AN EVALUATION OF INOTROPIC USE POST- CARDIAC SURGERY AT THE KENYATTA NATIONAL HOSPITAL

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DECLARATION

I hereby declare that this dissertation is my original work and to the best of my knowledge has not been presented elsewhere for approval and for the award of a degree, diploma or certificate.

I further declare that all material cited in this report which are not my own have been duly acknowledged.

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APPROVAL BY THE DEPARTMENT

This dissertation has been revised as per the recommendations made by the unit of Thoracic and Cardiovascular Surgery, Department of Surgery and the study was approved as per recommendations of Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee (KNH/UON ERC)

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LIST OF ABBREVIATIONS

AVR – Aortic Valve Replacement

CABG – Coronary Artery Bypass Graft

CI – Cardiac Index

CKD – Chronic Kidney Disease

CVP – Central Venous Pressure

DVR – Double valve replacement

ECG – Electrocardiogram

ERC – Ethics and Research Committee

KNH- Kenyatta National Hospital

LCOS- Low Cardiac Output Syndrome

LVD – Left Ventricular Dysfunction

LVEDP – Left Ventricular End Diastolic Pressure

LVEF – Left Ventricular Ejection Fraction

MAP – Mean Arterial Pressure

UON- University of Nairobi

ABSTRACT

Introduction: Cardiac Surgery in Kenya has evolved over the past few decades amid a myriad of challenges. One of these challenges appears to be low cardiac output syndrome as well as the minimum availability of published data. This study aims to evaluate the pattern of inotropic use post cardiac surgery in the critical phase.

Materials and Methods: The study is a retrospective cross-sectional design. A data collection sheet was used to retrospectively collect data post cardiac surgery between 2013 and 2016 in Kenyatta National Hospital. The pattern of inotropic use vis-a-vis various pre-operative and intraoperative factors was then compared to the duration and number of inotropes used while the patient was in the critical care unit. This data was analysed using Microsoft excel and SPSS v20

Results: 109 patient files were perused. The study showed a marked variance in the pattern of inotropic use post cardiac surgery in KNH with adrenaline use singularly being the most common (78%). There was no algorithm in systematic introduction of inotropes post cardiac surgery. Risk factors were correlated via t-tests to length of ICU stay with no significant findings which indicated that patients are kept unnecessarily longer in ICU. However, long cardiopulmonary bypass time was found to have a positive correlation to use of high dose inotropes as well as increased morbidity and mortality.

1.0 Introduction

Many sub-Saharan African hospitals are not particularly well known for cardiac surgery. We have a growing population of Africans including Kenyans seeking specialized surgery out of the country particularly in India. (1)

Cardiac surgery has particularly been affected in this area with extremely long waiting lists in the public hospitals. In the private sector in Kenya, the price of cardiac surgery is still far beyond the reach of the common Kenyan. Nonetheless even in instances of well-off Kenyans, there is generally a preference to seek surgical treatment in more advanced centres found outside the country. It has been found that patients find seek treatment in India with airfare, accommodation and treatment being far cheaper than treatment locally. (1)

Cardiac surgery requires a wholistic team approach stretching across various disciplines from cardiac nurses, perfusionists, cardiologists, cardiac anaesthetists, cardiac surgeons, medical technologists not to mention effective and up to date equipment for maximum efficiency. Failure in any of this leads to poor results with regards to the surgery. Various aspects of these failures will be highlighted in the text that follows particularly over the peri-operative period.

Left ventricular dysfunction is common immediately after cardiac surgery due to the reduced compliance and contractility of the cardiac muscle (2). Patients are at an increased risk of developing low cardiac output syndrome (LCOS) (3). Despite the availability of a wide range of inotropic agents for management of LCOS, no consensus exists regarding its treatment after cardiac surgery (4).

A thorough assessment of the risk factors predicting the use of inotropes has not been undertaken in our institution. At present, no specific protocol exists at KNH regarding the use of inotropes

post-cardiac surgery; this study elucidates the current practice and provides some data that could be used in future to formulate a policy for rational inotropic use.

A study on the thirty-day mortality done at the Kenyatta National hospital highlights increased mortality in our set up perhaps due to late patient presentation. It also suggests a need to bring down the mortality through improved preoperative preparation and a reduction in surgical ischaemic times (5).

The same study indicates that the most common cause of early mortality post cardiac surgery is low output failure and this accounts for over 50% of early mortalities (5). It is some of these hemodynamic variables and the influence made by inotropes on low cardiac output syndrome that this study examined.

From the above, several problems have been highlighted in our set up. This study emphasizes on peri-operative factors influencing the use of inotropes post cardiac surgery.

2.0 Literature review

Cardiac surgery began developing in the 1940's with a number of operations carried out without the cardiopulmonary bypass machine. These included, closure of a patent ductus, coarctation repair, Blalock-Taussig shunt, mitral commissurotomy and closure of atrial septal defects with the use of hypothermia (7).

About half a century ago, cardiopulmonary bypass was developed and first clinically used by John Gibbon Jr (8). Subsequently, teams at the Mayo clinic and University of Minnesota initiated the routine use of this novel technique in open heart surgery (9).

Documented reports of cardiac surgery in Africa date as far back as 1964 when surface cooling was used by Ghanaian surgeons to close atrial septal defects (10). However, there are various risk factors associated with open heart surgery and the consequences post-operatively to the cardiac muscles.

Immediately after severance from cardiopulmonary bypass, ventricular function is seen to improve however it then begins to worsen, reaching a nadir between 4 and 6 hours post-surgery with full recovery occurring 24 hours postoperatively (3). The rate of ventricular depression is more severe and recovery much longer in patients who had preoperative ventricular dysfunction. (3)

2.1 Epidemiology

Mortality post cardiac surgery has been declining steadily over the past 20 years despite the complexity of procedures (10,11). Open heart surgeries performed between 1951 and 1955 revealed a disastrous mortality rate, with reports indicating 18 patients who had been operated on had only 1 survivor (6).Over the years, there has been drastic improvements in the mortality rates. Operative mortality in elderly and high risk patients has continued to decline with a 34% relative risk reduction over a period of 10 years (12).

The rates in developing countries still remain high despite continued improvement (13). Only 1% of the cardiothoracic surgeons worldwide practice in Africa and only 1 cardiothoracic surgeon is present for 4 million inhabitants (9,13,14). Mortality in KNH still remains higher than that reported in developed nations with low cardiac output syndrome playing a key role amongst the myriad of complications post cardiac surgery (5). Other complications post-cardiac surgery include, myocardial infarction, asystole, ventricular tachycardia or fibrillation, tamponade, aortic dissection, acute renal failure, sepsis, respiratory insufficiency, pulmonary embolism, multi-organ failure and in hospital death (15).

2.2 Low Cardiac Output Syndrome (LCOS)

Low cardiac output syndrome is a well-known common post-operative complication with known haemodynamic and physiological attributes (11). It is a clinical condition characterised by a transient decrease in systemic perfusion or cardiac output secondary to myocardial dysfunction (16).

