HAEMODIALYSIS VASCULAR ACCESS FUNCTION IN DIALYSIS PATIENTS AT THE KENYATTA NATIONAL HOSPITAL

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DECLARATIONS

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

I dedicate this book to my parents, Mr and Mrs Ndinya, to my wife Evelyne and son Ethan for their overwhelming support and being a source of inspiration for me during the course of my studies.

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To the Almighty God for His grace and strength that enabled me carry out this study. Secondly, I offer my sincere gratitude to the following people who made this study possible: Dr Chacha for his supervision, dedication and assistance in performing all the Doppler ultrasounds in my study. My supervisors: Prof. Kayima, Prof. Mc'ligeyo, Dr Were, Dr Chacha for their guidance and supervision. My Statistician George Odinya for his help with the data analysis. The staff of Kenyatta National Hospital renal unit. All the patients who agreed to participate in the study. My family for their encouragement and prayers during my masters program.

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LIST OF ACRONYMS AND ABBREVIATIONS

AVF	-	Arteriovenous Fistula
AVG	-	Arteriovenous Graft
BFR	-	Blood Flow Rate
BUN	-	Blood Urea Nitrogen
CVC	-	Central Venous Catheter
DOPPS	-	Dialysis Outcome and Practice Pattern Study
ESRD	-	End Stage Renal Disease
HD	-	Haemodialysis
KNH	-	Kenyatta National Hospital
Kt/V	-	A method of assessing the amount of dialysis delivered in terms of urea removal.
NCDS	-	National Cooperative Dialysis Study
NKF-DOQI	-	National Kidney foundation – Dialysis Outcome Quality Improvement
RRT	-	Renal Replacement Therapy
SPSS	-	Statistical Package for Social Sciences
URR	-	Urea Reduction Ratio
VA	-	Vascular Access

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ABSTRACT

Background

The number of patients requiring renal replacement therapy (RRT) worldwide has been on the rise. Vascular access (VA) is the life-line for the majority of these patients when on haemodialysis (HD). VA related morbidity is a leading cause of hospitalization. Its function and patency is essential for efficient HD. There is a need to determine the VA performance to identify those that are dysfunctional since early intervention to improve blood flows would ensure longevity of use and preservation of future vascular access site options.

Objective

This study aims to evaluate the vascular access function in patients undergoing haemodialysis at the Kenyatta National Hospital (KNH).

Methods

This was a cross-sectional descriptive study. The participants were thirteen years and above, requiring RRT in the form of HD at the KNH renal unit, who gave written informed consent or assent. Consecutive sampling was employed to recruit 150 patients. A focused clinical examination was then undertaken to determine the type of VA. The peak and mean VA blood flow rate (BFR) were recorded during a single HD session. Pre and post dialysis blood samples were obtained for blood urea measurements used to determine the delivered dialysis dose. The mean VA BFRs for the session was then compared to the corresponding achieved dialysis dose. In addition, all patients with an arterio-venous fistula (AVF) fashioned had a Doppler Ultrasound evaluation of the vascular access.

Results

An analysis of the complete data of 150 patients was performed, the mean age of the study participants was 43 years. The cuffed tunnelled central venous catheter was the VA predominantly used by 46% of the study participants. The mean and peak blood flow was 311.5 mL/min and 368.3 mL/min respectively, non-cuffed non-tunnelled central venous catheter (CVC) performed poorly; only 47.5% achieved a mean blood flow rate above 300 mL/min as compared to AVF (87.5%) and cuffed tunnelled CVC (81.7%). The delivered mean Kt/V and urea reduction ratio (URR) were 1.5 and 69.8% respectively. Twenty-four percent of patients had a URR less than 65%. A higher mean blood flow rate was associated with a higher URR ($p=0.004$) and Kt/V ($p=0.009$). AVF stenosis was present in 12.5% and

thrombosis in 3% of patients. Aneurysms were the commonest complication in AVF at 46.9% but were not haemodynamically significant.

Conclusion

This study demonstrates that 74.7% of the vascular accesses in use for haemodialysis at the KNH renal unit delivered adequate blood flow rates. Cuffed tunnelled haemodialysis CVCs offered adequate blood flows and achieved good delivered dose of dialysis that were comparable to arterio-venous fistula. The non-cuffed non-tunnelled CVCs delivered poor blood flow rates and dialysis dose and were in use for longer than the recommended duration of two weeks. On the whole, arterio-venous fistula access had better blood flow rates and delivered dialysis dose, however there is need to have routine surveillance by measuring blood flow rates and delivered dialysis dose. Interventional procedures need also to be made affordable to prevent access loss.

CHAPTER ONE: INTRODUCTION

Background

Worldwide prevalence of chronic kidney disease is estimated to be between 8% to 16%; it is expected to rise disproportionately in developing nations driven by diabetes and hypertension (1). Renal replacement therapy in the form of dialysis or renal transplantation is a life saver for chronic kidney disease patients who progress to end stage renal disease (ESRD). The number of patients with ESRD requiring renal replacement therapy has continued to increase worldwide (2–4).

