
FACTORS ASSOCIATED WITH OPERATIVE MORTALITY AMONG PATIENTS
ADMITTED WITH THORACIC AORTIC ANEURYSM/DISSECTION IN
KENYATTA NATIONAL HOSPITAL: A RETROSPECTIVE COHORT STUDY

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DECLARATION

I declare that this dissertation is my original work and has not been presented for a degree in any other university. All material that is not my work has been duly acknowledged.

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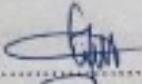
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ABBREVIATIONS AND ACRONYMS

AAA – Abdominal Aorta Aneurysm

AVF – Arterio-Venous Fistula

BMI – Body Mass Index

CCU – Critical Care Unit

CPB – Cardiopulmonary Bypass

CT – Computer Tomography

CVA- Cerebrovascular accident

DHCA-Deep Hypothermic Circulatory Arrest

ICU- Intensive Care Unit

KNH – Kenyatta National Hospital

LV- Left ventricle

MM- Millimetre

MRI – Magnetic Resonance Imaging

NHIF-National Hospital Insurance Fund

SCAD- Spontaneous Coronary Artery Dissection

TAA – Thoracic Aortic Aneurysm

TAD - Thoracic aorta dissection

TEVAR - Thoracic Endovascular Aneurysm Repair

TIA- Transient Ischaemic Attack

STJ – Sinotubular Junction

UoN – University of Nairobi

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ABSTRACT

Introduction: Thoracic aorta aneurysms (TAA) and Thoracic aorta dissection (TAD) are linked to significant morbidity and mortality. The incidence of death, undesirable post-operative complications and risk factors for mortality after undergoing open surgical repair for TAA/TAD remain largely unknown in Kenyatta National Hospital among patients undergoing management for TAA and TAD. Understanding the risk factors associated with operative mortality among patients with TAA and TAD would help improve patient selection for surgery hence reduce mortality and complications associated with the surgery.

Objectives: The objective of this study was to determine the rate of operative mortality and the risk factors associated with operative mortality among patients who underwent thoracic artery aneurysm/dissection surgical repair.

Methodology: This was a retrospective cross section study with a sample size of 31 cases. Data was collected from patient files retrieved from the records department at Kenyatta National Hospital. The study population included patients managed for thoracic aortic aneurysm/dissection at Kenyatta National Hospital from July 2010 to June 2020 through open surgical repair technique. Exposure variables were collected on socio-demographic, clinical factors, anatomical, radiological findings, intraoperative outcomes, the nature of the procedure done, time under Cardio-pulmonary bypass (CPB) and postoperative complications with the outcome variable as the 30-day mortality.

Data analysis: Stata 13.0 was used for data analysis. Means and medians were used to describe characteristics of the study participants. For univariate risk factor analysis Chi-

square were used for categorical data, and unpaired Students T-test for continuous data if it followed a normal distribution or Mann Whitney U test if data followed a non-normal distribution. Multivariate risk factor analysis using logistic regression and Survival analysis using the Kaplan Meier curve were used to assess for risk of mortality and other time related covariates.

Study results: The operative mortality rate was 34.6% (CI 17.9 – 54.3). Female patients constituted 51.61% of the total participants. Twenty-four patients (77.42%) were married, 13 (41.94%) had attained primary education and 26 (83.87 %) were not current smokers at the time of the study. Twenty-six patients (83.87 %) were referred for surgery by health facilities, 24 (77.42%) had hypertension, 3(9.68%) with diabetes mellitus and one with peripheral vascular disease.

Of the 31 patients reviewed, 29 were operated on: 21 (67.74 %) of these developed postoperative complications. Eighteen patients (27%) had bleeding as the most common post-operative complication. The statistically significant findings associated with operative mortality included extension of aneurysm to involve descending thoracic aorta (0.008), left common carotid artery (0.009) and left subclavian (0.009), Use of DHCA (0.041), retrograde cerebral perfusion (0.017), greater than 2 units transfused intra-operatively (0.002), prolonged length of surgery (0.049), prolonged CPB (0.002), cardiac failure (0.003), and pulmonary failure (0.001).

Conclusion: This study was of great importance to practicing cardiothoracic and vascular surgeons not only in KNH but also in Africa as a whole. Knowledge gap exists as pertains to factors associated with morbidity and mortality in the surgical management of thoracic aortic dissections and aneurysms especially in resource limited setups.

The factors associated with mortality in patients undergoing surgery for thoracic aortic aneurysms and dissection were well outlined. This knowledge will guide clinicians in careful selection of patients for surgical management and ensure improved surgical outcomes in the cardiothoracic unit. Subsequent reduction in mortality and reduction in postoperative complications is beneficial to the patients. Based on the research findings local evidence-based protocols can be setup to ensure a standardized approach to management of TAA/TAD at KNH.

CHAPTER ONE

INTRODUCTION

A true aortic aneurysm is a permanent localized dilatation of a diameter of 50% or greater than normal, comprising all layers of the arterial wall. A false aortic aneurysm is a localized dilatation with a breach in the intima plus or minus the media, but the adventitia remains intact (1). In an aortic dissection, blood leaves the normal lumen through an intimal tear and dissects inner from outer layers to cause a false lumen.

A thoracic aortic aneurysm may encompass the aortic root or ascending aorta (60%), descending aorta (40%), aortic arch (10%), or thoracoabdominal aorta (10%) segments (2).

Aneurysm/dissection are the most prevalent indication for aortic surgery.

Data on the prevalence of TAD/TAA in Kenya is inadequate. A retrospective study was conducted in KNH between the years 1998-2007 on all aortic aneurysms; from the abdominal aorta, two hundred and twenty-three (84.5%) aneurysms occurred. This was followed by (7.5%) descending aorta, (3.8%) ascending aorta and (1.9%) arch. In general, thoracic aorta was 15.5% of all cases. Both thoracic and abdominal aorta was involved in 2.3% of patients. (3).

Thoracic aortic dissections occurrence is estimated at 3-4 cases per 100,000 persons per year. (4) TAD incidence increases with age and more common in elderly male (4). Aortic dilatation (aneurysm) increases the risk of dissection though it's not a prerequisite to dissection (4).

KNH is the main referral hospital in our country (Kenya), it's the only public hospital currently offering thoracic aortic surgical care. The other available options are to seek

services in a private hospital or outside the country with the most preferred choice being India according to the ministry of health data. The costs of open surgical procedures or TEVAR in the private hospitals is prohibitive with estimated costs ranging from 10,000 to 25,000 United States dollars. On the contrary, the services are offered free of charge at KNH for patients registered under the NHIF scheme.

The cardiothoracic unit located at ward 4b in KNH handles thoracic aortic surgical patients, it has a 30-bed capacity with 5 bed ICU. The department is fully equipped to do open surgical thoracic aortic surgeries with post-operative care being offered at the unit ICU. TEVAR was introduced 6 months ago with the first case being done under fluoroscopy guidance in the cardiac catheterization laboratory.

Thoracic aortic surgery requires several professional ranging from cardiothoracic surgeons, cardiac anesthetists, perfusionists, cardiac theatre nurses, ICU trained nurses, cardiologists etc. The requisite properly working equipment and consumables for example- grafts, valves, sutures just to mention but a few are key in the success of the surgeries. Failure in any of the above leads to poor surgical outcomes.

Data is lacking in KNH as pertains to the incidence of mortality and contributory risk factors. The results of this study were key in providing information that will guide evidence-based practice to improve outcomes and reduce mortality. The data will also aid in formulating protocols in our local setup as pertains to the management of the thoracic aortic disease.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 The Epidemiology of TAA/TAD.

Reports from The Center for Disease Control and Prevention state that aortic aneurysm (thoracic and abdominal) are the fifteenth leading cause of death in individuals aged above fifty-five years and the nineteenth overall leading cause of death (5). Aneurysm/dissection are the most prevalent indication for aortic surgery.

During the first half of the 20th century, infectious aneurysms in the thoracic aorta were more common than AAA. As of 1952, autopsy studies showed a thoracic to abdominal aortic aneurysm ratio of 2:1 (6). As of 1964, the ratio had declined to less than 1 to 1, the main reason being a weakening frequency of the syphilitic aneurysms (7).

Data on the prevalence of TAD/TAA in Kenya is inadequate, a retrospective study was conducted in KNH between the years 1998-2007 on all aortic aneurysms, abdominal aorta were two hundred and twenty-three (84.5%) aneurysms. This was followed by 7.5% for the descending aorta, 3.8% for ascending aorta and 1.9% in the arch. In general, thoracic aorta was 15.5% of all cases. For both thoracic and abdominal aorta cases, 2.3% of patients were affected (3).

In a well-documented study in Malmö, Sweden, having a stable metropolitan populace and an autopsy rate of 83%, the total prevalence of thoracic aortic aneurysms between the years 1958 to 1985 was 489 apiece 100,000 autopsies in men and 437 apiece 100,000 autopsies in women (8). The prevalence of asymptomatic thoracic aneurysms was approximately 400/100,000 autopsies in sixty-five years old and approximately 670 per

100,000 autopsies in eighty years old. Thoraco-abdominal aneurysms made up 5 per cent of entirely asymptomatic thoracic aneurysms (8). A study from England and Wales that examined repetitive mortality figures, the number of demises following thoracic aortic aneurysms increased 17% in the years 1974 to 1984 (9). This upsurge rate was significantly lower than that of abdominal aortic aneurysms (53%). The study from Sweden, the incidence of dissection of the thoracic aorta was 3.2 per 100,000 autopsies in both male and females (8). The study from England and Wales, the number of deaths following the dissection increased ten per cent from 1974 to 1984 (9). Both studies, the number of deaths from aortic dissection exceeded the number from rupture of an aneurysm.

A whole country study on Icelandic population from 1992-2013 the prevalence of ascending TAD was 2.53 per 100,000 per year and remained constant through the course of the study. This opposed the recent observations of an increasing incidence. Within 30 days of the initial event, over half of patients die. The reduction of 30-day mortality rate and an increased long term survival rate indicates an enhanced general outcome in patients with this complex disease (10).

Most thoracic aortic aneurysms (TAAs) identified in patients over age 65 years are degenerative. Inflammatory disorders such as giant cell arteritis are also associated with TAA in this age group. TAA in less than 65 years is often associated with a genetic predisposition that can be familial or related to defined genetic disorders such as Marfan syndrome. Approximately 25 per cent of patients with thoracic aortic aneurysm (TAA) will also be found to have a AAA (11).

A larger familial component can be identified from TAA than previously thought. Studies conducted on Mendelian patterns in families of TAA patients recognized a definite familial

pattern. Further, the studies indicate 21% of patients with TAA have at least one family member with aneurysm (12).

2.2 The normal thoracic aorta anatomy

The thoracic aorta is divided into ascending, arch and descending portions. The ascending arises from the left ventricle, at the third sternocostal joint level. It courses upward and arches posteriorly and leftward at the level of second left sternocostal joint, where the arch begins and ends at the inferior border of T4 it lies lateral to the vertebral column. The descending portion takes a downward course and is left to vertebral bodies of T5-T12 in the posterior mediastinum and terminates as it goes through the median arcuate ligament between the diaphragm crurae anterior to T12 vertebral body (13).