This results in a deficiency between oxygen delivery and consumption at a cellular level leading to metabolic acidosis which if unchecked can result in multiple organ failure and death (10). It may

result from other systemic disease processes, but the highlight here was with regard to LCOS post cardiac surgery specifically requiring cardio-pulmonary bypass. It typically develops 4-6 hours after cardio-pulmonary bypass surgery.

Low cardiac output syndrome may also be defined as the need for postoperative intra-aortic balloon pump or inotropic support for >30 minutes in the intensive care unit (17,18); specifically, a cardiac index of less than 2l/min/m^2. Approximately a fifth of cardiac patients develop some form of cardiac dysfunction in the peri-operative period which is characterized by the inability to pump blood at normal end-diastolic pressures (19). In young children this figure is slightly higher at 25% (16).

2.3 Risk Factors

Cardiac surgery with cardiopulmonary bypass is the primary risk factor for LCOS. Other risk factors for post-operative LCOS include; age> 70 years, LVEF < 30%, prolonged QRS interval. increased time on CBP machine, reoperation. female sex, both hypo- and hyperthermia, systemic inflammation, residual cardiac lesions, electrolyte imbalances, diabetes and significant coronary disease (16).

2.4 Clinical Presentation

Tachycardia, hypotension, increased capillary refill time, decreased peripheral pulses , cool extremities, and decreased urine output are the commonest signs and symptoms in patients with post-operative LCOS (16). Other clinical manifestations of LCOS occur as a result of its consequences which include acute renal failure, neurologic and pulmonary complications as well as atrial fibrillation. (16,17,18)

2.5 Diagnosis

Diagnostic tests used in LCOS are both laboratory and imaging based. The full haemogram is performed to evaluate for anaemia, an electrolyte panel is done to rule out underlying electrolyte imbalances, arterial blood gas is evaluated for perfusion and metabolic disturbances due to the low circulation at the cellular level and a serial serum lactate level is done as a pointer to the perfusion adequacy (16). An arteriovenous difference in oxygen saturation also gives an indication of cardiac output and oxygen consumption which are of great practical clinical and prognostic value. (20) Due to the reduced perfusion, other features in the arterial blood gas would be those suggestive of compensated or uncompensated metabolic acidosis (16)

2.6 Treatment

The treatment of LCOS is multi-pronged. The goals include minimization of oxygen consumption, promotion of healing, reduction of risk for complications and providing emotional and educational support to the patient and close family members (16). The patient is given analgesics, anti-arrhythmics, inotropes and is provided with mechanical ventilation. Urine output should be monitored as low output increases morbidity through renal failure. (19,21)

2.7 The peri-operative period

The peri-operative period may be classified within distinct clinical scenarios: precardiotomy, failure to wean off bypass and postcardiotomy (19). These all differ with regards to diagnosis, monitoring and management but these periods contain valuable measurable indices which influence cardiac function post cardiac surgery. Cardiac output declines as a result of reduced ventricular contractility and compliance (3).

Using the peri-operative classification, precardiotomy heart failure or pre-operative factors include disease sequalae which may be causing chronic myocardial ischaemia. The dysfunctional myocardium may not have undergone irreversible damage. It may in fact be "stunned" to the point that revascularization greatly improves myocardial performance. In this instance, the longer disease process increases morbidity; inadequate myocardial protection to such a heart further aggravates post cardiac surgery cardiac dysfunction (19).

Failure to wean off bypass is in turn caused by a multitude of factors which may be procedure related or patient specific. A successful therapeutic approach requires knowledge of the underlying cause. These include inadequate myocardial protection, ischemia, infarction, myocardial hyperthermia, small blood vessels, incomplete revascularization of the heart, reperfusion injury, metabolic, uncorrected pathology, mechanical issues, conduction issues, pulmonary hypertension and right ventricular failure (19).

The above consists of intraoperative factors which play a role predicting LCOS. Other directly measurable intraoperative factors include length of cardiopulmonary bypass as well as aortic cross clamp time (11,19). Establishing predictors of LCOS as well as early diagnosis of LCOS can avert mortality and morbidity associated with LCOS (3,4,10).

In post cardiotomy cardiac failure, preservation of end organ function takes precedence. Maintenance of adequate cardiac output and blood pressure is obtained through optimization of preload and cardiac output in conjunction with positive inotropic and/or vasopressor drugs (19).

2.8 Predictors of inotropic use

Ahmed et al highlights pre-operative independent predictors of inotrope use in patients subjected to cardiopulmonary bypass including:

- Cardiac index (CI) ≤ to 2.5L/min/m^2
- LVEDP (left ventricular end diastolic pressure) ≥ 20mmHg
- LVEF (left ventricular ejection fraction) ≤ 40%
- Chronic Kidney Disease stage 3 to 5 (21).

These predictors are however specific to patients undergoing both CABG and AVR. In KNH, the only routinely measured factor in the list is the ejection fraction. Other known predictive factors of inotrope use post cardiac surgery include female gender, older age, history of congestive cardiac failure, emergency operation, recent myocardial infarction as well as left main coronary disease (21).

It should be noted that other factors such as chronic ischemic heart disease, left ventricular dysfunction in patients with moderate to severe valvular heart disease do not improve immediately after surgery (4). These may be considered pre-operative risk factors and are measurable in ECG and Echo.

A pre-operative echocardiogram with variables such as left ventricular ejection fraction and left ventricular end diastolic volume will give a quantitative function of the heart before the operation. A post-operative echocardiogram is also performed to quantify the function of the heart. Apostolakis et al also mentions left ventricular dysfunction as being a significant predictor of

post-operative morbidity and mortality (22). From the above it can be postulated that there are pre-operative, intra-operative and post-operative factors which play a major role in predicting the use of inotropic agents.

2.9 Inotropes

Inotropes are substances with excitatory and inhibitory actions on the heart and vascular smooth muscle as well as important effects on metabolic, central nervous system and presynaptic autonomic nervous system effects. (24)

Table 1 Receptors and effects of various inotropes (23,24)

Inotrope	Receptors				Cardiac effect	Major vascular effect
	α_1	β_1	β_2	Dopamine		
Dopamine	+++	++++	++	+++++	Intermediate dose: +ve chronotropy, +ve inotropy	Low dose: Coronary, renal, mesenteric vasodilation High dose: Vasoconstriction
Dobutamine	+	+++++	+++	nil	+ve inotrope +ve lusitropy weak chronotrope	Mild vasodilation
Noradrenaline	+++++	+++	++	nil	Minimal chronotropy +ve inotropy improved coronary flow	Vasoconstriction
Adrenaline	+++++	++++	+++	nil	+ve chronotropy +ve inotropy	Vasoconstriction
Milrinone	Nil	Nil	Nil	Nil	+ve inotrope	Vasodilation

Inotropic support post cardiac surgery haemodynamically optimises cardiac muscle function by improving tissue microvascular flow as well as oxygenation (23). Inotropes may be broadly categorized into catecholamines, phosphodiesterase inhibitors and calcium sensitizing agents. Catecholamines propagate action predominantly through α_1, β_1, β_2 and dopaminergic receptors. The density and proportion of these receptors thus modulate the physiological responses of inotropes in individual tissue. (24)

Catecholamines used in Kenyatta National Hospital include Dopamine, Dobutamine, Epinephrine and Norepinephrine while the phosphodiesterase inhibitor milrinone is used depending on availability.