In the year 2010, between 4.9 to 9.7 million people were estimated to require RRT, of which only 2.6 million people received treatment. This treatment gap is fuelled by the growing populations from low income nations in Africa and Asia. The number of people on RRT is projected to more than double to 5.4 million by the year 2030 (5).

Around the world, 70 to 80% of patients who need RRT are initiated on HD. In some countries like Hong Kong and Mexico peritoneal dialysis predominates as the preferred mode of RRT where 76% and 50% of patients respectively have been initiated on peritoneal dialysis (6). Vascular access is the life-line for the majority of these patients when on HD; its function and patency is essential for efficient HD. Low BFR and loss of patency of VA limit HD delivery, extends treatment times and results in under dialysis leading to increased morbidity and mortality (7).

Primary prevention measures of access dysfunction include use of central venous catheter locking solutions (heparin and citrate) and routine monthly blood flow rate surveillance for both CVC and AVF. Attempts to restore blood flows once dysfunction occurs include; saline flushes, use of fibrinolytics and mechanical disruption of fibrin sheath for CVCs and fistuloplasty or VA stenting for patients with AVF (8,9).

Haemodialysis access function can also be assessed by measuring the delivered dialysis dose. One method of assessing the dialysis dose is calculation of Kt/V (where K = urea clearance, t = dialysis time and V = total body water). This index reflects the efficiency of dialysis and has been shown to correlate with morbidity and mortality rate of patients on HD (10–12). Dialysis dose can also be assessed by measuring the urea reduction ratio (URR) (13). The URR is assessed by measuring blood urea levels before and after dialysis. The results of several surveys show that achieving a Kt/V of 1.2 or more and URR of 65% or more is effective in

improving outcomes of patients on HD (14). Hence achieving this goal remains one of the aims of HD.

In order to achieve the desired dialysis dose, one may be required to use high flux dialyzers, increase the blood flow rate (BFR), increase the flow of dialysate or increase the dialysis treatment time. Some of these methods like increased treatment times and use of high flux dialyzers cannot be used routinely due to economic constraints as well as the patients' reluctance to spend most of their productive hours on HD.

Short intermittent HD practice for patients on maintenance HD as currently done in most centers across the world and at the Kenyatta National Hospital involves prescription of high blood flow rates above 300 ml/min to achieve the recommended dialysis dose (15). Measuring the BFR across the HD vascular access is an important marker of VA function and ultimately a marker of delivered dialysis dose.

This study assessed the peak and mean BFR in the HD vascular accesses of patients undergoing maintenance HD at the Kenyatta National Hospital during a single dialysis session. The mean BFR was compared to the National Kidney Foundation-Dialysis Outcome Quality Initiative (NKF-DOQI) recommended set minimum VA blood flow rate of 300 mL/min. In addition, flow velocities of above 500 mL/min by Doppler ultrasound examination was used for patients with a fashioned AVF to define a good functional vascular access (8). Doppler ultrasound was also used to examine patients with AVF to describe the discernible causes of dysfunction. The VA mean blood flow rate for the session was also compared to corresponding URR and Kt/V.

CHAPTER TWO: LITERATURE REVIEW

2.1 Haemodialysis access

Maintenance of access to circulation continues to be the Achilles' heel of the HD procedure (16). Vascular access can be temporary (non-cuffed non-tunnelled CVC) for use in emergency cases or permanent. There are three types of permanent VA in use: Native arterio-venous fistulae (AVF), arterio-venous graft (AVG) and cuffed tunnelled CVC. The ideal permanent VA must provide longevity of use, have minimal complications and supply high enough blood flow to deliver the prescribed dialysis dose (17).

The native AVF is considered the best VA to initiate ESRD patients onto HD (9,18,19). Despite this, geographical variations exist worldwide in the types of VA used with developed countries using less of CVCs. In Australia among adult patients on HD, the prevalence of VA use for AVF, AVG and cuffed tunnelled CVC are 77%, 19% and 4% respectively (20). The analysis from the Dialysis outcomes and practice patterns study (DOPPS) compared data on VA usage patterns from 145 dialysis units in the United States (US) and 101 dialysis units in Europe and found that the AVF prevalence was 80% in Europe versus 62% in the US (21).

Data on access usage patterns in Africa is limited. In South Africa, the prevalence of AVF, AVG, cuffed tunnelled CVC and non-cuffed non-tunnelled CVC use was 50.9%, 6.1%, 38% and 5.1% respectively (4). In our set up at the Kenyatta National Hospital (KNH) *Soshi et al* in 2003 reported the prevalence of access usage for cuffed tunnelled CVC, AVF and non-cuffed non-tunnelled CVC at 65.2%, 27.3% and 7.6% respectively (22). The prevalence of CVC usage in Africa and in particular in our set-up is far in excess of the National Kidney Foundation–Dialysis Outcomes Quality Initiative (NKF-DOQI) recommendation that CVC be used in <10% of prevalent HD patients (8).