The ascending portion lies within the fibrous pericardium, its length ranges from 5-7cm and a diameter of 2.5 to 3 cm. It is further divided into aortic root which comprises of the annulus, aortic valve, sinuses of Valsalva and the origins of coronary arteries, the Sino tubular junction (STJ) is the transition point from root to the tubular portion. The STJ dimensions are 85% of the annulus diameter (13).

The arch further gives rise to 3 main branches namely, brachiocephalic trunk, left common carotid and left subclavian.

The descending gives rise to intercostal and subcostal arteries, superior and inferior bronchial branches, and variable branches to the esophagus, mediastinum and pericardium.

The aortic size diminishes from proximally distally, however, the diameter of the vessel at any given point of reference varies with age, sex, body weight and height with age being the strongest correlation. The ascending aorta has been defined to have a diameter of

<2.1cm/m² and <1.6cm/m² of the descending aorta. The average measurements per segment are listed in Table 1(13)

Table 1: The average measurements per segment

| ANATOMICAL REGION | SIZE IN MM |
|---------------------|------------|
| Annulus | 20-31 |
| Sinuses of Valsalva | 29-45 |
| STJ | 22-36 |
| Tubular ascending | 22-36 |
| Arch | 22-36 |
| Tubular descending | 20-30 |

Histologically the aortic wall comprises of the intima, media, and adventitia. The intima is a thin inner layer abutting the lumen, composed of endothelial cells and small quantities of subendothelial connective tissue. The media is parted from intima by internal elastic lamina and comprises of elastic fibers, smooth muscle cells and connective tissue. It offers structural support, vasoreactivity and elasticity. External elastic lamina separates media and adventitia which is the outer layer abutting perivascular space, it's made up of

connective tissue, nutrient vessels (vasa vasorum) and autonomic nerves (Nervi vasorum) (14).

2.3 Thoracic Aorta Aneurysm /Dissection

A true aortic aneurysm is a permanent localized dilatation, of a diameter of fifty per cent greater than normal, involving the entire layers of the arterial wall. A false aortic aneurysm is a localized dilatation with a breach in the intima plus or minus the media, but the adventitia remains intact (1). Aneurysms can also be distinguished by morphology. The most common aneurysms are fusiform aneurysms, which is a circumferential enlargement of the arterial wall. Saccular aneurysms affect only part of the arterial circumference. Etiologic classification divides aneurysms into degenerative, congenital, infective aneurysms, inflammatory, mechanical (post stenotic, associated with AFV), anastomotic and chronic post-traumatic (15).

In an aortic dissection, blood leaves the normal lumen through an intimal tear and dissects the inner layers from outer layers to form a false lumen. Two hypotheses exist in which one considers intimal tear to be the precursor lesion: Larson and Edwards found in a sample of 158 specimens examined found a tear in all of them (16). Occasionally a discrete intimal tear not identifiable and its hypothesized that a vasa vasorum rupture with subsequent intramedial hematoma is the inciting event (17). It's considered acute if duration less than 14 days and chronic thereafter. Most of the patients present with complications beyond two weeks thus this definition has been recently revised. Booher and colleagues presented a new classification system with four-time domains: hyperacute (<24 h), acute (2–7 days), sub-acute (8–30 days), and chronic (>30 days) (18).

The commonly used anatomic classification for aortic dissections is the DeBakey and Stanford. DeBakey I dissections arise from the ascending aorta, extend to the aortic arch, and commonly beyond the arch distally. Type II dissections are confined to the ascending aorta. Type III dissections are located in the descending aorta. Dissections beginning at the descending aorta and extending proximally to the arch and ascending aorta are type 3. Stanford type A are dissections that involve the ascending aorta, arch and the descending thoracic aorta. Stanford type B are dissections that are only limited to the descending aorta. Rarely, dissections that begin in the descending aorta can also extend proximally to involve the aortic arch and the ascending aorta. This is a special case of type B dissection and is termed as retro-A dissection (19).

2.4 Natural History of Thoracic Aortic Aneurysm/Dissection.

The standard ascending aneurysmal aorta grows by 0.10 cm annually, whereas descending TAAs grow by 0.29 cm every year (17). Aneurysms with more diameters tend to grow more swiftly (17). Such dimensions may have measurement errors for majority of CT scanners and hence caution in applying these measurements inpatient care. Besides, tortuosity and dilatation of the aorta alter accurate measurements of aortic parameters. TAAs with familial traits, have a more rapid growth rate of 0.21 cm/y (combined ascending and descending TAA) in comparison to sporadic TAAs (0.16 cm/y) and as well present earlier (12). Syndromic TAA growth rates also vary. A rate of 0.1 cm/y is noted in patients with Marfan's syndrome, whereas patients with Loeys-Dietz syndrome can grow more rapidly than 1.0 cm/y, resulting in the average age of mortality at 26 years (12, 20).

Based on the aortic size, the risk of rupture or dissection is predictable. According to studies, aortic diameter directly correlates with risk of complications (rupture, dissection).

The yearly risk of rupture or dissection is around 2% for TAAs between 4.0 and 4.9 cm while nearing 7% for TAAs more than 6.0 cm (9). A rapid increase in the likelihood of rupture or dissection in diameters more than 6.0 cm for ascending TAA and 7.0 cm for descending TAA has been documented (9). Elective surgical intervention is advocated for at these dimensions. However, in patients with acute symptoms, bicuspid aortic valve, connective tissue disease or a rapidly enlarging diameter, an early intervention is advocated for (9).

Natural history of aortic dissections varies quite significantly with an aneurysm. In a large series study of acute ascending aortic dissections conducted in the 1930s, 40% succumbed immediately, 70% within twenty-four hours, 94% within one week and all patients had died at one week (21).

Recent studies still report high mortality rates, in which if proximal and distal dissections are left untreated 50% died within 48 hours, 84% at 1 month and 90% at 3 months. 8% survival rate at 1 year was recorded, data at 9 years showed 100% of patients as deceased (22). Distal aortic dissection had a 75% survival rate at 1 month (23).

2.5 Etiology/risk factors for TAA/TAD

Studies done have identified several causes and risk factors associated with thoracic aortic disease.

Degenerative- This can be further classified as cystic medial degeneration or arteriosclerotic. Approximately 80% of TAA is associated with cystic medial degeneration. Characteristic features include- fragmentation and loss of elastic tissues and smooth muscle cells. The inflammatory component is also noted, significantly the enlargement involves

the proximal aorta (24). Arteriosclerosis, which is majorly characterized by atheromatous changes, however, the exact pathogenesis leading to aneurysms has not yet clearly been established.

Congenital/Developmental

Marfan syndrome - is an autosomal dominant disorder characterized by FBN1 gene mutations, ultimately leading to defective glycoprotein fibrillin. This leads to a weak medial aortic layer due to decreased microfibrils which are component of the elastic tissue (25). Others include Ehlers-Danlos syndrome which is characterized by defective collagen 3 synthesis (26). Loeys-Dietz syndrome which results from mutated transforming growth factor receptor cells 1 and 2 genes (27).

Inflammatory

Several inflammatory disorders predispose individuals to the development of TAD/TAA, these include giant cell arteritis, Behcet's, Kawasaki disease and Takayasu arteritis

Infections

Infections account for two per cent of the thoracic aortic aneurysms. The common causative organisms are staphylococcus aureus, mycobacterial and syphilitic (28). The mechanism commonly involves hematological seeding with deposition of infected emboli into an arteriosclerotic or traumatic intima (29).

Chronic-Posttraumatic

Represent a very small percentage in which the mechanism involves blunt chest trauma. The descending thoracic aorta is commonly involved, disruption of part of the aortic wall

leads to a contained hematoma in the peri-aortic tissue. A false aneurysm develops when no intervention is undertaken (18).

Risk factors

- I. **Age.** A key risk factor is old age with most patients diagnosed at 60-70 years. A study done had a mean age of 63.1 years (30).
- II. **Raised blood pressures.** Persistently raised systolic blood pressures (above 150mmhg) were present in 72.1 % of the patients. (30)
- III. **Dyslipidaemia.** High cholesterol (serum total cholesterol ≥ 7.55 mmol/L) has a positive correlation with increased risk of TAA/TAD (31).
- IV. **Body Mass Index.** Positive and a significant correlation exists between high BMI greater than 25 and the risk of developing TAA/TAD (31).
- V. **Smoking Status.** AAA was associated with a high percentage of smokers (80.22%) at the time of participation. It was more in current smokers than past smokers, it was directly proportional to the smoking duration, the number of cigarettes smoked daily and depth of inhalation during smoking. It declined over time from the point of quitting (27).

2.6 Clinical features/Diagnostic criteria

A greater majority of the patients are asymptomatic. Symptoms most often develop late in the progression of the disease. The ascending aortic aneurysm can cause pain as well as features of heart failure because of a dilated annulus leading to aortic valve regurgitation (32).

Aortic arch aneurysms can also present with neck and jaw pain. Recurrent laryngeal nerve compression may cause hoarseness of voice, whereas stridor and dyspnea is a consequence of tracheal compression (33). Dysphagia though rare is also because of esophageal compression (34).

Descending thoracic aneurysms are mostly asymptomatic with pain being the commonest symptom (5).

Sudden onset, severe anterior chest pain is the typical presentation in acute aortic dissection. Varying degrees of visceral malperfusion may occur based on the site, extent and involvement of branch vessels. Not infrequently, neurological signs appear in the acute setting, ranging from short lasting to longstanding central nervous symptoms. This ranges from loss of consciousness, paraparesis or paraplegia. New appearing aortic valve regurgitation, pericardial effusion, or myocardial ischemia are associated with acute proximal dissection (29). Rarely can you find a patient with a SCAD with aortic annulus dilatation, clinically chest pain is the main complaint. A high index of suspicion should warrant coronary angiography as part of the imaging screen (35)

2.7 Diagnostic Imaging.

Imaging modalities for TAD / TAA are mainly done to avail information with the goal of diagnosis confirmation, classification, intimal tear localization, the extent of disease and urgency of surgery.

The available modalities are CT scan, echocardiography which may be transthoracic or trans-esophageal as well as cardiac MRI. The commonly used modality is contrast-

enhanced CT angiography which has the advantages of wide availability, affordable, less invasive and a timely modality (36).

Cardiac echocardiography also gives information on aortic valve function, which is a key factor in planning for surgery.

A study involving 1139 patients with aortic dissection comparing the accuracy of TEE, CT scan and MRI concluded that the three modalities produced clinically similarly reliable diagnostic values for approving or ruling out thoracic aortic dissection, with a pooled sensitivity of 98-100% and specificity of 95-98% which were comparable between the three modalities (37).

2.8 Management of TAA/TAD.

TAA/TAD is associated with significant morbidity and mortality. If left untreated prognosis is poor mainly due to fatal hemorrhage when they rupture. A study on the incidence and mortality rates showed 41% of ruptured TAA arrived at AED but overall mortality was 97% to 100%, hence efficient screening methods for diagnosis of TAA must be incorporated, features indicating high-risk rupture need prompt recognition and the number of operations for ruptured TAA must be escalated to reduce this high mortality rate (38).