These drugs particularly the catecholamines have dose dependent action. The spectra of drugs to choose all affect myocardial performance by having an effect on the variables of cardiac output through various receptors (24). It is therefore important to recognize the dose-response relationship, to consider route and rate of administration, and to take into account the presence of other drugs as well as the abnormal pathophysiology of the patient.

Effective and safe use of inotropes and vasodilators in critically ill patients is most readily achieved when there is a systematic plan for introducing the drug. This involves evaluating its effects and adjusting those hemodynamic variables that can be controlled (4,24). Improper use of inotropes results in increased risk of tachycardia, dysrhythmia and myocardial ischaemia with a poor prognosis on the post cardiac-surgery patient (21).

3.0 Rationale

The mortality rates post cardiac surgery are generally on a downward trend worldwide due to improved knowledge, skill and equipment. The level of care in the intensive care units has also remarkably improved. Despite this downward trend worldwide, the morbidity and mortality rates in Kenya may be above the average internationally. The mortality meetings in the cardiothoracic ward in KNH between 2014 to 2016 have put the mortality at 25% post cardiac surgery compared to 3.4% internationally according to Mazzeffi et al; however, this must be interpreted with caution because of our small sample size.

Several factors may contribute to these elevated rates, however a prominent one is end organ damage that occurs secondary to left ventricular dysfunction leading to low cardiac output syndrome. Inotropic support is vital in patients with LCOS as it augments the action of the cardiac muscles. There are several different classes of inotropes and the type used largely depends on the underlying mechanism causing LCOS.

Different hospitals have protocols that they implement during inotropic use in patients post cardiac surgery leading to improved outcomes. These protocols are based on hemodynamic and peri-operative risk factors. At the KNH, we currently do not have any existing local protocol defined for patients with LCOS despite the higher relative morbidity and mortality rates. This study elucidates the existing approaches used in inotropic support at the KNH in patients post-cardiac surgery, and the outcomes. This data could be used towards forming a protocol based on local epidemiology for future reference in order to improve the morbidity and mortality outcomes in our patients.

4.0 Research Question

What are the perioperative risk factors in cardiac surgery, pattern of inotrope use and outcomes at the Kenyatta National Hospital?

5.0 Objectives

5.1 Main Objective

- To determine the pattern of inotropic use post cardiac surgery at Kenyatta National Hospital.

5.2 Specific Objectives

1. To determine the perioperative risk factors in cardiac surgery at the Kenyatta National Hospital.
2. To determine pattern of inotropic use with regards to various peri-operative risk factors at the Kenyatta National Hospital.
3. To determine the in-hospital mortality rate of cardiac surgery patients.

6.0 Methodology

6.1 Study Design

This was a retrospective cross-sectional study of the patients operated from 2013 to 2016

6.2 Study Area Description

Kenyatta National Hospital is the largest referral and teaching Hospital in East and Central Africa. It has a capacity of 1,600 beds; 24 outpatient and specialist clinics and more than 6,000 staff members.

6.3 Study Population

The population of interest was drawn from patients who underwent elective open-heart surgery at the Kenyatta National Hospital over 3 years. The period was from January 2013 to December 2016 a period during which there were regular open-heart surgeries. The records were sourced from the Records Department, Kenyatta National hospital.

The inclusion criteria were:

- Adults ≥ 18 years of age.
- Any elective open-heart surgery in KNH.

The exclusion criteria were:

- Patients younger than 18 years of age.
- Patients with incomplete records with respect to data collection tool

6.4 Sample Size

The sample size was determined using the formula (25):

$$n^1 = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where

n^1= sample size with finite population correction

N=Population of post cardiac surgery patients in KNH during the target study period estimated at 225 patients (average of 75 patients per year over a 3-year period)

Z= 1.96 Z statistic for 95% level of confidence

P= Expected proportion of all patients any one of the specific types of inotropes in the post-cardiac surgery period in KNH (since there are no existing published estimates a P of 0.5 was assumed based on recommendations by Naing et al)

d=Precision (0.05)

Thus, based on the formula above the sample size for this study was 143

6.5 Sampling method

Convenient sampling method was to be used until the appropriate sample size was attained. Only 109 out of 143 patient files were acquired.

6.6 Data and Statistical analysis

The data was analyzed using Statistical Product and Service Solutions (SPSS Version 20) and Microsoft Excel 2013. Descriptive analysis of continuous variables (e.g. patient age, weight, arterial pressures and ventricular fractions) involved calculating a measure of central tendency (mean or median) and a measure of spread (standard deviation or ranges) depending on the normality of distribution. For categorical variables including gender, and type of surgery, percentages of patients with each level of the factor was calculated and presented using frequency tables.

The pattern of inotropic use was determined by measuring the number, dosage and duration used for each post cardiac surgery patient Means and medians were used for continuous variables while proportions were used for categorical variables. Any association between dosage and the number of inotropes used and specific pre-operative (e.g. specific type of heart lesion, ejection fraction) and intra-operative (e.g. cardiac bypass time) parameters were determined using independent t-test.

Hospital mortality rates were calculated and presented as a percentage (95% CI). The actual confidence interval was however 72% due to the inability to acquire up to 143 complete records. Finally, inferential analysis was used to determine risk factors associated with perioperative outcomes in cardiac patients. Mean difference was calculated to compare means of continuous variables in patients with and without the risk factors and T-test applied in determining statistical significance. For categorical risk factors percentages were calculated by proportion. Multivariable analysis of risk factors that are significantly associated with perioperative outcomes were conducted and Odds ratio (95% CI) reported for independent predictors of perioperative outcome. All statistical tests were to be determined at the alpha level of 0.05.

6.7 Data Collection and Data Analysis

Collection was done through input of patient file records into the study questionnaire. The data was then transferred to Microsoft Excel 2013 and SPSSv20. Confidentiality was observed and no patient names featured in the questionnaire. Consent was sought from patients who are still on follow up at the hospital using a phone verbal consent form. Data collection was done by myself and research assistant, a medical officer

Frequency tables and summary statistics were made for demographic and patient characteristics of the subjects post cardiac surgery. Continuous variables were presented as means and standard deviations. Student's *t*-test was used for differences in continuous variables.