2.2 Central venous catheter dysfunction

A broad range of definitions for CVC dysfunction have been documented in the literature and include; VA low blood flow rates, frequent HD machine arterial and venous pressure alarms, poor conductance during HD, and poor urea clearance based on decreasing URR or Kt/V calculations (23). The NKF⁄DOQI guidelines define VA dysfunction as failure to attain a sufficient extracorporeal blood flow of > 300 mL/min with a pre-pump arterial pressure more than negative -250 mmHg (8).

CVC dysfunction is a common complication encountered in clinical practice (24). The 1 year primary patency rates of tunnelled haemodialysis CVCs range between 65% to 75% (25,26). Early CVC dysfunction can occur from mechanical factors like mal-positioning of the distal tip, kinking in the subcutaneous tissue, tight ligature or early fibrin sheath formation (27,28). Thrombosis which occurs later can be intraluminal or periluminal and is the primary reason for CVC dysfunction. This leads to untimely removal of 17% to 33% of CVCs (29,30) and consequently loss of VA in 30% to 40% of patients (31).

2.2.1 Pathogenesis of central venous catheter dysfunction

Virchow's triad describes the interplay of turbulent blood flow, hypercoagulability, and disruption in vessel walls as an impetus for thrombus formation (32). Endothelial and vessel wall damage occurs during CVC insertion; its continued presence in the vessel lumen creates turbulent flow and that triggers the coagulation cascade further. The cycle is perpetuated by manipulations and lumen reversals during HD to improve blood flows (27,33).

Another cause of dysfunction is fibrin sheath formation. This is composed of proteins, lipoproteins and coagulation factors. Fibrin sheath is a normal biological response to a foreign object inserted into the blood stream. Several studies have shown that it can form as early as 24 hours within insertion of CVCs (34,35). It then evolves over weeks to months to form collagen and recruit smooth muscle cell migration (35). The formation of fibrin sheath starts at the point of contact between the CVC and the vessel wall, coats the entire length of the CVC and can create a one-way valve mechanism that decreases blood flow through the CVC (36). This complex interaction results in further activation of the coagulation system beyond which the intrinsic fibrinolytic system can overcome and thrombosis ensues which further worsens blood flow through the CVC (33).

2.2.2 Evaluation of central venous catheter dysfunction

Early detection of CVC dysfunction is essential as it is easier to salvage and thus leads to preservation of future VA sites and prevention of under dialysis. Assessment of a CVC can be done at the bedside to identify dysfunction. Clues include: HD blood pump flow rates below 300 mL/min, HD machine arterial pressure monitor more than negative -250 mmHg, HD machine venous pressure monitor above 250 mmHg, low conductance during HD, decreasing urea clearance as demonstrated by declining URR or Kt/V and inability to aspirate blood freely using a syringe from the CVC (8).

2.3 Native AVF and AVG dysfunction

A common cause of native AVF dysfunction is failure to mature (before the access can be utilized for haemodialysis). The reason for this is not well understood but the lesion observed is a juxta-anastomotic stenosis (37). Secondary failure of an AVF access is usually due to venous stenosis leading to thrombosis. The same pathology occurs in AVG at sites of vascular and graft anastomosis (38). The thrombotic episodes occasionally cannot be resolved leading to loss of vascular access in 80% of the cases (39,40).

2.3.1 Pathogenesis of AVF and AVG dysfunction

The media and intima of blood vessels at the site of stenosis in AVF and AVG undergo neointimal hyperplasia (41,42). In addition, in AVG, there is adventitial angiogenesis and a large number of macrophages that line the perigraft region (43,44).

The initial events in neointimal hyperplasia include: altered haemodynamics at the graft–vein or artery–vein anastomosis as a result of turbulence and compliance mismatch between noncompliant graft/artery and compliant vein (45,46), surgical injuries to blood vessels at time of access creation (37), inflammatory mediators attracted to the surgical site due to presence of the graft (44), graft injury during the cannulation of access at every dialysis session (47) and effect of uremia exacerbating endothelial dysfunction which precedes access creation (48).

Following these events, endothelial and smooth muscle injury results in the proliferation and migration of smooth muscle cells and myofibroblasts from the media into the intima to form the lesion of venous neointimal hyperplasia. This process is mediated via cell cycle regulators, cytokines, chemokines and adhesion molecules (49). The cytokine predominantly thought to trigger neointimal hyperplasia in response to the turbulence and vascular injury is platelet derived growth factor (PDGF) (50).

2.3.2 Evaluation of AVF/AVG dysfunction

Simple measures such as inspection of the arm with an AVF or AVG can detect aneurysms or failure of the fistula to collapse on elevation of the arm with the AVF may suggest presence of stenosis. In general, VA blood flow rate less than 600 ml/min in AVG and less than 400 to 500 ml/min in AVF (9) has been used to define dysfunction.