As pertains to dissection, acute Stanford type A carries a 17.6 mortality before arrival to hospital (10), risk of death at 24 hrs. was 21.4% for patients who made it to hospital and 30-day mortality of 45.2% (10).

Treatment modalities range from conservative medical management, open surgical repairs, and endovascular surgical repair. The decision making on treatment modality largely

depends on whether elective or emergency setting, the size, site and the extent of the TAA/TAD. Characteristics of patients including operative mortality risk and patient preference also influence the chosen treatment option.

Medical management has a limited role, however, it's used in small aneurysms whose operative risk is higher than rupture risk or risk of dissection, medical management slows aortic growth rate and is used in conjunction with serial imaging for conservative management. The common modality is the use of antihypertensive, especially beta-adrenergic blockers. Commonly used beta-blockers include Atenolol, bisoprolol and metoprolol. An open-label, randomized β -blocker treatment trial was used in patients with MFS, it concluded that a reduction in aortic root growth rate and generally a reduction in aortic complication were conferred benefits. (39). Smoking cessation and statin use have added benefits.

Surgical intervention is recommended with increased sizes, a study on the likelihood of rupture when compared to the size concluded that at 5 years the total likelihood of rupture was zero percent for aneurysms of 4cm diameters or less, 16% (with 95% Confidence Intervals being 4%-28%) for patients with a diameter range of 4 to 5.9 cm, and 31% (95% CI, 5% -56%) in those with 6cm or larger diameters (40). Average diameter of the aneurysm recorded before rupture was 6.3 ± 0.3 cm. surgical intervention is recommended before the critical dimension of 6cm. However, 5cm is recommended in genetic diseases like MFS. Aneurysm with symptomatology should be operated on without consideration of the size.

Broadly the operative modalities are classified as open surgical repair and thoracic endovascular aneurysm repair (TEVAR). Two key determinants on approach are the location of aneurysm/ vascular anatomy and general physiologic reserve of the patient (41).

Type of surgery varies with the location of the aneurysm. Open surgical repair is largely undertaken in ascending aortic aneurysm when or no valvular involvement is noted, also aneurysms involving the arch and branch vessels. Indications for open surgery are shown in Table 2

Table 2: The indications for TAA open surgery repair

- a) Persistent pain
- b) Aortic valve involvement
- c) LV strain/coronary artery involvement
- d) Diameter >5.5 cm/rapidly expanding(>0.5cm/year) for patients with no comorbidities
- e) Threshold increased to 6cm in patients with increased operative risk
- f) Collagen vascular diseases e.g., Marfan syndrome threshold reduced to 4 cm
- g) Compressive symptoms e.g., dysphagia, dyspnoea
- h) Evidence of dissection

Stanford A aortic dissection is managed by open surgery under CPB. Aortic valve-sparing or replacement is dependent on the integrity of the aortic valve leaflets and its functionality as determined by the preoperative echocardiogram.

Uncomplicated Stanford B dissection is treated conservatively with medical management which mostly entails adequate blood pressure control, follow up and monitoring for developments of any complications, however with the advent of endovascular surgeries, preemptive stenting is a recommendation to prevent late complications. (42)

Stanford B dissections complicated by any of the following require surgical intervention:

- Visceral organ or extremities hypo-perfusion
- Advancing dissection
- outside-aortic blood accumulation (nearing rupture)
- Uncontrollable pain
- Hypertension not responding to treatment
- Early onset false lumen

Options available are open surgery which is however linked with increased morbidity and mortality as compared to TEVAR.

TEVAR though limited in availability, cost hindrances and lack of adequately trained personnel is the preferred treatment modality in aneurysms and dissections of descending thoracic aorta. Conservative management is applicable in uncomplicated Stanford type B dissections and small size aneurysm.

Open aneurysm repair is a major operation and carries risks to the patient such as:

- Myocardial infarction
- arrhythmias
- severe post-operative hemorrhage
- Neurological deficit (TIA, CVA)
- the embolic phenomenon with ischemia to different organs,
- spinal cord ischemia (paraplegia, Quadriplegia)
- kidney injury from prolonged ischemia
- graft and surgical site infection.

Thus, elective TAA repair should only be done if the risk of rupture surpasses the risk related with repair and that is when aneurysm diameter is greater than 5.5cm (11, 19).

a. Open Surgical Repair

1. ASCENDING AORTA

Patients with aneurysm 5-6cm in diameter require open surgery, additional criteria are symptomatology either due to large size or aortic valve regurgitation. The ascending aorta is replaced plus or minus aortic valve if regurgitation via echo is moderate to severe. Rapidly growing aneurysms >0.5cm/yr. require surgery. The procedure is done under CPB and moderate systemic hypothermia. The aorta is replaced with the appropriate size tube graft and the aortic valve replaced if diseased. Bentall's procedure involves aortic valve

replacement, coronary re-implantation plus ascending aorta graft repair, whereas David's procedure involves aortic valve-sparing procedure.

2. AORTIC ARCH

Isolated arch aneurysms are rare and mostly involve ascending aorta as well. The arch replacement is done under deep hypothermic circulatory arrest with various techniques being applied for neuroprotection, these include deep hypothermia, retrograde or antegrade cerebral perfusion and head being packed with ice. Electroencephalic monitoring is used. The surgery ranges from partial to full aortic arch replacement using tubular grafts with anastomosis of the arch vessels. Elephant trunk a 2 staged procedure is used in cases where the aneurysm extends into the descending thoracic aorta (43). 1st stage involves the arch replacement, and graft is pushed towards the descending aorta 'the elephant trunk' which was used for anastomosis during the descending aneurysm replacement.

3. DESCENDING THORACIC AORTA

Aneurysm of the descending thoracic aorta is replaced through a posterolateral thoracotomy through the 5th or 6th costal interspace with extending of incision depended on location plus extend of the aneurysm.

b. Endovascular Aneurysm Repair (TEVAR)

Intraluminal stent placements into descending thoracic aorta as well as the arch have now become the preferred treatment modality in selected patients in centers where endovascular surgery is available. The minimally invasive nature of the procedure confers benefits which by far outweigh the open procedures. Femoral access is used to deploy the stent via a sheath and guidewire under fluoroscopic guidance. The expandable stent-graft is deployed

within the aneurysm lumen to isolate the aneurysm from the circulation. A study done in the United States of America (USA) involving 8697 patients with descending thoracic aneurysm comparing the open surgical repair with TEVAR showed decreased incidence of mortality and associated central nervous, cardiac and respiratory systems complications after surgery with favor towards TEVAR (44).

The invention of stent grafts that are fenestrated and branched has made repair of aneurysms of the arch with endovascular techniques easier (45).

c. Hybrid Approaches.

Aneurysm of the arch and the descending thoracic aorta traditionally required a 2 staged elephant trunk procedure, this resulted in higher post-operative complications and death rates, however, the completion can now be done via endovascular placement of a stent with minimal mortality. Imaging after procedure must be done to identify ongoing pressurization of the aneurysm and to confirm the strength of repair. The second stage portion of these complex aneurysm repairs were further simplified by improvements in implant designs and delivery systems (46).

d. CPB.

Cardiopulmonary bypass is routinely used for open thoracic aortic surgery in KNH. Aneurysms involving the arch warrant the use of deep hypothermic circulatory arrest alone or together with either antegrade or retrograde brain perfusion to ensure brain protection during surgery (47). Patients are cooled to different core temperatures with moderate hypothermia at 28 degrees Celsius or deep hypothermia ranging from 18 to 22 degrees Celsius. DHCA is used as a brain-protective technique when the arch is aneurysmal. The

length of CPB has been acknowledged as an isolated risk factor leading to acute kidney injury (48) as well as mortality (49). In a study of 122 patients, CPB time of over 4 hours was linked with an increased likelihood of death (49).

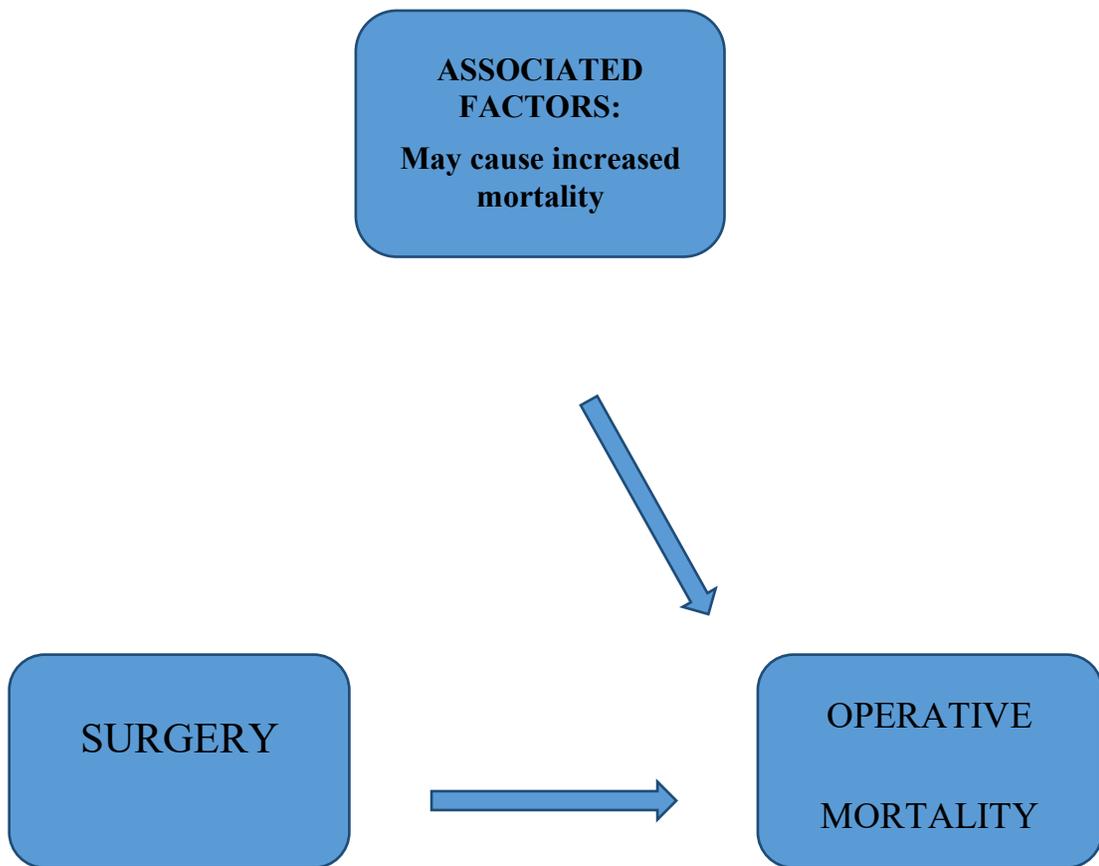
2.7 Postoperative Management at KNH

TAA/TAD repairs are major operations often requiring CPB with full heparinization, and in some cases deep hypothermic circulatory arrest, the current KNH protocol involves admission of all patients to the Critical Care Unit (CCU) facility in the immediately after surgery. Once the stable discharge to the ward is undertaken. The key parameters are optimal organ functions, the key organs being cardiovascular, renal, hepatic, cerebral and motor functioning.