Differences in various means of peri-operative risk factors were displayed on charts and graphs. Linear graphs were used to show trend particularly for continuous variables.

6.8 Study Limitations

Since this was a retrospective study, it was susceptible to selection bias, missing data sets as well as some confounders which were not recorded. There were missing files and incomplete data to the point that only 109 files were acquired with complete data. In addition, some of the pre-operative factors especially that of pre-operative echo are user dependant meaning that the exact values are not easily reproducible. Measurement of left ventricular dysfunction was not possible because of the inconsistency in measured values with some echocardiographers not placing them in the echo report.

7.0 Ethical Consideration

Ethical approval was sought from the Kenyatta National Hospital - University of Nairobi Ethics and Research Committee (KNH-UoN ERC) and the Department of Surgery, School of Medicine, University of Nairobi. The study was approved.

Consent for retrospective studies presents a dilemma. Verbal phone consent was acquired from the surviving participants due to the complexities involved in their physical appearance.

8.0 Results

A total of 133 files were perused of which 109 had met the study inclusion criteria; - 24 files had incomplete data in the follow up notes.

Table 2: Patient Characteristics

Parameter	Male	Female
Number	36 (33%)	73 (67%)
Age (Mean)	30.97	30.65
Age (Median)	27	30
SD (Age)	17	10
Weight (Mean)	55.44	58.02
Severe pulmonary hypertension	9 (25%)	17 (23%)
Ejection Fraction <40%	3 (8%)	8 (11%)
Mitral valve • Regurgitation • Stenosis	 15 (47%) 13 (36%)	 27 (37%) 15 (20%)
Mitral Valve replacement	23 (64%)	43 (57%)
Aortic Valve • Regurgitation • Stenosis	 2 (6%) 4 (11%)	 9 (12%) 7 (9%)

Aortic Valve Replacement only	3 (8%)	6 (8%)
Tricuspid annuloplasty	9 (25%)	11 (14%)
DVR	5 (14%)	13 (17%)
ASD/VSD	7	2
CABG	1	1
Bental	0	2

The patients ages ranged from 18 up to 75 years. The female patients were much more at 73 (77%) compared to male patients at 36.

It was also found that 9 (25%) of the male patients had severe pulmonary hypertension in the pre-operative echo while 17 (24%) of the female patients had the same. The ejection fraction was less than 40% in 3 of the male patients and 8 of the female patients. Left ventricular dysfunction was one of the readings meant to be measured from the echo but this was inconsistently reported in the cardiac echo and for this reason it was not measured leaving ejection fraction as the only component measuring the heart function.

In the both male and female, mitral regurgitation was the most common valve pathology with 47% of the males being affected compared to 36% of the females. Mitral stenosis affected 36% of the males in the study while 20% of the females were affected. A total of 23 (64%) of the males underwent single mitral valve replacement compared to 43 (57%) of the females.

Aortic regurgitation affected 2 out of the 36 male patients compared to 9 out of the 76 female patients while aortic stenosis affected 4 male and 7 females in the study. Only 3 males in the

overall study underwent aortic valve replacement only compared to 6 females. It was also noted that 9 (25%) of males in the study underwent tricuspid annuloplasty compared to 11 (14%) females.

There were 5 double valve cases amongst the male patients and 13 amongst the female patients. Other operations done included 6 ASDs for the males, 1 VSD for the males, 2 ASDs for female, a single CABG in both male and female patients, 2 Bentals amongst the females as well as a pulmonary valvotomy and mitral valve repair.

8.1 Risk factors

Only 14 (12.8%) out of the total number 0f 109 patients were found to have the following risk factors. Left ventricular dysfunction and pulmonary hypertension are discussed under a separate heading. These included:

Table 3: Risk factors

Risk factor	**Number affected**
Hypertension	5
Diabetes	2
Chronic renal failure	2
Chronic pulmonary disease	2
Previous cardiac surgery	3

8.2 Severe tricuspid regurgitation and tricuspid annuloplasty

Twenty-nine (26.6%) patients were found to have severe tricuspid regurgitation. Only 19 of these patients had tricuspid annuloplasty done representing 66%.

8.3 Cardiac Bypass time & Cross-clamp time

The cardiac bypass time ranged from 52min up until 360min. The aortic cross clamp time ranged from 28min to 240min. The mean cardiac bypass time was 105min while the mean aortic cross clamp time was 69min. The median cardiac bypass time was 90min while the median aortic cross clamp time was 60min. The standard deviation for cardiac bypass time was 55min while the standard deviation for aortic cross clamp time was 49min.

An independent t-test was done to compare the influence of CPB time to the use of high dose inotropes at 48hrs:

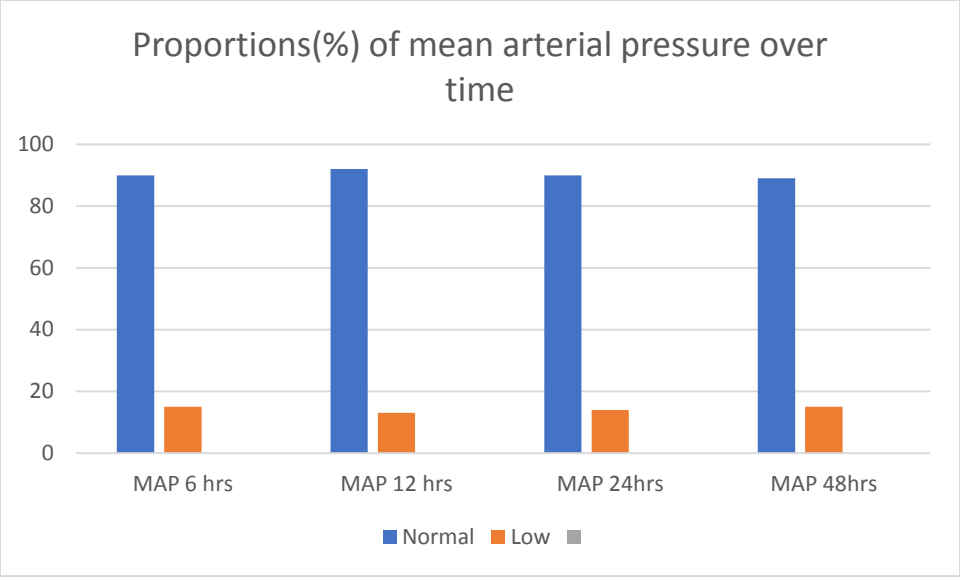
	Inotrope 48	N	Mean	Std. Deviation	p-value
CBP time	H	26	132.08	55.533	0.004
	N	81	96.32	53.957	

The mean difference was found to be statistically significant with a p-value of 0.004

8.4 Mean arterial pressure post cardiac surgery

Values of MAPs were taken at 6 hours, 12 hours, 24 hours and 48 hours post cardiac surgery. The values were placed in ranges meaning normal was considered anything above 60 while low was considered anything below 60. A trend of the MAP values was superimposed for all the 109 patients.