Direct and indirect techniques of blood flow measures exist; the direct methods are Doppler ultrasound and magnetic resonance angiography. The indirect methods include; ultrasound

dilution, glucose infusion technique, urea dilution, differential conductivity and In line dialysance (51).

Doppler ultrasound is a direct technique for measuring VA blood flows that has been used in various studies (52–54). It is operator dependent and requires an accurate measurement of the cross-sectional diameter of the VA (55,56). Despite these limitations, serial VA blood flow measurements by use of Doppler ultrasound has been shown to help in identifying early stenotic lesions, their location and severity (9). Early intervention when stenotic lesions are identified will result in reduction of VA thrombosis, preservation of VA and improved quality of dialysis.

2.4 Vascular access morbidity and mortality

Mortality risk is dependent on the type of vascular access. Studies have demonstrated that CVCs have the highest risk followed by AVG and AVF in descending order (57,58). Relative risk of death associated with CVC compared to AVF have been reported between 1.4 to 3.4 fold higher (59–61) and is driven by infectious causes (59). Data from 616 patients followed up for 3 years in the Choices for Healthy Outcomes in Caring for ESRD Centre CHOICE study by Astor et al demonstrated increased mortality of CVC and AVG at 50% and 26% respectively as compared to AVF (62).

However Di Iorio et al in their analysis of data from the uremic registry of Campania (southern Italy) demonstrated that CVC use in both incident and prevalent chronic dialysis population is associated with significantly increased hospitalization, mortality rate and relative risk of death compared to patients using AVF; after correction for age, malnutrition, haemoglobin, albumin and co- morbidities, the difference in mortality disappeared (63).

Failure of an AVF to mature; its complications related to VA stenosis or thrombosis and the need for hospitalization for VA related procedures is the leading cause of morbidity with its use (64,65).

2.5 Haemodialysis prescription

The Kt/V formula (where K = urea clearance, t = dialysis time and V = total body water) is a method of assessing the delivered dialysis dose in terms of urea clearance. It is derived from the Daugirdas formula $Kt/V = -\ln(R - 0.03) + [(4 - 3.5R) \times (UF/W)]$, where UF is the ultra-filtration volume in liters, W is the post dialysis weight in kg, and R is the ratio of the post dialysis to pre-dialysis urea (66). URR is calculated by the equation (pre-urea - post-urea)/pre-urea.

The NKF-DOQI HD Adequacy Work Group has recommended conventional thrice-weekly HD for all people who need dialysis therapy with the minimum target Kt/V of 1.2 mL/min/1.73m^2 or URR of at least 65% for patients with residual renal function (RRF) above 2 mL/min/1.73m^2 (67). Despite these recommendations, twice weekly HD is quite common in many parts of the developing world, and occasionally in Europe and the United states (68,69). It is recommended that twice weekly HD patients should be a highly select group with considerable amounts of residual renal function. A target Kt/V of above 2.0 per session should be aimed at, and this is extrapolated from urea kinetics in those receiving thrice weekly HD (70).

2.5.1 Blood flow

Blood flow rate which is determined by the quality of the VA, is the most important rate limiting step for urea clearance. Higher blood flow rates will optimize dialyzer performance. During intermittent HD, VA BFRs are maintained at 350 to 450 mL/min for AVF (64) and above 300ml/min for CVC dialysis (8). Patients with lower BFR are at risk of receiving inadequate dialysis (71). Observational studies have demonstrated that low or declining access blood flow predicts subsequent access failure (72,73). VA blood flows are affected by access related factors like VA stenosis or thrombus formation and systemic hemodynamics like blood pressure and cardiac output as well as vascular size (74).

2.5.2 Dialysate Flow

The diffusive clearance of a solute is directly proportional to the dialysate flow, This relationship is linear for dialysate rate up to 500 mL/min (75). Low dialysate flow rates result in nearly complete saturation of the effluent dialysate with respect to urea and limits clearance. To overcome this, higher dialysate flows between 500 to 800 mL/min are used to maintain a higher concentration gradient for diffusion of urea, and therefore, the urea clearance rate is higher. The usual dialysis solution flow rate is 500 mL/min and a faster flow rate is 800 mL/min. An increase from 500 mL/min to 800 mL/min (60%) produces a 10 to 15% increase in clearance (76).

2.5.3 Dialysis time

The usual conventional HD prescription is currently thrice-weekly sessions of 180-240 min duration (77). Mixed results of the effect of time on dialysis adequacy have been reported in observational studies and clinical trials.