After aortic surgery, patients are at an increased likelihood of cerebrovascular accident, delirium, reduced cardiac output, respiratory collapse, kidney failure, coagulation disorders, sepsis, bleeding, superficial wound infection (50). Patients experiencing any of the above complications have a considerably higher death rate when compared to those with no such post-operative morbidities (51).

2.8 CONCEPTUAL FRAMEWORK

Figure 1: The conceptual framework of interaction of various variables



CHAPTER THREE

3.0 STUDY QUESTIONS, JUSTIFICATION AND OBJECTIVES

3.1 STUDY QUESTIONS

1. What is the rate of mortality among patients undergoing open surgical repair for TAA/TAD at KNH
2. What are the factors influencing mortality among these patients.

3.2 JUSTIFICATION OF THE STUDY

KNH is the main national referral hospital in Kenya which treats majority of the thoracic aortic surgical patients in the country.

In this hospital, TAA/TAD is treated by either conservative medical management, TEVAR or open surgical repair. Open surgical repair for TAA/TAD has been performed at Kenyatta National Hospital (KNH) for more than 40 years. However, patients' characteristics, outcomes for open surgical repair including rates of mortality and contributing factors remain largely unknown. No studies have been done to evaluate the success of open surgical repair in this hospital / region.

Thus, availability of data on mortality rates and associated factors arising from open surgical repair are lacking. Absence of adequate information hinders the practitioners from making evidence-based decision in patient care. A clear understanding of our mortality rate and the contributory factors, by retrospectively analyzing the patients managed in our local setup is of utmost importance. This information will help the cardiothoracic and vascular unit team at KNH design protocols based on data collected in the unit as pertains to care of

TAA/TAD patients. This knowledge will help to improve patient selection for surgery, reduce morbidity and mortality associated with open surgical repair and improve hospital-based outcomes from open surgical repair.

Improved outcomes will increase patient confidence subsequently leading to increase in number of patients seeking for health care services at KNH. The results of this study will significantly contribute to the development of the Thoracic and Cardiovascular surgery service Nationally.

3.3 OBJECTIVES

Main. To determine the operative mortality rate and factors influencing operative mortality for patients undergoing open surgical repair due to TAA/TAD at KNH.

Specific Objectives

1. To determine the operative mortality rate among patients undergoing open surgical repair due to TAA/TAD at KNH.
2. To determine the risk factors associated with operative mortality in patients undergoing open surgical repair for TAA/TAD at KNH.

CHAPTER FOUR

4.0 MATERIALS AND METHODS

4.1 STUDY DESIGN

The design of the study was a retrospective cross-sectional design.

4.2 STUDY PERIOD

The data for this study were collected from patient files spanning ten years between January 2010 and December 2020.

4.3 STUDY SITE

The study was carried out at the Kenyatta National Hospital (KNH) health information office, where files for patients to be recruited into the study were retrieved, data collected and analyzed. KNH is the national public referral hospital where most cases of TAA/TAD are referred and managed owing to availability of expertise. Data were derived from theatre registers, ICU registers and ward registers. The specific patient files tracked and retrieved from the main health information (Records) office. On average one to three thoracic aortic aneurysm repairs are carried out in a month.

4.4 STUDY POPULATION

Comprised of all patients of 18 years and above who had a confirmed diagnosis of TAA/TAD and who had open surgical repair at KNH between years January 2010 and December 2020.

4.4.1 Inclusion Criteria

All the patients above the age of 18 years with a diagnosis confirmed to be TAA/TAD who were managed for at KNH.

4.4.2 Exclusion Criteria

1. Patients with thoracoabdominal aortic aneurysms.
2. Patients with TAA/TAD who were transferred from KNH to other hospitals.
3. Patients who did not undergo open surgical repair for TAA/TAD.

4.5 SAMPLE SIZE DETERMINATION

To calculate the sample size for the estimate of the incidence of mortality for the 95% confidence interval the following formula will use (Cochrane, 1977):

$$\text{Sample size } n = \frac{[DEFF * Np(1-p)]}{[(d^2/Z^2_{1-\alpha/2} * (N-1) + p * (1-p))]}$$

Population size (for finite population correction factor or fpc)(N) = 130

Z value for p = 0.99 or 99% confidence intervals = 2.58

P = Estimated prevalence / incidence (Estimated mortality incidence is 5.5%)

d = Desired level of precision (0.05)

Hence a sample size of 68 persons were required. This sample will also be sufficient for logistic regression purposes as I were assessing 5 risk factors (52).

4.6 SAMPLING

A systematic random sampling method of patients who underwent open surgical repair due to TAA/TAD between the years 2010 – 2020 was used.

From a population of 130 participants, to derive n^{th} patient, total patient population (130) divided by sample size (68) = 1.9 thus approximately 2nd patient.

A list of patients operated during the study period was developed from patients' records/registry. From this list every 2nd patient was recruited into the study until a sample size of 68 is arrived at.

4.7 SCREENING, RECRUITMENT AND ENROLLMENT

Data sources for this study were the patient files, theatre registers, ICU registers and ward registers for patients who underwent TAA/TAD surgery at Kenyatta National Hospital during the period 2010-2020. Data were collected using a specifically designed questionnaire form. Potential participants were identified from the registers. These are the patients who had a diagnosis of TAA/TAD entered at admission/discharge and fulfilling the inclusion criteria. Their registration numbers were identified, and the files retrieved from the records department for data collection. From the admission notes, pre-operative investigations and evaluation, theatre notes, ICU notes and daily ward notes, those who underwent surgery were identified and data collected. For mortality analysis, patients admitted at KNH for TAA/TAD and having undergone surgery who died within the hospital, were determined and data collected.

4.8 STUDY VARIABLES

Using the data collection sheet (Appendix 1), the following variables were derived from the patients' records.

4.8.1 Exposure variables

These covariates were used to predict the occurrence of mortality and other post-operative complications. They will include Sociodemographic factors such as age, sex, marital status, physical address, level of education, mode of referral and initial place of diagnosis.

Information on Lifestyle factors such as smoking history, and medical factors such as the presence of comorbidities e.g., hypertension, diabetes mellitus, connective tissue disorders, and peripheral arterial disease among others were collected.

Clinical factors information to be collected included, first presenting symptoms such as chest pain, back pains, shortness of breath, difficult breathing, low blood pressure, and whether TAA/TAD was diagnosed as an incidental finding.

Time-related information included-date when the first diagnosis was made, date of admission to KNH, date of surgery, length of operation in minutes, time under CPB, date of admission and discharge to ICU and ultimate date discharge from hospital or death.

Anatomical and Imaging findings included, size of the aorta in mm, whether aneurysm was leaking, dissected, whether arch vessels were involved and presence of intramural thrombus.

Treatment information included whether the patient underwent surgery, type of surgery and whether was admitted in ICU.

4.8.2 Outcome variables

The occurrence of mortality was the key outcome variable.

Other outcomes investigated included, information on whether the patient developed complications postoperatively and the nature of complications including, bleeding, neurologic injury, cardiac failure, respiratory failure, wound sepsis and dehiscence, embolic phenomenon, deep vein thrombosis, graft infection, myocardial infarction, acute kidney injury, chronic kidney injury, etc.

4.9 DATA COLLECTION

A structured data collection tool (Appendix 2) developed based on the study protocol was used to retrieve information from the patient file records which are available at the Health Records and Information office of the Kenyatta National Hospital, Clinic 19.

Trained data collectors who were postgraduate cardiothoracic and vascular surgery residents of the university of Nairobi were used to fill all questions in the data collection tool.

4.10 QUALITY ASSURANCE PROCEDURES

Data collectors were trained for one day to ensure that they understood the protocol and data collection procedures including retrieval of information from files and filling of data collection form.

Data collection forms were counterchecked on collection from the data collectors to ensure all parts were filled adequately.

Data entry was done using a Epi-Info 3.5.4. A second data entry officer counter-checked entered data to ensure consistency of information.

Already entered data collection forms was stored in a locked safe for a period of 3 years after which they were disposed.

CHAPTER FIVE

5.0 RESULTS

A total of 31 records of patients managed surgically for Thoracic Aortic Aneurysm at KNH during the study period were retrieved. Two were excluded because of incomplete records or failure to meet the inclusion criteria. Therefore 29 patient records were analyzed, and results are reported in the order of 1) Sociodemographic characteristics, 2) Clinical Characteristics, 3) Surgical factors 4) Complications and 5) Mortality.

5.1 SOCIAL DEMOGRAPHIC FACTORS OF PATIENTS

Participants were aged 18 and above and majority were between 66-75 years. Female patients constituted to more than half 16(51.61%) of the total participants. Twenty-four (77.42%) were married, 13 (41.94%) had attained primary education and 26 (83.87 %) were not current smokers at the time of the study. Twenty-six patients (83.87 %) were referred for surgery by health facilities. No significant association with mortality was found amongst socio-demographic characteristics as shown by Fisher's exact p value.

Table 5: Socio-demographic characteristics of patients with TAA

| Variable | Category | Frequency | Proportion (%) | Fishers exact <i>p</i> value |
|-----------------|-----------------|------------------|-----------------------|-------------------------------------|
| Age groups | <55 | 18 | 64.3 | 0.703 |
| | >55 | 10 | 35.7 | |
| Sex | Male | 15 | 51.7 | 0.245 |
| | Female | 14 | 48.3 | |