Chart 1 : MAP post cardiac surgery



The bar graph indicates that majority of patients had a normal trend of MAPs at 6hr, 12 hrs, 24hrs and 48hrs post cardiac surgery. The range of patients with below normal MAP post cardiac surgery ranged between 13% and 15%.

8.5 Central Venous Pressure monitoring post cardiac surgery

Values of CVP were measured at 6 hours, 12 hours, 24 hours and 48 hours post cardiac surgery. The values of low, normal or high were used to describe the values with low being below 8, normal being up to 13 and high values above 13.

Table 4: CVP values

	CVP 6hrs	CVP 12hrs	CVP 24hrs	CVP 48hrs
Low	28 (26%)	12 (11%)	7 (6%)	3 (3%)
Normal	56 (51%)	69 (63%)	73 (67%)	71 (65%)
High	21 (19%)	24 (22%)	22 (20%)	20 (18.3%)

8.6 Urine output post cardiac surgery

Values of urine output in ml/kg were measured at 12 hours, 24 hours and 48 hours post cardiac surgery. The values of low or normal were used to describe the amount with low being below 0.75ml/hr/kg and normal being above this value.

Table 5: Urine output

	Urine 12hrs	Urine 24hr	Urine 48hr
Low output	30 (28%)	19 (17%)	17 (16%)
Normal output	79 (72%)	90 (83%)	92 (84%)

The trend shows that there was a higher percentage of urine output below normal at 12hrs with some element of recovery towards the 24hr and 48hr mark with regards to most of the patients

A t-test was done to compare the CBP time and urine output 48hrs post cardiac surgery where N was normal output and L was low output.

Table 6: Urine output at 48hrs vs Cardiopulmonary bypass time

Urine at 48hrs	N	Mean	Std. Deviation	p-value
CBP time N	90	95.00	37.046	0.134
L	14	121.14	59.940	

The mean CBP of patients with low urine output at 48hrs was higher though the p value (0.134) was not found to be statistically significant

8.7 Peripheral circulation post cardiac surgery

This was measured at 12 hours and at 24 hours with the differences being either cold or warm. There were 16 (15%) patients who had cold peripheries at 12hrs post-surgery. Of these 2 still had cold peripheries at 24 hours while the rest had warm peripheries. On the other hand, there were 91 (85%) patients with warm peripheries at 12 hours. Of these 2 (2%) changed to cold peripheries at 24hrs while the rest still had warm peripheries. These two patients later became mortalities.

8.8 Ventilation post cardiac surgery

Ventilation was checked at 24 hrs and at 48 hrs in the study set.

Chart 2: 24 hours post cardiac surgery

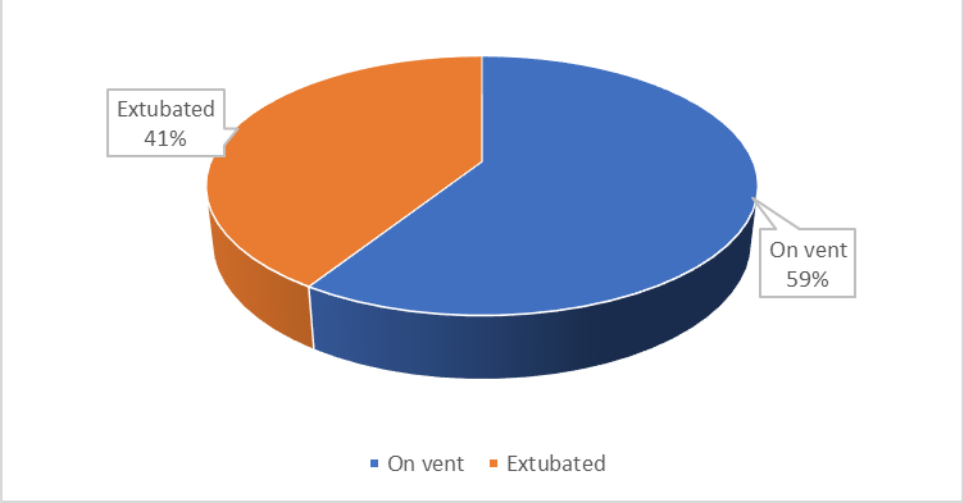
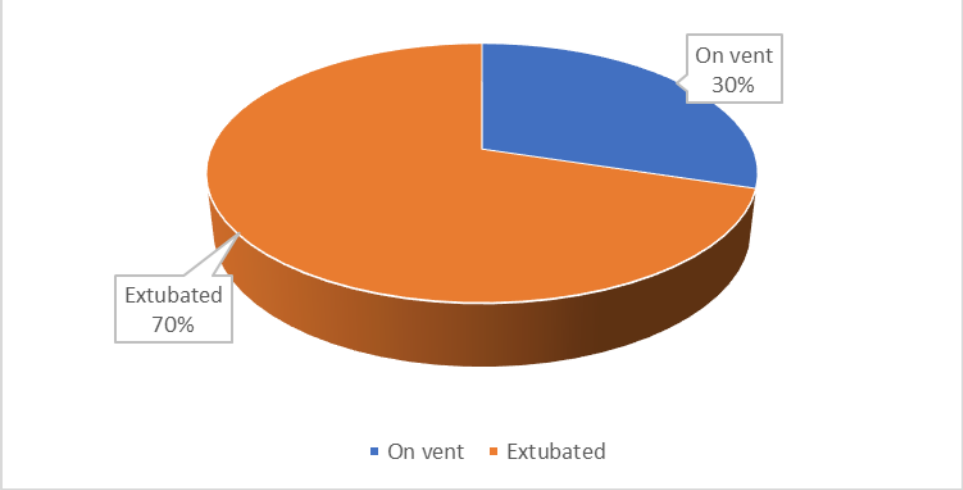