Observational data suggest that the positive effects of prolonged times of dialysis treatment or increased dialysis frequency translate into improved patient survival (78). *Saran et al* in her analysis of the DOPPS study noted that the adjusted risk of dying was 19% higher in patients treated for 211 min to 240 min and 34% higher in patients whose sessions lasted less than 211 min compared to those whose time on HD was more than 240 min. The time benefit varied among the continents being greatest in Japan and lowest in the US but it was significant in all cases (79).

Similar results from observational studies have not been replicated in clinical trials. In the first randomized clinical trial among patients with ESRD on HD, the National Cooperative Dialysis Study (NCDS), patients were divided into four groups on the basis of blood urea nitrogen level and dialysis time. The relationship between treatment time and patient outcome in this study did not reach statistical significance (p=0.06). The study results led to the development of Kt/V formula, which uses urea as a marker of low molecular weight (LMW) uremic toxins (80).

More consideration has been given to the reduction of urea than time on HD during dialysis prescription (77). Hence more recent trials like the landmark HEMO study compared lower dialysis dose (Kt/V of 1.2) versus higher dialysis dose (Kt/V of 1.6) and found no difference in mortality or cardiac events (81).

2.6 Justification

The availability of transplantation is less accessible, therefore haemodialysis remains the major renal replacement modality used worldwide. It supports life despite complete cessation of renal function. This is achieved at a considerable cost to the community and inconvenience to the patient.

Vascular access is the cornerstone of the haemodialysis treatment. The performance of VA is a major determinant of treatment outcomes, an indicator of quality of care in a program and a lifeline to a majority of patients who have no access to transplantation.

In the current literature a few studies have looked at the relationship of suboptimal performing vascular accesses and delivered dialysis dose. VA dysfunction is amendable and maintaining a good functional access is a key strategy in short intermittent HD especially in our set-up given our limited resources and congestion in our dialysis unit. This was a quality improvement study aimed at setting in place a surveillance program for VA function as well as a step towards increasing interventions to prolong VA survival.

2.7 Research question

What is the adequacy of haemodialysis and vascular access function among patients undergoing haemodialysis at the Kenyatta National Hospital?

2.8 Study Objectives

2.8.1 General Objective

To evaluate the haemodialysis and vascular access function in patients undergoing haemodialysis at the Kenyatta National Hospital.

2.8.2 Primary Objectives

i. To describe the vascular access blood flow rates in patients using AVF or CVC for Haemodialysis.
ii. To determine the dialysis dose delivered through AVF or CVC for the session of dialysis (by measuring URR and Kt/V).
iii. To determine the prevalence of significant stenosis and thrombosis in patients with native arteriovenous fistula in the study population as diagnosed by Doppler ultrasound.

2.8.3 Secondary Objective

To assess the relationship between mean blood flow rate through vascular accesses namely, AVF or CVC and the achieved dialysis dose (URR and Kt/V).

CHAPTER THREE: METHODOLOGY

3.1 Study Design

Cross sectional descriptive study.

3.2 Study Setting

The study was carried out at the renal unit, Kenyatta National Hospital, a teaching and national referral hospital located in Nairobi, Kenya. The renal unit has 24 haemodialysis machines. It provides services for inpatient acute kidney injury cases and emergencies, as well as outpatient services. On average the unit performs 60 sessions of haemodialysis per day scheduled in three different shifts with each session lasting about 240 minutes. Patients on maintenance HD are scheduled on a twice weekly inter-dialytic period with emergency cases scheduled as determined by the nephrologist.

3.3 Study Population

The study population comprised of all patients undergoing haemodialysis at the Kenyatta National Hospital.

3.4 Sample size calculation

Considering the finite population of 200 patients dialyzing in the renal unit, the Daniel formula for finite population (less than 10,000) (82) was used as follows:

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

Where

n' = sample size with finite population correction,

N = size of the target population of patients on regular haemodialysis in KNH renal unit= 200

Z = Z statistic for 95% level of confidence = 1.96

P = Estimated proportion of dialysis patients with mean blood flow rate >300 ml/min = 89.5% (Moist et al, 2006).

d = margin of error = 5%

$$= \frac{200 \times 1.96^2 \times 0.895 \times 0.105}{0.025^2 (200-1) + 1.96^2 \times 0.895 \times 0.105}$$

n = **149**

The minimum sample size for this study was 149 patients dialyzing at KNH renal unit, and there were 150 patients enrolled into the study.

3.5 Inclusion criteria

i. Age thirteen years and above

ii. Patients on haemodialysis for at least 1 week

iii. Blood pressure above 90/60 mmHg

iv. Written informed consent

v. Written informed assent for those less than eighteen years.

3.6 Exclusion criterion

Patients who did not complete 4 hours of haemodialysis

3.7 Sampling method

Consecutive sampling was used, with each patient who fulfilled the inclusion criteria being included in the study in order to achieve the minimum required sample size.

3.9 Screening and recruitment

The principal investigator (PI) and two research assistants (registered Nurses of higher national diploma level in nephrology) screened the patients undergoing hemodialysis in the renal unit for eligibility. Patients who met the inclusion criteria were selected. The patients were then given all the relevant information about the study and those who gave written informed consent (Appendix I & II) or assent for those less than 18 years (Appendix III) were recruited.