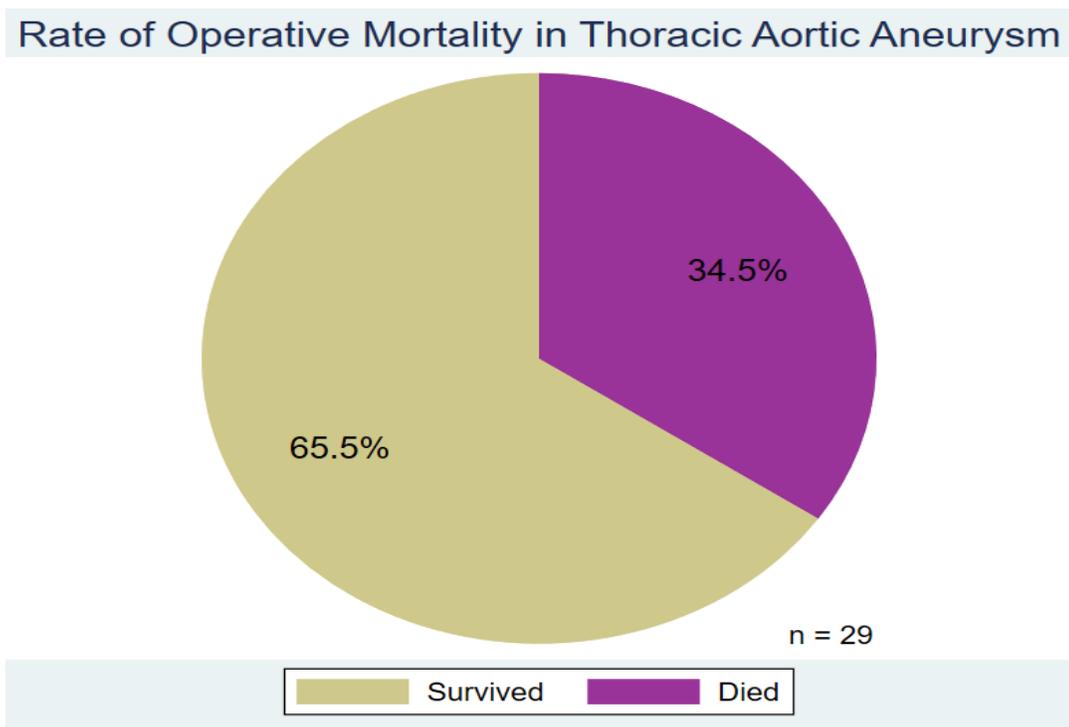
| | | | | |
|-----------------|-----------|----|------|-------|
| Marital status | Married | 21 | 77.8 | 0.677 |
| | Single | 6 | 22.2 | |
| Education level | Primary | 12 | 41.4 | 0.482 |
| | Secondary | 8 | 27.6 | |
| | Tertiary | 9 | 31.0 | |
| Smoking status | Yes | 5 | 17.2 | 0.576 |
| | No | 24 | 82.8 | |

5.2: CLINICAL CHARACTERISTICS OF PATIENTS WITH TAA

5.2.1 Incidence of mortality

Out of the 29 study subjects, 10 died which represents an operative mortality rate of 34.5% (CI 17.9 – 54.3).

Figure 2: Pie chart indicating the operative mortality rate in TAA



5.2.2 Comorbidities

Twenty-two (75.9%) patients had hypertension, 3(10.3%) with diabetes mellitus and one (3.6%) had peripheral heart disease as well as Hemorrhagic CVA and only 2 (6.9%) had Marfan's syndrome. No significant association with mortality was found amongst clinical factors as indicated by Fisher's exact test.

Table 6: Co-morbidities among patients with TAA

| Variable | Frequency n = 29 | Proportion (%) | Fisher's exact <i>p value</i> |
|-----------------------------|-----------------------------|-----------------------|--|
| Hypertension | 22 | 75.9 | 0.161 |
| Diabetes mellitus | 3 | 10.3 | 0.265 |
| Marfan's syndrome | 2 | 6.9 | 0.111 |
| Peripheral arterial disease | 1 | 3.6 | 0.655 |
| Hemorrhagic CVA | 1 | 3.6 | 0.345 |

5.2.3 First presenting symptoms among patients

The most common first presenting symptoms was chest pains in 23 (74.2%) of the participants, followed by shortness of breath in 17 (54.8%), and difficulty in breathing in 15 (48.4%). Others were back pain at 5 (16.1%), low bp 1 (3.2%) and incidental finding 1 (3.2%). First presenting symptoms were not associated with occurrence of mortality as indicated by non-significant Fisher's exact p values.

Table 7: Summary table indicating the frequencies of the first presenting symptom.

| Variable | Frequency n = 29 | Proportion (%) | Fisher's exact <i>p value</i> |
|---------------------|-----------------------------|---------------------------|--|
| Chest pain | 23 | 74.2 | 0.191 |
| Shortness of breath | 17 | 54.8 | 0.248 |
| Difficult breathing | 15 | 48.4 | 0.248 |
| back pain | 5 | 16.1 | 0.092 |
| Easy fatigability | 8 | 27.6 | 0.419 |
| Palpitations | 6 | 20.6 | 0.331 |
| Low limb swelling | 4 | 13.8 | 0.105 |
| Cough | 2 | 6.9 | 0.111 |
| Ascites | 2 | 6.9 | 0.111 |
| Confusion | 1 | 3.5 | 0.345 |
| Stroke | 1 | 3.5 | 0.345 |
| low BP | 1 | 3.5 | 0.483 |
| Incidental finding | 1 | 3.5 | 0.483 |

The mean duration of symptoms in 27 study subjects was 48.7 days, SD 122.3, range 1 – 520, with a median of 6. It not significantly associated with mortality on student t test, p value 0.377.

5.2.4 Aneurysm characteristics

Various characteristics of the aneurysm were assessed and presented below. Risk factors of mortality were assessed in the bivariate analysis using the Fishers exact test

Table 8: Characteristic of the Aneurysms

| Variable | Category | Frequency | Proportion (%) | Fishers exact p value |
|------------------------------|-----------------------------------|-----------|----------------|-----------------------|
| Aneurysm location | Aortic root | 24 | 85.7 | 0.615 |
| | Ascending | 26 | 92.9 | 0.548 |
| | Arch | 7 | 25.9 | 0.139 |
| | Descending | 7 | 22.2 | 0.008 |
| Aneurysm type | True | 29 | 100.0 | na |
| | Dissected | 20 | 69.0 | 0.311 |
| | Stanford A | 18 | 90 | 0.653 |
| | Stanford B | 2 | 10 | 0.653 |
| Arch vessels involved | Brachio-cephalic | 8 | 27.6 | 0.255 |
| | Left common carotid artery | 4 | 13.8 | 0.009 |
| | Left subclavian | 4 | 13.8 | 0.009 |
| Intramural thrombus | Present | 26 | 89.7 | 0.733 |

Out of 26 measurements, the mean for maximum aortic diameter was 77.5mm (SD 142, Range 54 – 98, Median 76) and not significantly associated with risk of mortality as indicated by p value derived from Wilcoxon rank sum test p value 0.87.

5.3 SURGICAL FACTORS OF THE TAA/TAD PATIENTS

5.3.1 Type of procedure

The most common procedure carried out was the Bentall's procedure, followed by David's

Table 9: Surgical factor of patients with TAA

| Variable | Categories | Frequency | Proportion (%) | Fishers exact p value |
|---|----------------------------------|-----------|----------------|-----------------------|
| Surgery type | Bentall's procedure | 24 | 82.8 | 0.424 |
| | David's procedure | 2 | 6.9 | 0.421 |
| | TEVAR | 1 | 3.5 | 0.655 |
| | Wheat's Procedure | 1 | 3.5 | 0.655 |
| | Graft repair of descending aorta | 1 | 3.5 | 0.345 |
| DHCA | Used | 5 | 17.9 | 0.041 |
| CBP machine | Used | 27 | 96.4 | 0.643 |
| Retrograde Cerebral perfusion | Yes | 3 | 12.5 | 0.017 |
| Antegrade Cerebral perfusion | Yes | 2 | 7.7 | 0.529 |
| Intraop transfusion | Yes | 21 | 72.4 | 0.066 |
| Number of intraop transfused pints | <2 | 19 | 7.1 | 0.002 |
| | >2 | 7 | 26.9 | |
| ICU admission | Yes | 29 | 100 | 0.036 |
| | No | 0 | 0 | |
| No. of pints transfused in ICU | <2 | 9 | 50 | 0.50 |
| | >2 | 9 | 50 | |

| | | | | |
|----------------|----|---|------|-------|
| FFPs transfuse | <2 | 9 | 64.3 | 0.023 |
| | >2 | 5 | 35.7 | |

5.3.2 Time related surgical factors

Table 10: Table showing time related surgical factors

| Variable | Categories | N | Mean | Standard deviation | 95%CI | Range | Median | Student t test p value |
|---------------------------------|------------|----|-------|--------------------|---------------|-----------|--------|------------------------|
| Length of operation (min) | Survived | 19 | 392.3 | 104.9 | 341.8 - 442.9 | | | 0.049 |
| | Died | 10 | 509.8 | 204.3 | 363.7 - 655.9 | | | |
| | Combined | 29 | 432.8 | 154.0 | 374.2 - 491.4 | 180 - 900 | 445 | |
| CPB time (min) | Survived | 18 | 204.7 | 42.2 | 183.7 - 225.7 | | | 0.002 |
| | Died | 10 | 343 | 161.5 | 227.5 - 458.5 | | | |
| | combined | 28 | 254 | 119.9 | 207.6 - 300.6 | 78 - 600 | 205 | |
| DHCA time (min) | | 6 | 47.5 | 34.2 | | 20 - 115 | 37.5 | 0.143 |
| Duration in ICU (days) | | 21 | 5.9 | 2.9 | | 2 - 16 | 5 | 0.684 |
| No. of days in the hospital | | 21 | 12.6 | 6.0 | | 3 - 28 | 12 | 0.952 |
| Duration to death after surgery | | 7 | 9 | 7.1 | | 2 - 20 | 6 | |

5.4 POSTOPERATIVE COMPLICATIONS

Of the 29 were operated on, 19 (65.5%) of these developed postoperative complications.

Eighteen patients (62.06%) had bleeding as the most common post-operative complication.

Figure 3: Pie chart showing the rate of complications

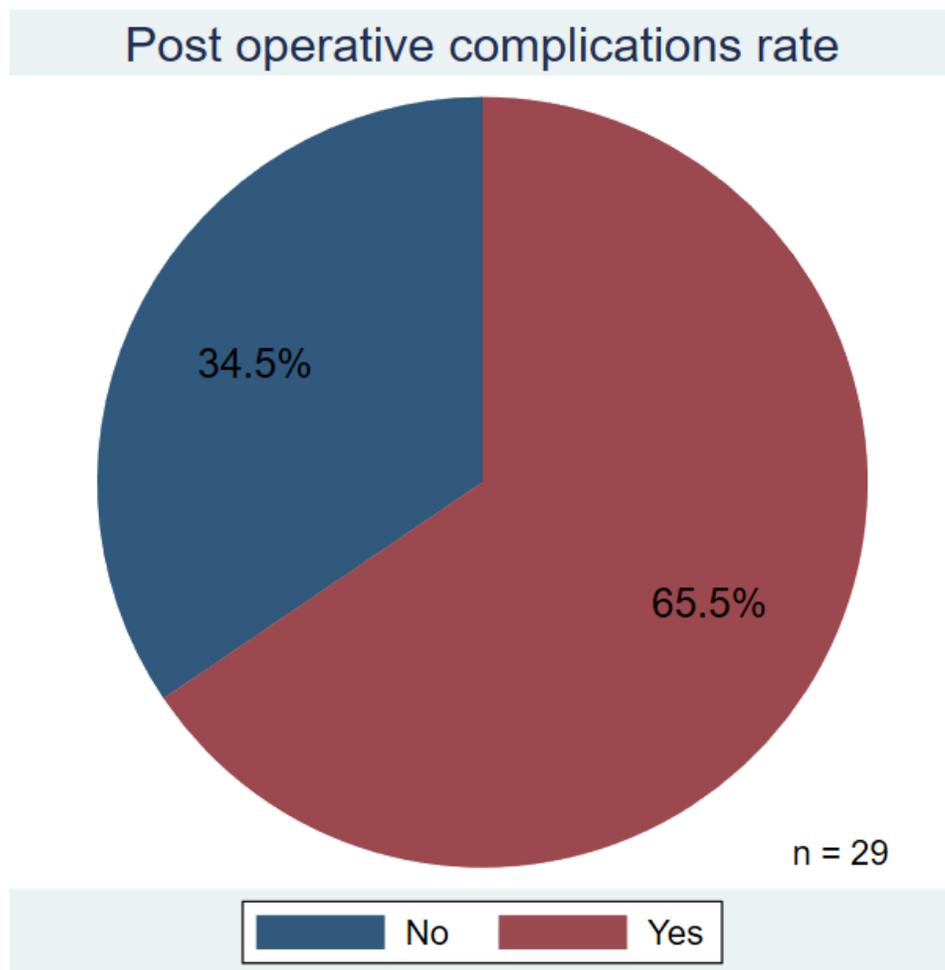


Table 11: Table showing occurrence of complications after surgery

| Variable | N | Frequency | Proportion % | P value |
|--------------------------|-----------|------------------|---------------------|----------------|
| Bleeding | 24 | 18 | 75 | 0.202 |
| Neurologic injury | 21 | 2 | 9.5 | 0.648 |
| Cardiac failure | 26 | 13 | 50 | 0.003 |
| Pulmonary failure | 25 | 9 | 36 | 0.001 |
| Wound infection | 24 | 2 | 8.3 | 0.507 |
| Wound dehiscence | 25 | 2 | 8 | 0.490 |
| Acute kidney injury | 26 | 9 | 34.6 | 0.538 |
| Paraparesis | 26 | 1 | 3.9 | 0.731 |