Chart 3: 48hrs post cardiac surgery



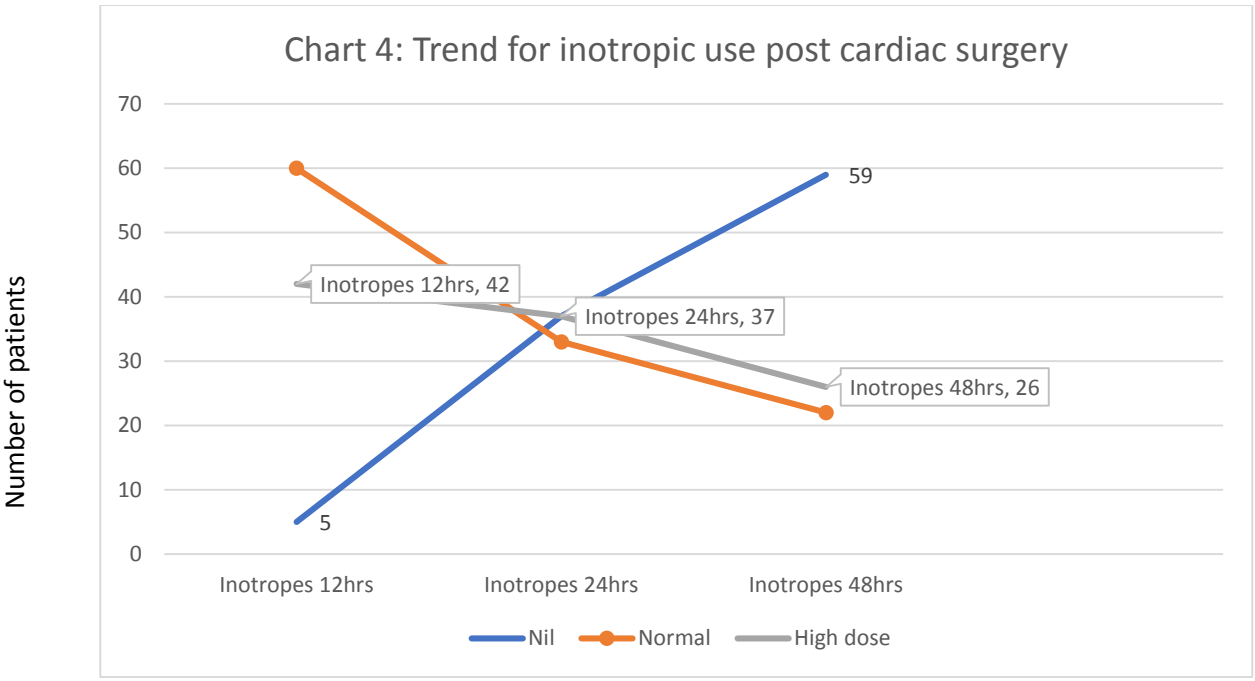
From the above, it can be noted that majority of patients at 59% were still on the vent at 24hrs post cardiac surgery. This amount increased to 70% as at 48hrs post cardiac surgery

8.9 Inotropic use

The specific inotrope used in all patients was documented. The duration of use over 12 hours, 24 hours and 48 hours was also indicated with a differential of nil, normal or high. Normal indicated use of any single inotrope while high indicated use of more than one inotrope and nil indicated that inotropic support via intravenous infusion had been stopped.

Table 7: Inotrope use post cardiac surgery

	Inotropes 12hrs	Inotropes 24hrs	Inotropes 48hrs
Nil	5 (4.6%)	37 (35%)	59 (55%)
Normal	60 (56%)	33 (31%)	22 (21%)
High dose	42 (39%)	37 (35%)	26 (24%)



The chart shows the general trend with regards to inotropic use post cardiac surgery in KNH. The chart nil inotropes increases over 48hrs indicating a reduction in inotropic use as time progresses. The normal and high doses are also seen to generally reduce over time as well.

The pattern of inotropic use was skewed with the following combinations coming into play:

Table 8 : Combination of Inotropes used

Inotrope	Number (%)
No inotropes	4 (3%)
Adrenaline only	74 (69%)
Noradrenaline only	2 (1.8%)
Dobutamine only	3 (2.8%)
Dopamine only	2 (1.8%)
Adrenaline and Dobutamine	8 (7.4%)

Inotrope	Number (%)
Adrenaline and Dopamine	7 (6.5%)
Adrenaline and milrinone	3 (2.8%)
Noradrenaline and milrinone	1 (1%)
Dopamine, adrenaline and milrinone	3 (2.8%)
Adrenaline, Noradrenaline & Dopamine	1 (1%)

8.10 Length of ICU stay

The length of ICU stay ranged from 1 to 10 days with a mean of 4.2 days and a median of 3 days. There were 23 (21.5%) patients who stayed longer than 5 days in ICU. It was noted that 5 of these patients had pre-operative risk factors including previous cardiac surgeries for 2, 2 with hypertension and one with chronic pulmonary disease. Five of the patients had undergone more complex surgeries with 3 having had a double valve replacement while 2 had Bental's procedure. Of the 23 patients with long stay ICU the mean ejection fraction was 52% with a median of 55%. However, 5 (21.7%) of the patients had an ejection fraction less than 40%.

The mean CBP time of these patients was also 152min which was much higher than the mean at 105min. A t-test was done comparing the CBP time longer than 3 hours to length of ICU stay:

Table 9: Length of ICU stay and CBP time

	CBP time	N	Mean	Std. Deviation	p-value
ICU stay	<=180	98	4.20	1.6	0.903
	>180	7	4.29	2.6	

The mean difference of 0.09 days was not statistically significant (p=0.903)

Also noted was that 53% of the same patients had severe pulmonary hypertension and 73% of the patients were on high dose inotropes as of 48hrs past the surgery. Sixty eight percent of the patients also had low urine output.

A t-test was done to compare ICU stay to the presence of severe pulmonary hypertension.

Table 10: Length of ICU stay and PAH

	PAH	N	Mean	Std. Deviation	p-value
ICU stay	Severe	25	4.44	2.022	0.441
	Normal/Moderate	80	4.14	1.597	

The mean difference of 0.30 days was not statistically significant (p=0.441)

Table 11: Length of ICU stay and gender

	Gender	N	Mean	Std. Deviation	p-value
ICU stay	Male	36	4.56	1.949	0.133
	Female	69	4.03	1.543	

An independent sample t-test was performed to ascertain if there are differences in the length of stay in ICU for male and female patients. The mean difference of 0.53 days was not statistically significant (p=0.133)

Table 12: Length of ICU stay and DVR

	DVR	N	Mean	Std. Deviation	p-value
ICU stay	Yes	17	4.00	1.541	0.582
	No	88	4.25	1.737	

A t-test comparing length of double valve replacement and length of ICU stay was done and was not statistically insignificant (p=0.582)

Table 13: Length of ICU stay vs mitral regurgitation or mitral stenosis

	Mitral	N	Mean	Std. Deviation	p-value
ICU stay	MR	49	4.00	1.399	0.174
	MS	34	4.50	1.927	

The mean difference of 0.50 days was not statistically significant (p=0.174)

8.11 Mortality

In this study, there were 14 mortalities. The mortality rate for this sample size was 12.8%

Table 14: Day vs Mortality

	Mortalities
Day 0/1	3 (2 on table)
Day 2	3
Day 3	3
Day 4	2
Day 6	1
Day 10	1
Day 13	1

Of the 11 mortalities who did not die on the table:

Table 15: Other mortalities

		Value
Gender	Male	4 (45%)
	Female	6 (55%
Low MAPs 48hrs post op		9 (81%)
CVP at 48hrs post op	Low	2 (18%)
	Normal	1 (9%)
	High	8 (73%)
Pulmonary hypertension	Severe	8 (73%)
	Moderate	1 (9%)
	Normal	2 (18%)
Peripheries at 48hrs	Warm	2 (18%)
	Cold	9 (82%)
Urine output	Normal	2 (18%)
	Low	9 (82%)
Vent at 48hrs		11 (100%)
High inotropes at 48hr		11 (100%)

According to the above, 9 (82%)of the patients had LCOS indicated by the clinical findings. Five of the patients were also on triple inotropes before mortality

Of the 3 other mortalities, two who died on table 2 had severe pulmonary hypertension. No other readings were done because the patient did not reach ICU, but the cardiopulmonary bypass time was over 5 hours. The other patient who died on day 0 had severe pulmonary hypertension and was on cardiopulmonary bypass for 4 and a half hours. The patient only had readings immediately post op and required emergency sternotomy for resuscitation after transfer to ICU.