3.10 Procedures

3.10.1 Clinical methods

A brief history of vascular access use was taken from each patient focused on the type, site and other previous VA used. Physical examination focused on patient's weight before and after dialysis and blood pressure measured before dialysis. The patient's weight was measured in kilograms to the nearest 100 grams, using a digital Ashton Meyer weighing scale. Blood pressure was measured using a mercury sphygmomanometer, on the non-dominant arm while the patient is seated at rest. The dominant arm was used if the non-dominant had an AVF fashioned.

3.10.2 Laboratory methods

All blood draws were done by the principle investigator and the 2 trained research assistants. Each patient had 2 ml of pre-dialysis blood sample for BUN collected using a technique void of dilution with saline or heparin (see appendix IV) and an immediate 2ml Post dialysis blood sample for BUN drawn using the slow flow technique (see appendix V). The blood samples were then transferred to a plain partial draw vacutainer (red top) and transported to the KNH renal laboratory within one hour of sample withdrawal. The samples were then analyzed using the *biolis 50i superior machine.*

3.10.3 Measurements of blood flow across the vascular access

Dialysis was performed using a *Nipro surdial 55 plus or Gambro AK96 HD machines*. The assessment of peak flow was performed during the first 1 hour of the treatment by the principal investigator and the trained assistants to eliminate error caused by decreases in cardiac output or blood pressure related to ultra-filtration. The measurement was done as described here.

The HD blood pump speed was set at 250 mL/min at initiation of HD. The speed was then adjusted up or down at rate of between 5 mL/min to 10 mL/min within the HD pre-pump arterial pressure limits of above -250 mmHg and HD post-pump venous pressures limits of below 250 mmHg. A sustained maximum BFR for at least 5 minutes performed at a single treatment within the arterial and venous pressure limits was considered the VA peak BFR. Mean blood flow rate for the session was an automated recorded average from the HD machine blood pump after completion of HD.

Patients with an AVF subsequently underwent a Doppler ultrasonography (using a *Sonosite Fujifilm M turbo ultrasound machine and a high frequency 9 MHz linear array transducer*) of their VA and this was done within 2 hours post dialysis by an interventional radiologist. The following criteria were used for color Doppler diagnosis of AVF abnormalities:

i. **Fistula stenosis** was a circumscribed constriction of the vessel lumen within the AVF vein or in the region of the color Doppler flow stream with turbulent high velocity systolic flow and low diastolic flow by spectral Doppler.
ii. **Fistula thrombosis** was an echogenic mass (thrombus) protruding into the vessel lumen, associated with partial or complete occlusion of the lumen.
iii. **Fistula aneurysm** was a circumscribed region of dilatation of the AVF lumen with distinct borders filled with color Doppler flow signals of low velocity.

The VA blood flows for each patient was then compared to the corresponding URR and Kt/V after the dialysis session to determine the access performance in relation to the achieved dialysis dose. Kt/V was calculated using the Daugirdas formula $Kt/V = -\ln(R - 0.03) + [(4 - 3.5R) \times (UF/W)]$, where UF is the ultrafiltration volume in liters, W is the post dialysis weight in kg, and R is the ratio of the post dialysis to pre-dialysis urea (66). URR was calculated by the equation (pre-urea - post-urea)/pre-urea.

3.11 Quality Assurance

All Doppler ultrasound scans were performed using a single machine, the *Sonosite Fujifilm M-turbo*. The PI and the radiologist underwent orientation on the utilization of the machine from a technician at Sonosite Inc. (Nairobi), prior to embarking on the study. Consensus was achieved between the PI and radiologist on the methodology of acquisition and measurement of images, prior to the onset of the study, and that ensured uniformity of definitions and standardization of measurement. All Doppler ultrasound scans were performed by a single experienced radiologist in order to reduce intra-observer variability in image acquisition.

Standard operating procedures for specimen collection was followed; labeling was done after sample collection to minimize pre-analytical errors. To ensure quality, the renal laboratory machines were calibrated periodically. Standards and controls were run with each batch of tests. Every 20^{th} sample was taken to an external laboratory (the lancet laboratory) for quality control. Verification of results was done together with the laboratory technician and accurate

transcription of results to the case report forms was ensured. The weighing scale was zeroed and calibrated before each use.

3.12 Study variables

3.12.1 Outcome Variables

The primary outcome variables was the peak and mean BFR in the HD vascular access, URR and KT/V. An adequately functioning VA was defined as blood flow rates above 300 mL/min. In addition, for patients with an AVF access, Doppler ultrasound blood flow rates above 500 mL/min.