P values derived to assess association between complications and occurrence of mortality. Cardiac and pulmonary failure were significant at 5%.

In the bivariate analysis, bleeding was associated with cardiac failure, $p=0.013$ and acute kidney injury, $p=0.037$

Cardiac failure was associated with pulmonary failure, $p=0.001$ and acute kidney injury, $p=0.006$

5.5 RISK FACTORS FOR MORTALITY

In the bivariate analysis, the risk factors for mortality included, location of aneurysm at descending aorta (0.008), left common carotid artery (0.009) left subclavian (0.009), Use of DHCA (0.041), retrograde cerebral perfusion (0.017), Higher number of intra-operative transfused pints (0.002) greater than 2, ICU admission (0.036), use of Fresh frozen plasma transfusion (0.023), prolonged length of surgery (0.049), Prolonged CPB (0.002), cardiac failure (0.003), and pulmonary failure (0.001) (Table 12).

Table 12: Risk factors for mortality

| Risk factor | P value |
|--|----------------|
| Descending thoracic aorta | 0.008 |
| Left common carotid | 0.009 |
| Left subclavian | 0.009 |
| DHCA | 0.041 |
| Retrograde cerebral perfusion | 0.017 |
| More than 2 of transfused pints intra-op | 0.002 |
| ICU admission | 0.036 |
| FFPs transfusion | 0.023 |
| Cardiac failure | 0.003 |

| | |
|-----------------------------|-------|
| Pulmonary failure | 0.001 |
| Prolonged CPB | 0.002 |
| Prolonged length of surgery | 0.049 |

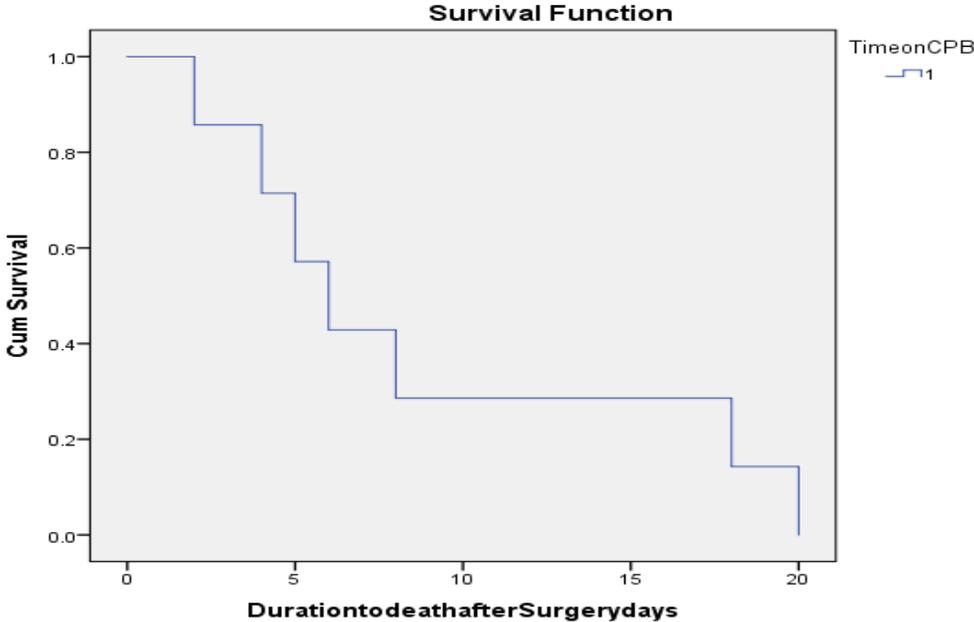
5.6.3 Time to mortality and associated risk factors

Table 13: Kaplan Meier and log rank test were used to compute respective values in the table below.

| Participant | Time under CPB (minutes) | Length of surgery (hours) | Time to mortality (days) |
|-------------|--------------------------|---------------------------|--------------------------|
| 27 | 78 | 3.67 | 6 |
| 17 | 160 | 7.00 | 5 |
| 18 | 174 | 4.30 | 18 |
| 24 | 348 | 7.0 | 2 |
| 23 | 360 | 7.33 | 4 |
| 14 | 390 | 9.33 | 8 |
| 7 | 480 | 11.00 | 20 |

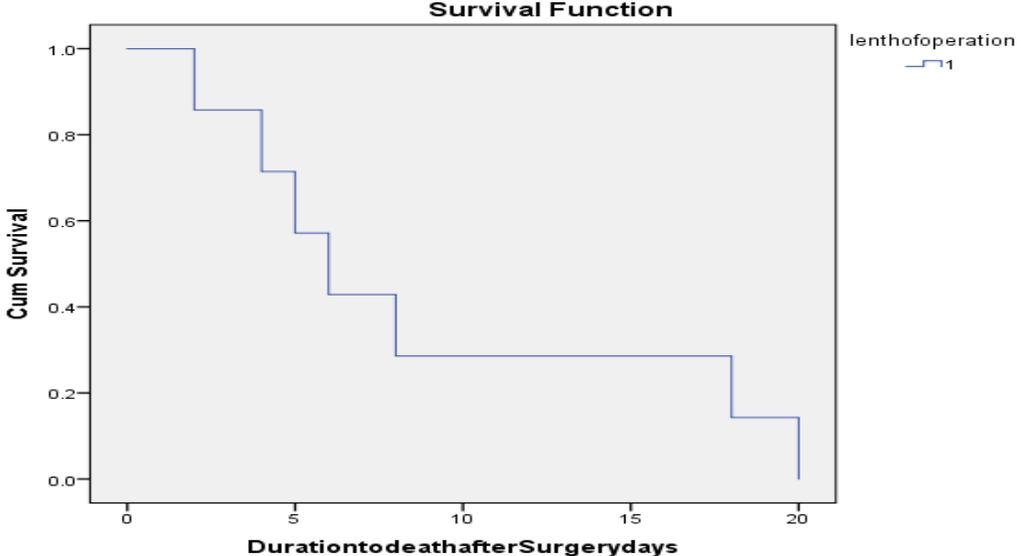
The Kaplan Meier curve depicts that as time passes by, survival rate decreases. However, mortality was higher in the immediate postoperative period but as days progressed, mortality decreased. Survival rate at day 5 is 50% and at day 7 it is 70%.

Figure 4: Kaplan-Meier Survival Curve of Mortality- Time on CPB



The Kaplan Meier curve depicts that as time passes by, survival rate decreases. However, mortality was higher in the immediate postoperative period but as days progressed, mortality decreased. Survival rate at day 5 is 50% and at day 7 it is 70%. There are similarities of survival for both time on CPB and length of surgery.

Figure 5: Kaplan-Meier Survival Curve of Mortality-Length of Surgery



5.6.4 Length of operation as a predictor of mortality

Cut off times for mortality as based length of operation were determined using the Receiver Operator Characteristics (ROC). The AUC was 0.647 which is a relatively poor model fit for predicting mortality. However, the figure 6 below shows the ROC curve.

Figure 6: ROC curve for mortality based on length of operation.

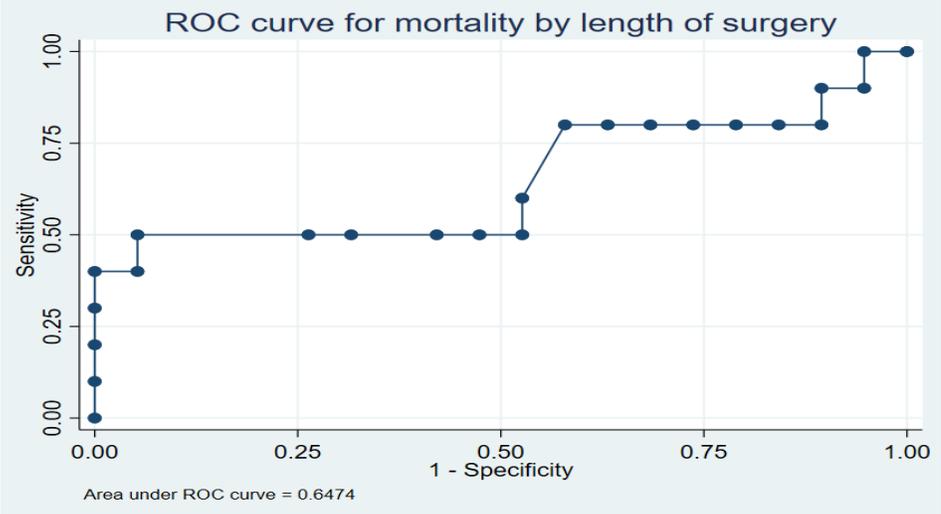


Table 14: The cut offs for length of operation and occurrence of mortality.