9.0 Discussion

Low cardiac output is one of the known complications post cardiac surgery which causes increased morbidity and mortality(1,2,3). The risk factors for LCOS were already highlighted in the introduction of the text. Low cardiac output has a multipronged method of management. One of the methods is systematic introduction of inotropes immediately while weaning a patient from cardiopulmonary bypass. No consensus exists regarding the methods of their introduction.(12,13)

This study aimed to elucidate the pattern of inotropic use post cardiac surgery in KNH, the morbidity and mortality post cardiac surgery in KNH as well as the peri-operative risk factors associated with differential use of inotropic agents post cardiac surgery.

Table 8 shows the pattern of inotropic use post cardiac surgery in KNH. There were 11 different combinations of inotropes recorded with adrenaline only being the most commonly used inotrope. There is quite a large variance in inotrope use in KNH which confirmed the lack of a protocol governing the systematic introduction of inotropes post cardiac surgery.

During the study period, milrinone was not a commonly available inotrope due to its price and the few instances it was available was due to a visiting surgical team from outside the country. Nonetheless, in the few instances used, the patients were found to have previously had severe pulmonary hypertension. In those situations, it was favourably used due to its effect on right heart failure.

Another factor influencing the variance in pattern of inotropic use was surgeon/anaesthetist preference with everyone having their own preference on use of inotropes whether it was with regards in rate of increase of inotropes as well as there dosage. During the study period, the patients were either managed in the main KNH ICU which is the anaesthesiologists domain with

some being managed in the cardiothoracic ICU which is more of the cardiothoracic surgeons domain. All of these seemed to influence use of inotropes as well as length of ICU stay with patients being retained longer than normal particularly in the main hospital ICU so as to have an available ICU bed. KNH is severely limited in terms of number of ICU beds for the total number of patients. This may also explain the lack of a statistically significant length of ICU stay between single valve and DVR patients.

At present, there has been an increased availability of inotropes particularly milrinone which would definitely have influenced this studies pattern of inotropic use however a consensus on a pattern or algorithm for the systematic use of inotropes post cardiac surgery does not exist in KNH which would certainly help in the management of post cardiac surgery patients especially since they are currently managed by both the cardiothoracic surgeons and the cardiac anaesthesiologists.

As noted in Table 2 above, majority of the patients were of female gender. Female gender is considered a risk factor for LCOS(15) but in this study female gender was not associated with LCOS. despite the female to male mortality being 8:5. Table 10 confirms that there was no statistical significance between male and female patients for length of ICU stay. However, it should be noted that our data set had a variety of other independent risk factors which may have played a bigger role in determining ICU stay compared to the patient gender. The period of stay in the KNH ICU also has other confounding factors such as the need for an ICU bed for a different patient.

The most common open-heart surgery performed in KNH is MVR and this is mainly for the most common lesion of mitral regurgitation as a result of RHD. The 2nd most common lesion is mitral stenosis followed by aortic regurgitation in males and aortic stenosis in females. In our data set however, there was no difference of note between the initial pathology of the patient with regards

to different valve pathologies and patient morbidity except with the more complex valve procedures such as DVR with tricuspid annuloplasty and Bental's procedure which all had higher morbidity. These values however did not show statistical significance in the t-tests most likely because of the influence of other multivariate factors and a small sample size. The length of ICU stay was also not necessarily dependent on the patients state as mentioned above. It should be noted that the more complex surgeries also had longer CPB times meaning the morbidity was further increased.

A comparison between patients with low urine output at 48hrs and mean CBP time (Table 6) showed that though the mean CBP was higher in the subset of patients with low urine output, it was of no statistical significance. It should be noted that the high variance of the CBP times played a role in the subset of those patients who had low urine output at 48hrs post cardiac surgery.

Another peri-operative factor found to influence morbidity was severe pulmonary hypertension. A t-test comparing severe pulmonary hypertension to length of ICU stay (Table 10) was found not to be statistically significant. However, patients in KNH are sometimes kept in ICU for longer periods of time than expected to have an ICU bed booked especially if the patient is in the main ICU. At the time of the study, milrinone was not readily available in KNH hence the increased morbidity for pulmonary hypertension. The other peri-operative factor which made a marked difference in morbidity of patients was CPB time.

In the group of patients who had severe tricuspid regurgitation only 66% had tricuspid annuloplasty done. This may have influenced the morbidity and mortality as shown in the subset of patients who still had a high CVP at 48hrs and long ICU stay.

Left ventricular function was also not precisely measured in these patients due to the non-standardised method of reporting echocardiograms which are performed by both technologists and cardiologists. It is also known that echocardiograms are user dependent. In our study set, using ejection fraction alone did not reveal large mean differences in morbidity. This could be because of the different valve pathology where mitral regurgitation gives a false impression of the ejection fraction which has a direct effect on the different t-test for statistical significance. It would be prudent to use a larger sample size to confirm some of these values in future or obtain more standardised echocardiograms to better determine the role played by cardiac function as a peri-operative risk factor

Our sample size showed a mortality rate of 12.8% compared to the previously recorded KNH mortality post cardiac surgery of 20%. It should however be noted that an adult mortality rate has not been calculated in KNH with 20% mortality rate including the paediatric cardiac heart surgery. The mortalities in this study however showed the strong role played by previous risk factors especially previous cardiac surgery as a predictor of a higher mortality rate. Majority of these patients also developed LCOS indicating the need for better understanding of management of LCOS towards reducing the mortality post cardiac surgery. Despite the lack of statistical significance between severe pulmonary hypertension and ICU stay, Table 15 shows 73% of the mortalities had severe pulmonary hypertension which indicates a possible correlation to morbidity and mortality. This potentially has implications for patient selection before cardiac surgery and risk stratification of various patients with regards to both patient counselling and planning for surgery.

The current availability of other inotropes such as milrinone may have greatly improved the management of this risk factor in influencing mortality and morbidity post cardiac surgery.

10.0 Recommendations

The methods of record keeping in KNH should be digitalized. If this is not possible, a database of patients operated on by the cardiothoracic team should be kept to facilitate both follow up of patients as well as future studies. A number of the records were incomplete and a number of the files were untraceable especially the mortalities which are files separately from the other patients.