3.12.2 Explanatory Variables

Explanatory variables were collected to determine if there is an association between these variables and blood flow rate in the CVC and AVF. To explore participant factors that impact on access function the following data were collected: age and gender of the patient, co-morbidities, height, weight, duration of dialysis, duration of access since creation, the site and type of vascular access.

3.13 Data management

3.13.1 Data Collection

Data was collected by use of structured Case Report Forms (CRF) specifically designed for this study (see appendix VI). During data collection the patients' case notes were reviewed and study specific information were identified and entered into the corresponding CRF. Patients were also interviewed to verify the information on the case notes and give any additional information.

3.13.2 Data Privacy

Standards to protect personal data were followed. Data collection instruments had minimum possible subject identifiers; only the first name and a serial number were entered in the study questionnaire and specimen labels.

3.13.3 Data Storage

The filled questionnaire and laboratory results forms (data forms) were verified for completeness by the principal investigator. The data forms were kept in a secure lockable cabinet only accessible by the PI and the statistician. The data was entered electronically

using the Statistical Package for Social Sciences (SPSS) version 23, (SPSS Inc., Chicago, IL, USA). Upon completion of entry, the hard copy forms were used to clean and verify correctness of the entered data and then stored safely in the lockable cabinet. The electronic file was backed up in three compact discs and stored offsite.

3.14 Statistical Analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 23. Univariate analysis for categorical data e.g. sex was presented as frequencies/proportions and for numerical data e.g. age was presented using measures of central tendency such as mean and standard deviation (SD). Blood flow rates were analysed and presented as a mean (SD); categories using different cut offs was done and number of patients in each category was presented as percentages. Patients who achieved the desired dialysis dose using URR and Kt/V were presented as a percentage with 95% confidence interval (CI). Bivariate analysis testing associations between delivered dialysis dose and mean blood flow rate was done using regression analysis. All statistical tests were interpreted at 5% level of significance ($p = 0.05$).

3.15 Ethical Considerations

The study was undertaken after approval by the department of internal medicine, university of Nairobi and the KNH - UON scientific and ethical research committee. Patients eligible to participate in the study were included only after providing consent/assent following the process as outline.

The PI informed all the patients of the purpose of the research, the procedures involved and disclosed the full details of all the tests to be done. They were assured that participation was voluntary and no medical attention was to be denied should they decline to participate. They were also informed of the medical benefits and also physical and psychological harms to their satisfaction prior to being included in the study. The PI assured them of full and free access to their results and therapeutic interventions were recommended and pursued where need arose, according to the accepted standards of practice.

Confidentiality was strictly maintained and all data were stored securely, only revealed upon a need to know basis. All costs regarding investigations in this study was borne by the principal investigator. Following the full explanation and acceptance by the patient of the above, they were requested to sign the consent or assent form (Appendix). All patients recruited in this study underwent the standard haemodialysis care as offered at KNH – Renal Unit. Only

specimen needed for the study, (2 mL of venous blood) were obtained from the patient before and after dialysis. Patients with a fashioned AVF also had a Doppler ultrasound scan of their access done. The study results were communicated to the patients and physician attending to them.

CHAPTER FOUR: RESULTS

4.1 Recruitment

In a period of 3 months (January 2016 to March 2016) 156 consecutive patients on haemodialysis in the renal unit, KNH, were screened for eligibility to our study (Figure 1). In all, 150 patients met the inclusion criteria and gave consent.