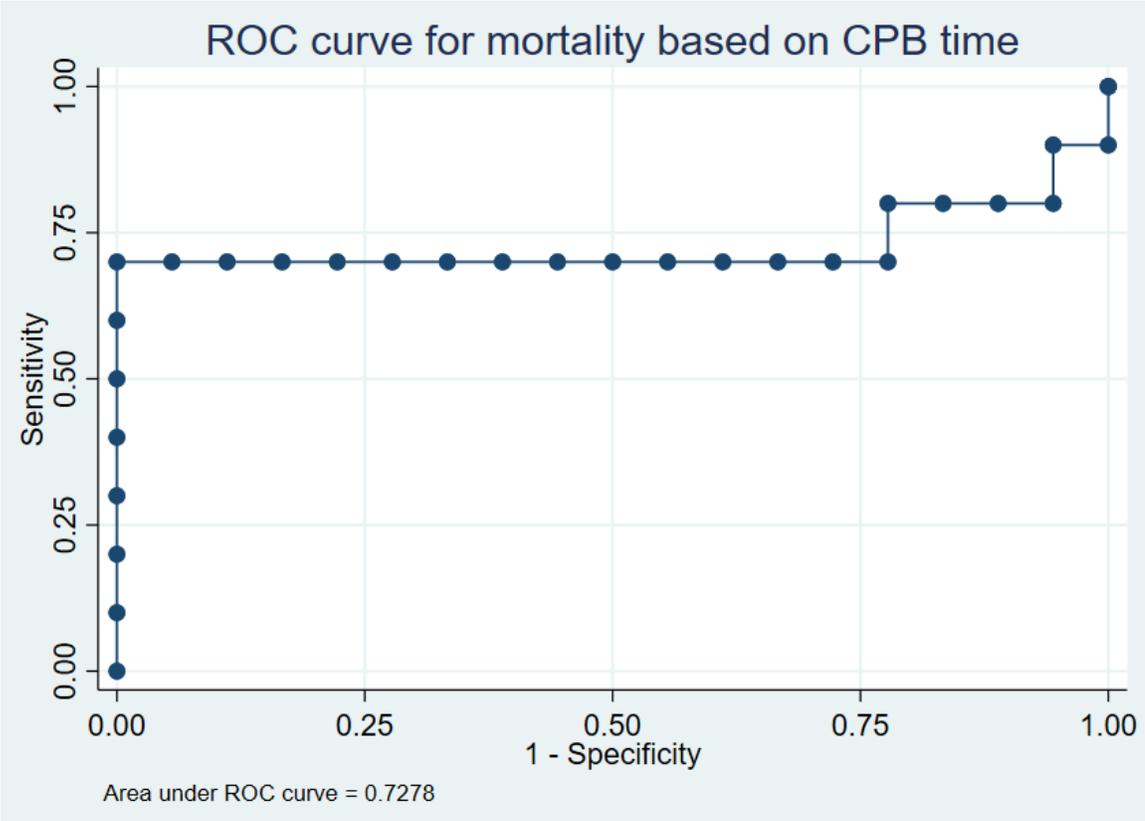
Detailed report of sensitivity and specificity

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR- |
|------------|-------------|-------------|----------------------|--------|--------|
| (>= 180) | 100.00% | 0.00% | 34.48% | 1.0000 | |
| (>= 220) | 100.00% | 5.26% | 37.93% | 1.0556 | 0.0000 |
| (>= 240) | 90.00% | 5.26% | 34.48% | 0.9500 | 1.9000 |
| (>= 258) | 90.00% | 10.53% | 37.93% | 1.0059 | 0.9500 |
| (>= 260) | 80.00% | 10.53% | 34.48% | 0.8941 | 1.9000 |
| (>= 268) | 80.00% | 15.79% | 37.93% | 0.9500 | 1.2667 |
| (>= 300) | 80.00% | 21.05% | 41.38% | 1.0133 | 0.9500 |
| (>= 323) | 80.00% | 26.32% | 44.83% | 1.0857 | 0.7600 |
| (>= 345) | 80.00% | 31.58% | 48.28% | 1.1692 | 0.6333 |
| (>= 356) | 80.00% | 36.84% | 51.72% | 1.2667 | 0.5429 |
| (>= 420) | 80.00% | 42.11% | 55.17% | 1.3818 | 0.4750 |
| (>= 440) | 60.00% | 47.37% | 51.72% | 1.1400 | 0.8444 |
| (>= 445) | 50.00% | 47.37% | 48.28% | 0.9500 | 1.0556 |
| (>= 450) | 50.00% | 52.63% | 51.72% | 1.0556 | 0.9500 |
| (>= 460) | 50.00% | 57.89% | 55.17% | 1.1875 | 0.8636 |
| (>= 470) | 50.00% | 68.42% | 62.07% | 1.5833 | 0.7308 |
| (>= 480) | 50.00% | 73.68% | 65.52% | 1.9000 | 0.6786 |
| (>= 540) | 50.00% | 94.74% | 79.31% | 9.5000 | 0.5278 |
| (>= 557) | 40.00% | 94.74% | 75.86% | 7.6000 | 0.6333 |
| (>= 560) | 40.00% | 100.00% | 79.31% | | 0.6000 |
| (>= 660) | 30.00% | 100.00% | 75.86% | | 0.7000 |
| (>= 680) | 20.00% | 100.00% | 72.41% | | 0.8000 |
| (>= 900) | 10.00% | 100.00% | 68.97% | | 0.9000 |
| (> 900) | 0.00% | 100.00% | 65.52% | | 1.0000 |

5.6.5 Duration of CPB time as predictor of mortality

The time under CPB was evaluated in reference to mortality with Receiver operator curves. The Area Under the curve (AUC) was 0.728 which shows that CPB is a good fair fit for predicting mortality. Figure 7 below shows the roc curve of mortality as predicted by the time under CPB.

Figure 7: ROC curve for mortality as predicted by CPB time



The cut offs for mortality as predicted by time under Cardiopulmonary bypass are indicated in the table 15.

Table 15. The cut offs for CPB time predicting mortality

Detailed report of sensitivity and specificity

| Cutpoint | Sensitivity | Specificity | Correctly Classified | LR+ | LR- |
|------------|-------------|-------------|----------------------|---------|--------|
| (>= 78) | 100.00% | 0.00% | 35.71% | 1.0000 | |
| (>= 138) | 90.00% | 0.00% | 32.14% | 0.9000 | |
| (>= 160) | 90.00% | 5.56% | 35.71% | 0.9529 | 1.8000 |
| (>= 163) | 80.00% | 5.56% | 32.14% | 0.8471 | 3.6000 |
| (>= 168) | 80.00% | 11.11% | 35.71% | 0.9000 | 1.8000 |
| (>= 171) | 80.00% | 16.67% | 39.29% | 0.9600 | 1.2000 |
| (>= 174) | 80.00% | 22.22% | 42.86% | 1.0286 | 0.9000 |
| (>= 180) | 70.00% | 22.22% | 39.29% | 0.9000 | 1.3500 |
| (>= 182) | 70.00% | 27.78% | 42.86% | 0.9692 | 1.0800 |
| (>= 191) | 70.00% | 33.33% | 46.43% | 1.0500 | 0.9000 |
| (>= 192) | 70.00% | 38.89% | 50.00% | 1.1455 | 0.7714 |
| (>= 198) | 70.00% | 44.44% | 53.57% | 1.2600 | 0.6750 |
| (>= 200) | 70.00% | 50.00% | 57.14% | 1.4000 | 0.6000 |
| (>= 202) | 70.00% | 55.56% | 60.71% | 1.5750 | 0.5400 |
| (>= 208) | 70.00% | 61.11% | 64.29% | 1.8000 | 0.4909 |
| (>= 209) | 70.00% | 66.67% | 67.86% | 2.1000 | 0.4500 |
| (>= 216) | 70.00% | 72.22% | 71.43% | 2.5200 | 0.4154 |
| (>= 232) | 70.00% | 77.78% | 75.00% | 3.1500 | 0.3857 |
| (>= 246) | 70.00% | 83.33% | 78.57% | 4.2000 | 0.3600 |
| (>= 269) | 70.00% | 88.89% | 82.14% | 6.3000 | 0.3375 |
| (>= 320) | 70.00% | 94.44% | 85.71% | 12.6000 | 0.3176 |
| (>= 348) | 70.00% | 100.00% | 89.29% | | 0.3000 |
| (>= 360) | 60.00% | 100.00% | 85.71% | | 0.4000 |
| (>= 380) | 50.00% | 100.00% | 82.14% | | 0.5000 |
| (>= 390) | 40.00% | 100.00% | 78.57% | | 0.6000 |
| (>= 460) | 30.00% | 100.00% | 75.00% | | 0.7000 |
| (>= 480) | 20.00% | 100.00% | 71.43% | | 0.8000 |
| (>= 600) | 10.00% | 100.00% | 67.86% | | 0.9000 |
| (> 600) | 0.00% | 100.00% | 64.29% | | 1.0000 |

CHAPTER 6:

6.0 DISCUSSION

Thoracic aorta aneurysms (TAA), a clinically silent disease in the initial stages has been linked to significant morbidity and mortality. Knowledge gap exists as pertains to factors associated with morbidity and mortality in the surgical management of thoracic aortic dissections and aneurysms especially in resource limited setups. Data on the prevalence of TAD/TAA in Kenya is inadequate. This study aimed to determine the operative mortality and the risk factors associated with operative mortality among patients who underwent thoracic artery aneurysm/dissection surgical repair. Understanding the risk factors associated with operative mortality among patients with TAA and TAD would help improve patient selection for surgery hence reduces mortality and complications associated with the surgery.

To achieve the objective, we included 29 patients who had a confirmed diagnosis of TAA/TAD and who had open surgical repair at KNH between years January 2010 and December 2020. Most of the patients accounting for 83.87% were referred to KNH by other health facilities as it was the main referral hospital in the country and the only public hospital offering thoracic aortic surgical care. This was an indication that the services are not easily accessible to a greater percentage of the population.

From our study, the rate of mortality among patients undergoing open surgical repair for TAA/TAD at KNH was 34.5%. The reported 30-day operative mortality rate from other studies is 5 – 10% (53, 54). In a study by Karam Nam et al, 2020, assessing 8 year period mortality in patients undergoing thoracic aorta replacement surgery in Korean hospitals indicated that in-hospital mortality was 8.6% in high volume hospitals, 10.7% in medium volume and 21.9% in low volume centers (55). From these studies we derive that in-hospital mortality in our facility is higher and nearly coincides with low volume centers. Another study conducted by Alessandro Varicca et al in Milan Italy between 1990 and 2007 which involved a total of 375 patients who underwent Bentall's operation demonstrated an overall in-hospital mortality of 4.5% (56). In comparison to above two studies a significant difference in mortality is noted. This statistically significant difference could be attributed to: KNH being a low volume center hence limited surgical experience which leads to longer duration of surgery and CPB time, limited resources i.e. absence of transesophageal echocardiography in theatre and lack of adequate postoperative care i.e. lack of cardiac intensivist in I.C.U, limited availability of blood and blood products, lack of devices like intra-aortic balloon pumps and extra-corporeal membrane oxygenation to aid patients with significantly compromised hemodynamics etc. In addition, our patients presented with advanced disease as demonstrated by the size of maximal aortic diameters, hence the higher mortality rate.

TAA is a life-threatening condition associated with high mortality. After aortic surgery, patients are at an increased risk of developing major complications most commonly hemorrhage, cardiac failure, pulmonary failure, acute kidney injury, delirium, coagulation disorders, sepsis, superficial wound infection (50). Recent study on the incidence and

mortality rates showed 41% of ruptured TAA arrived at AED but overall mortality was 97% to 100%, elective operations for TAA/TAD must be escalated to reduce this high mortality rate associated with rupture (38).