Considering the wide array of inotropes available, it would be prudent to form an algorithm towards the systematic introduction of inotropes post cardiac surgery to better manage LCOS. The current availability of milrinone has greatly helped in the management of severe pulmonary hypertension in patients with valvular heart disease.

Due to the team approach towards managing these patients in ICU, an open line of communication between the anaesthesiologists and cardiac surgeons should be maintained especially with regards to the critical patients such that introduction and/or tapering off of inotropes should be done in a systematic manner while reducing morbidity of the patient.

The cardiac echos especially for the open heart patients should be standardised with regards to reporting so as to be able to capture all the pre-operative factors that may influence inotrope use post cardiac surgery.

Prudent ICU care with regards to discharges to the ward would also give a clearer picture of the morbidity of these patients. It should be noted that the mean stay of patients in ICU post cardiac surgery in KNH is higher than the mean stay in more advanced countries

With regards to the mortalities in the unit, considering the risk factors, patients should be classified as high risk and appropriate measures undertaken towards a team approach so as to improve prognosis of these patients. The additive euroscore is used worldwide to predict cardiac surgical

procedures performed on cardiopulmonary bypass. However, it has been found to be inapplicable to the Kenyan population because of a difference in weight of risk factors. Nonetheless the same study which confirmed this also recommends the need to develop a local scoring system to better predict outcomes of patients post cardiac surgery. (26)

11 Appendices

11.1 Verbal Consent Script

(English transcript)

An Evaluation of inotropic use post-cardiac surgery in KNH

Hello, my name is [state your name]. I'm working on a study being conducted by Fredrick Mitema from the University of Nairobi's Department of Surgery, Cardiothoracic unit. Do you have a few minutes to discuss the study?

- If yes, continue below.
- If no, but the potential subject is interested in participating, determine a better time to call back to discuss the study.
- If no, thank them for their time.

We are inviting you to take part in this study because you underwent open heart surgery between 2013 and 2016 at Kenyatta National Hospital. The purpose of this study is to compare medication used immediately after your operation while you were in the intensive care unit and how it was influenced by your specific heart condition. We would also be looking into details of your operation from your file.
If you agree to take part in this study, we will be asking you whether or not you agree to us going through your file to collect this information
All the information collected will be anonymous and will not have any immediate or long-term effects on your health. It may however benefit other patients who undergo open heart surgery in future. There is no external funding for the study, and it is being undertaken as part of completion of the Master of Medicine Degree by Dr Fredrick Mitema. You will also not be paid whether you agree or disagree for us to peruse through your KNH file.
Does this sound like something you'd be willing to participate in?

- If yes, continue below.
- If no, thank them for their time.

The information collected from your file will be kept anonymous and only with Fredrick Mitema and his supervisors at the university of Nairobi once the data is collected. It will be destroyed within 3 years from the time of commencement of this phone call.

Do you have any questions? Do you agree to participate in this study?

☐ Yes: Document oral consent below

☐ No: Thank them for their time.

Name of Subject: Tel No.

_____

Person Obtaining Consent

I have read this form to the subjects. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. The subject has provided oral consent to participate in this study.

_____

Name and Title (Print)

_____ _____

Signature of Person Obtaining Consent Date

(Kiswahili transcript)

Habari, Jina langu ni [sema jina lako hapa]. Ninafanya utafiti pamoja na Fredrick Mitema kutoka Chuo Kikuu cha Nairobi, Idara la upasuaji wa kifua na moyo. Je! Una dakika chache ili kujadili hili jambo?

- If yes, continue below.
- If no, but the potential subject is interested in participating, determine a better time to call back to discuss the study.
- If no, thank them for their time.

Tunakualika kushiriki katika utafiti huu kwa sababu ulipata upasuaji wa moyo kati ya 2013 na 2016 katika Hospitali ya Taifa ya Kenyatta. Kusudi la utafiti huu ni kulinganisha dawa iliyotumika mara moja baada ya operesheni yako wakati ulipokuwa katika kitengo cha huduma kubwa na jinsi ilivyoathiriwa na hali yako ya "valve" ya moyo na nguvu ya moyo wako. Pia tutaangalia maelezo ya operesheni yako kutoka kwa faili yako.

Ikiwa unakubali kushiriki katika utafiti hili, utaulizwa kama unakubalianansi kupitia faili yako kukusanya taarifa hizi.

Taarifa zote zilizokusanywa hazitajulikana ovyo na hazitakuwa na madhara kwa afya yako. Inaweza hata hivyo kuwasaidia wagonjwa wengine ambao watafanyiwa upasuaji wa moyo mbeleni. Hakuna fedha ya nje ya utafiti huu ila inafanyika kama sehemu ya kukamilisha Shahada ya uzamili katika Madawa ya Daktari na Dr Fredrick Mitema. Unafaa kujua pia hakuna malipo kwa kubaliana nasi kupitia faili yako ya KNH.

Je! Hii inaonekana kama kitu ungependa kushiriki?

- If yes, continue below.
- If no, thank them for their time.

Taarifa zilizokusanywa kutoka faili yako zitahifadhiwa bila kujulikana na Fredrick Mitema pekee. Taarifa hizi za utafiti hazitawekwa zaidi miaka 3 kutoka leo ilhali zitatupiliwa mbali.

Je! Una maswali yoyote? Je! Unakubali kushiriki katika utafiti huu?

☐ Yes: Document oral consent below

☐ No: Thank them for their time.

Name of Subject: Tel No.

_____

Person Obtaining Consent

I have read this form to the subject. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. The subject has provided oral consent to participate in this study.

_____

Name and Title (Print)

_____ _____

Signature of Person Obtaining Consent Date

11.2 Data Collection Sheet

Study Number	Age	Gender	Weight Height

Type of surgery done	Risk factors
○ Mitral Valve Replacement ○ Aortic Valve Replacement ○ Tricuspid annuloplasty ○ CABG ○ Other _____	○ Hypertension ○ Diabetes ○ Chronic Renal Failure ○ Chronic pulmonary disease ○ Previous Cardiac surgery

Pre-op Cardiac echo

Ejection fraction: _____ Left Ventricular dysfunction _____ Pulmonary hypertension	Lesion Mitral Valve: MS_____ MR_____ Aortic Valve: AS_____AR_____ Tricuspid: TR_____

Intra-op

Cardiopulmonary Bypass time _____ Cross clamp time _____

Post-op	6hrs	12hrs	24hrs	48hrs	Day3	Day4	Day5		
Mean arterial pressure									
CVP									
Peripheral circulation warm/cold									
Urine (0-0.5ml/kg) V Low 0.5-0.75ml/kg) Low									
On Vent (Yes/No)									
Inotrope (dosage)	6hrs	12hrs	24hrs	48hrs	Day3	Day4	Day5	Day6	
Adrenaline									
Noradrenaline									
Dopamine									
Dobutamine									
Milrinone									

Length of ICU stay	Mortality + Day

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