 0.0198 was arrived at after subjecting the means to a student's T-test. This shows that the average CPBT in minutes and the average AKI diagnosis were statistically significantly different. A prolonged CPBT is an independent risk factor associated with CSA-AKI[37][59][60]. Ali et al in a study conducted in Egypt found mean CPBT of 155 minutes and 129 minutes in the CSA-AKI group and non-AKI group, respectively[21]. This is comparable to our study. Similar findings were obtained by Sirvinkas et al (134±62.02 vs 100.59±43.59 minutes in the AKI vs non-AKI groups)[36]. Measures to shorten CPBTs should be taken as this would in turn reduce the occurrence of CSA-AKI. These measures include improved surgical skills by the surgeons, proper planning of each OHS preoperatively, and preoperative optimization of patients in terms of hemoglobin level and coagulation profile.

The mean XCT was 87.8±49.5 minutes. The patients that developed AKI had a mean XCT of 96.5±7.2 95% (95% CI 81.7-111.2) compared to a mean of 79.2±4.0 (95% CI 71.2-87.3) in the patients who did not have AKI; giving a P-value of 0.0271. Thus the difference in XCT was found to be statistically significant in our study. Prolonged XCT is associated with the occurrence of CSA-AKI according to Karim et al[38] and Lee et al[28]. Steps aimed at reducing XCTs should be adopted. These measures are similar to those described above for reducing CPBT.

Chi squares were used to determine the association between AKI and existence of comorbidities. All the P-values derived for the various comorbidities were greater than 0.05 (DM- not determined, hypertension-0.707, heart failure-0.215, HIV-not determined). Thus no statistically significant correlation was found between occurrence of CSA-AKI and comorbidities. Our study was not powered enough to determine the correlations between CSA-AKI and different preoperative comorbidities. A study by Lee et al noted no significant association of CSA-AKI and the presence of DM[28]. Based on Machado et al, presence of

DM did not confer a higher risk of CSA-AKI, but the use of insulin increased the risk three-fold[20]. Many other studies on this topic found that presence of comorbidities increased the risk of developing CSA-AKI. Mangano et al established that CCF, DM and previous myocardial revascularization are independent risk factors for the occurrence of CSA-AKI[10]. Preoperative presence of hypertension is predictive of the development of CSA-AKI according to Leballo et al[41]. Rodrigues et al determined that CCF, COPD, MI within the prior 30 days, and PAD are independently associated with CSA-AKI[22].

4.2 CONCLUSION

AKI following OHS is common and close monitoring of RFTs should be done after OHS so that it is not missed. The occurrence of AKI following OHS is significantly associated with both prolonged CPBT and XCT. The association between CSA-AKI and comorbidities was not determined.

4.3 STUDY LIMITATIONS AND DELIMITATIONS

This study being retrospective, we were unable to obtain all data related to the parameters of interest. However, data validation was adequate as we went through both physical and electronic medical records before the selection of records. Patients with less than two serum creatinine readings may have had AKI but would be missed resulting in the majority of their records being excluded, this may have introduced a selection bias.

4.4 STUDY RECOMMENDATIONS

Frequent monitoring of RFTs after OHS is recommended so that CSA-AKI is not missed. This will aid in prompt diagnosis of CSA-AKI, timely initiation of treatment and thus reduction in morbidity and hospital stay.

Measures to prevent the occurrence of CSA-AKI such as optimization of renal function and hemoglobin prior to surgery should be encouraged.

Measures to shorten CPBT and XCT should be employed to minimize the chance of CSA-AKI. These include improved surgical skills (obtained through trainings, simulations and mentorship) and adequate preparations for surgeries.

Further research preferably a prospective study is required to better characterize the predictors of CSA-AKI such as comorbidities, age, gender, and preoperative renal dysfunction.

APPENDICES

5.1 ETHICAL APPROVAL LETTER

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Ref: KNH-ERC/A/23

16th January 2023

KENYATTA NATIONAL HOSPITAL APPROVED 16 JAN 2023 KNH/UoN-ERC P.O. Box 20723 - 00202 NAIROBI

Dr. Onesmas Nakhwanga Abdul
Reg. No. H58/34211/2019
Dept. of Clinical Medicine and Therapeutics
Faculty of Health Sciences
University of Nairobi

Dear Dr. Abdul,

RESEARCH PROPOSAL: THE PREVALENCE AND FACTORS ASSOCIATED WITH ACUTE KIDNEY INJURY IN PATIENTS UNDERGOING OPEN HEART SURGERY AT KENYATTA NATIONAL HOSPITAL; A RETROSPECTIVE STUDY (P764/10/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P764/10/2022.** The approval period is 16th January 2023 – 15th January 2024.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

5.2 BUDGET

Item	Quantity	Unit Cost (Kshs)	Total (KShs)
Study assistants	2	20,000	40,000
Stationery	Forms and booklets		40,000
Statistician	1	30,000	50,000
ERC fee	2	2,000	4,000
Contingency		30,000	30,000
Total (Kshs)			**174,000**

Table 7: Budget

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