This study indicated a mean age of 48.53 which shows that our population is younger. This shows that in contrary to a study by David Sidloff et al(30), on mortality from thoracic aortic diseases and associations with cardiovascular risk factors that suggested majority of patients diagnosed with TAA had a mean age of 63.1 years. Older age is a recognized risk factor for TAA; however, in this study the variable was statistically non-significant. The data also suggested the incidence of TAA was comparable between males and females. This was in contrast with studies that indicated the prevalence is higher in men (8).

TAA has been associated with co-morbidities and from a study carried out the commonest co-morbidities were hypertension and dyslipidemia (31). For our study, the commonest comorbidity was hypertension with an incidence 77.42%. Comparatively, studies have showed higher prevalence of hypertension comorbidity among TAA patients (30). However, there was also a relatively high number 28 (90.32) who did not have other co-morbidities (e.g., diabetes). Only 1 (3.23%) of the study participants had peripheral arterial disease.

A greater majority of the TAA patients are asymptomatic. Symptoms most often develop late in the progression of the disease. Sudden onset, severe anterior chest pain is the typical presentation in acute aortic dissection with our data suggesting that majority of the patients 74.19% presented with chest pains. Other notable symptom was shortness of breath as results showed 54.84% presented with the symptom. The mean duration of symptoms in days was 49.58. This may suggest that TAA presents with an indolent course in our

hospital. Moreover, patients could have been seen in other facilities prior to visiting KNH where initial medical management was instituted before referral. TAA/TAD presents as a silent disease in the early stages, symptoms develop in advanced disease, as evidenced by our study the mean of the maximal aortic dimensions was 77.5 mm.

The anatomical pattern also influences outcome, higher incidence of bleeding as a complication was experienced in patients whom the aneurysm or dissection involved the arch vessels (p 0.009) and descending thoracic aorta (p 0.008) and similarly a higher mortality rate. Cardiopulmonary bypass time and length of operation was also noted to be longer in patients with TAA/TAD involving the the arch vessel and descending aorta.

From our study, most of the patients 21 (67.74%) out of the 31 experienced postoperative complications. After aortic surgery, patients are at an increased likelihood of complications, and this study demonstrated a correlation between cardiac failure and pulmonary failure complications with occurrence of mortality after surgery. There were statistically significant at p values of 0.029 and 0.01 respectively. These results build on existing evidence and compares to a study by Maung Hlaing, MD et al (51). that indicated patients who experience such complications had a considerably higher death rate as compared to those with no such post-operative morbidities.

TAA/TAD has been greatly associated with significant morbidity and mortality and if left untreated prognosis is poor mainly due to fatal hemorrhage when the aneurysm ruptures. Time factor is very important in treatment and management of TAA/TAD, Koji K et al (49) study on preoperative risk factors for hospital mortality in acute type A aortic dissection determined that the length of CPB has been acknowledged as an isolated risk factor leading to mortality, with CPB time of over 4 hours linked with an increased

likelihood of death. Conversely, our study showed a correlation between time under Cardiopulmonary bypass machine and duration of surgery with time to mortality and this was statistically significant at p value 0.002 and <0.001 respectively.

Contrary to the hypothesis that there is no association between mortality and the independent variables, a multivariate analysis was done on these variables which had a statistical significant of 5%. The variables included anatomical pattern, length of operation, length of CPB use, cardiac failure, severe hemorrhage, acute kidney injury and pulmonary failure as post-operative complications, smoking status preoperatively, clinical presentation before surgery i.e., difficulty breathing, shortness of breath and chest pains and age in years. From our findings we rejected the null hypothesis and concluded that there was an association between mortality and the selected independent variables. This implied that patients with the aforementioned factors were at a higher risk of developing complications and subsequent death. The reliability of this data however is impacted by the small sample size and a relatively larger cohort would generalize our results.

It is worthwhile to note that this study had significant limitations. Firstly, this was a retrospective study making it susceptible to selection bias, missing data and measurement errors. Secondly, the sample size was small curtailing the generalizability of the study. Thirdly, data we used were directly extracted from the available database contained during hospitalization hence information before hospitalization was unavailable making the data inconclusive. Therefore, we could not control the outcome of assessment or exposure. Studies on larger cohorts are needed to generalize our main findings of our present study.

Survival analysis

The Kaplan-Meier graphs depicted what trends of survival for both time on CPB and length of surgery. The data indicated that as time passed, survival rate increased. However, mortality was higher in the immediate postoperative period but as days progressed, mortality decreased. These results for survival were similar for both time on CPB and length of surgery. A similar study by Kebba N et al (57), gave a possible explanation that, at beginning the freshly operated patients were still at risk for adverse outcomes because sometimes the operations were done when they are still physiologically decompensated. The immediate postoperative period was just an extension of this unstable time. As postoperative period progresses and the derangements continue to be corrected, the chances of occurrence of mortality are reduced.

6.1 CONCLUSION

TAA is a disease that affects mostly younger people in our population and progresses even faster in patients with co-morbidities which are mostly non-communicable lifestyle diseases. Due to lack of advanced health services in many hospitals, TAA is diagnosed late when the disease has already progressed hence increasing the mortality and morbidity rate. The operative mortality rate together with the mortality rate amongst patients who developed complications post-operation were very high proving that this disease is fatal. Selection of patients for the open aortic surgery should be evidence-based on the presence of an underlying conditions, physiological status of the patient and anatomical extent of the disease. Intra-operatively considerations and measures should be put in place to reduce

the total operative time, time under CPB and the total blood transfusion. Post-operatively measures should be put in place for timely recognition and correction of post-operative complications. The significant postoperative complications associated with increased mortality being hemorrhage, cardiac failure, pulmonary failure and acute kidney injury.

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APPENDIX

APPENDIX 1: CONSENT FORM

I Dr. Joseph Mutie, a registrar in the Cardiothoracic Unit of Department of Surgery, University of Nairobi, would like to seek consent from the Research and Administration department/Office of the Kenyatta National Hospital to Conduct a research study entitled, **FACTORS ASSOCIATED WITH OPERATIVE MORTALITY AMONG PATIENTS ADMITTED WITH THORACIC AORTIC ANEURYSM/DISSECTION IN KENYATTA NATIONAL HOSPITAL: A RETROSPECTIVE COHORT STUDY.**

This study entails using patients' files to derive estimates of mortality and associated risk factors among patients undergoing open surgical repair for Thoracic artery aneurysms / thoracic artery dissection at Kenyatta National hospital.

Information derived from this study will help improve the process of patient selection for open surgical repair and therefore reduce mortality and morbidity associated with this procedure.

No patient identifying information were collected.

Results of this study was shared with the hospital management among other stakeholders to help improve local policies and guidelines on patients on surgical management for TAA/TAD

.....
Hospital representative

.....
Principal Investigator

APPENDIX 2. DATA COLLECTION TOOL

MANAGEMENT OF THORACIC AORTIC ANEURYSM/THORACIC AORTIC
DISSECTION AT KENYATTA NATIONAL HOSPITAL; A TEN-YEAR
RETROSPECTIVE COHORT ANALYSIS OF MORTALITY, TREATMENT OUTCOMES
AND SOCIODEMOGRAPHIC TRENDS.

DATE OF COLLECTION..... SERIAL NUMBER.....

BIODATA

1. SEX:
 - a. Male
 - b. Female
2. AGE: _____ (years)
3. MARITAL STATUS:
 - a) Single
 - b) Married

4. EDUCATION LEVEL:

- a) None/no formal education
- b) Lower primary (class 1- class 4)
- c) Upper primary (class5- class 8)
- d) Secondary (Form 1-Form 4)
- e) Tertiary institution

5. CURRENT SMOKER

- a) Yes NUMBER OF PACK YEARS.....
- b) No.....
- c) CEASED SMOKING..... NO. OF YEARS SINCE CESSATION..... PACK YEARS SMOKED.....

6. MODE OF REFERAL

- a) Self
- b) Health Facility

CLINICAL DETAILS

PATIENT CO MORBIDITIES

- 7. Hypertension yes / no
- 8. Diabetes mellitus yes / no
- 9. Connective tissue disorder yes / no

10. Peripheral arterial disease yes / no

11. Others.....

FIRST PRESENTING SYMPTOMS

12. chest pain Yes / No

13. back pain Yes / No

14. shortness of breath Yes / No

15. difficult breathing Yes / No

16. low BP _____mmHg Yes / No

17. Incidental finding Yes / No

18. Other.....

19. Date the diagnosis was first made (dd/mm/yr)

20. Duration of symptoms.....days

Computed Tomographic Angiogram (CTA) scan findings:

21. Size of aorta: maximal aneurysm diameter.....mm

Aneurysm location

22. Aortic root -yes/ no

23. Ascending – yes/no

24. Arch-yes/no

25. Descending-yes/no

Type of aneurysm

26. True-yes/no/no information

27. False-yes/no/no information

28. dissected aorta:

a) YES

b) NO

c) NO INFORMATION

29. If dissected STANFORD CLASSIFICATION (A OR B).....

30. Leaking aneurysm

YES

NO

NO INFORMATION

31. Presence of intramural thrombus

a) YES

b) NO

c) NO INFORMATION

ARCH VESSELS INVOLVED.

32. Brachiocephalic artery---YES/NO

33. Lt common carotid artery---YES/NO

34. Lt subclavian artery ----YES/NO

35. NO INFORMATION

36. Where the diagnosis was first made

37. Date of admission to Kenyatta National Hospital (dd/mm/yy)

.....

38. Surgical Intervention

a) YES

b) NO

39. Date of Surgery: (dd/mm/yr)

.....

41. Type of surgery

1. Bentall's procedure

2.Davids procedure

3.arch replacement

4.Elephants trunk

5.descending aorta replacement

6. TEVAR

7. Other type.....

42. Length of operation: Minutes

43. Cardiopulmonary bypass (CPB) machine usageyes/no

44. Length on CPB..... minutes

45. Deep Hypothermic Circulatory Arrest (DHCA).....YES/NO

46. Length of DHCA.....

47. Retrograde cerebral perfusion---yes/no

48. Antegrade cerebral perfusion...yes/no

49. Intra-operative transfusion... yes/no

50. Number of units transfused.....

51. Length of operation: Minutes

52. Admitted to ICU

a. YES

b. NO

53. Date of admission to ICU (dd/mm/yr.)

.....

54. Date of discharge from ICU (dd/mm/yr.)

.....Days in ICU.....

55. Date of discharge from hospital (dd/mm/yr.)

56.days in hospital post-operation.....

57. Patient developed complications post operatively.

a) Yes

b) No

Postoperative complications patients developed during hospital stay.

58. Bleeding. yes/no

If yes how much blood drained via UWSD.....Units of blood transfused in
ICU.....Patient required re-operation.....yes/no

59. Neurologic injury. yes/no

If yes.... transient / permanent.

Head imaging—yes /no..... if yes.

Findings.....
.....

60. Cardiac failure. yes/no

61. Pulmonary failure. yes/no

62. Wound sepsis. yes / no

63. Wound dehiscence. yes / no

64. Embolic phenomenon yes / no

65. Deep vein thrombosis yes / no