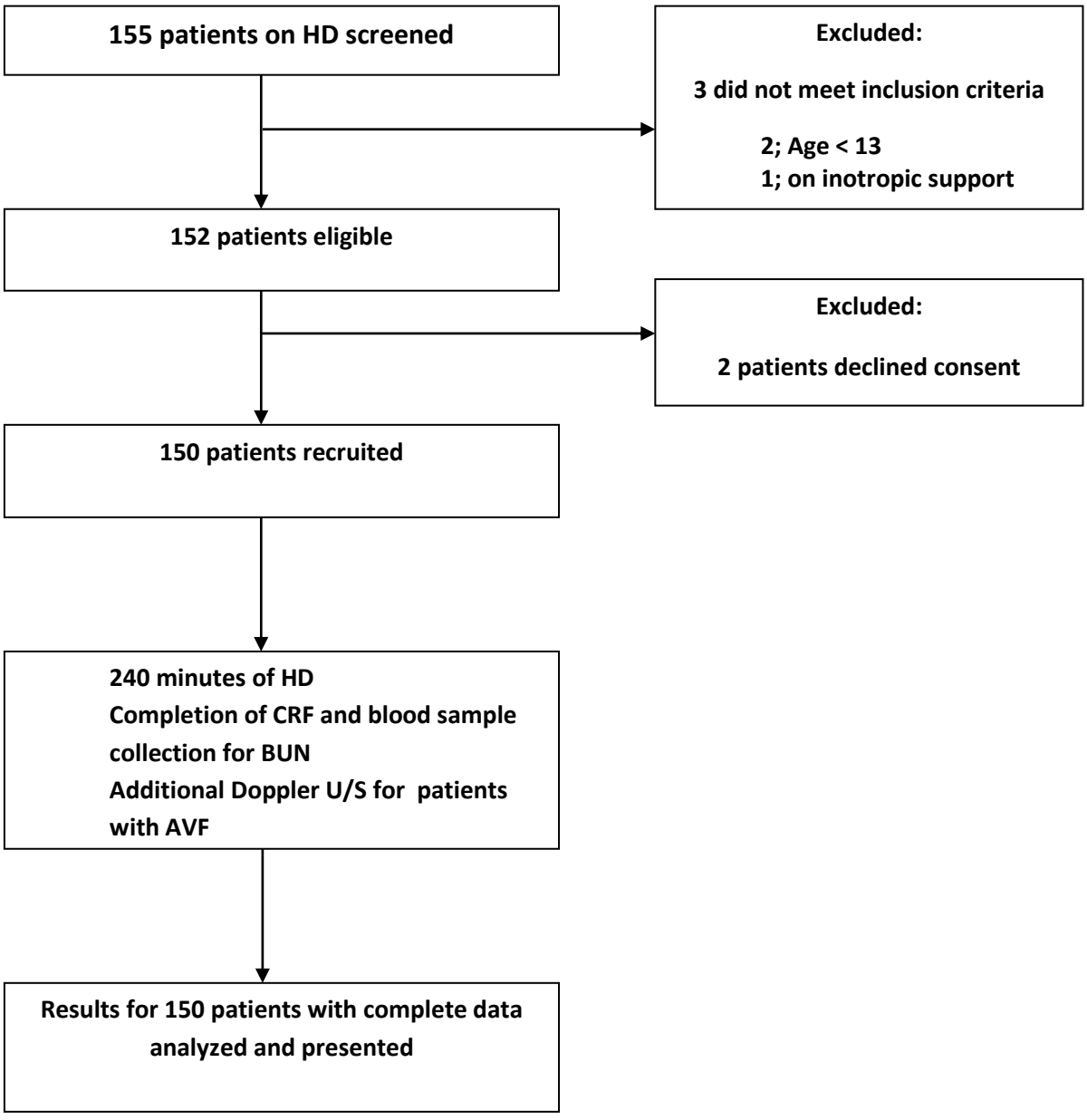

Figure 1. Patient Recruitment flow chart in the study

4.2 Demographics characteristics

The baseline demographic and clinical characteristics of the 150 patients studied were as shown in table 1 below. The male to female ratio is 1:1. Majority of the patients studied were young with 85 patients (61.3%) aged 50 years and below. There were 16 (10.7%) patients with documented multiple causes of kidney disease. Hypertension and glomerular disease were the leading underlying causes of kidney disease and comprised of 67 (44.7%) and 50 (33.3%) of patients respectively. The duration of haemodialysis ranged from 2 weeks to 19 years with a mean and median duration of 1.9 years and 10.5 months respectively. One hundred and fourteen patients (76 %) had received dialysis for less than 2 years (24 months).

Table 1.Baseline demographic and clinical characteristics of the study patients

	Characteristic	Statistics
1.	Gender	Number (%)
	Male	76(50.7)
	Female	74(49.3)
	Total	150(100)
2.	Age	Year
	Mean	43.25
	Median	43.00
	Minimum	14
	Maximum	80
3	Age clusters (year)	Number (%)
	14 -– 20	12(8.0)
	21 -– 40	58(38.7)
	41 -– 60	57(38.0)
	> 60	23(15.3)
	Total	150(100)
4	Cause of kidney disease	Number (%)
	Hypertension	67(44.7)
	Glomerulopathy	50(33.3)
	Diabetes	29(19.3)
	Others	11(7.3)
	Obstructive uropathy	9(6.0
5	Clustered duration of HD (Months)	Number (%)
	0 – 12	84(56)
	13 – 24	30(20)
	25 – 48	15(10)
	>49	21(14)

4.3 Vascular access and dialysis characteristics

4.3.1 Vascular access usage

The most common type of vascular access in use was a cuffed-tunnelled central venous catheter by 70 (46.%) individuals. The non-cuffed non-tunnelled catheters were used by 46 (30.7%) of the individuals. Arteriovenous fistulae were used by 34 (22.7%). Almost all the patients 145 (97%) were initiated on haemodialysis using a central venous haemodialysis catheter as shown in figure 2. The commonest site of insertion was the subclavian vein (87 %). Internal jugular vein had 12% while femoral vein comprised 1%. Of all the patients initiated on haemodialysis using a central venous catheter, 59% had access site changed for various reasons as shown in figure 3. Arterio-venous fistula access sites were brachiocephalic access (53%), radiocephalic (44) and one patient brachiobasilic (3%). In general arterio-venous fistula were in use for a longer duration as shown in figure 4. with the longest duration in use of 18 years.

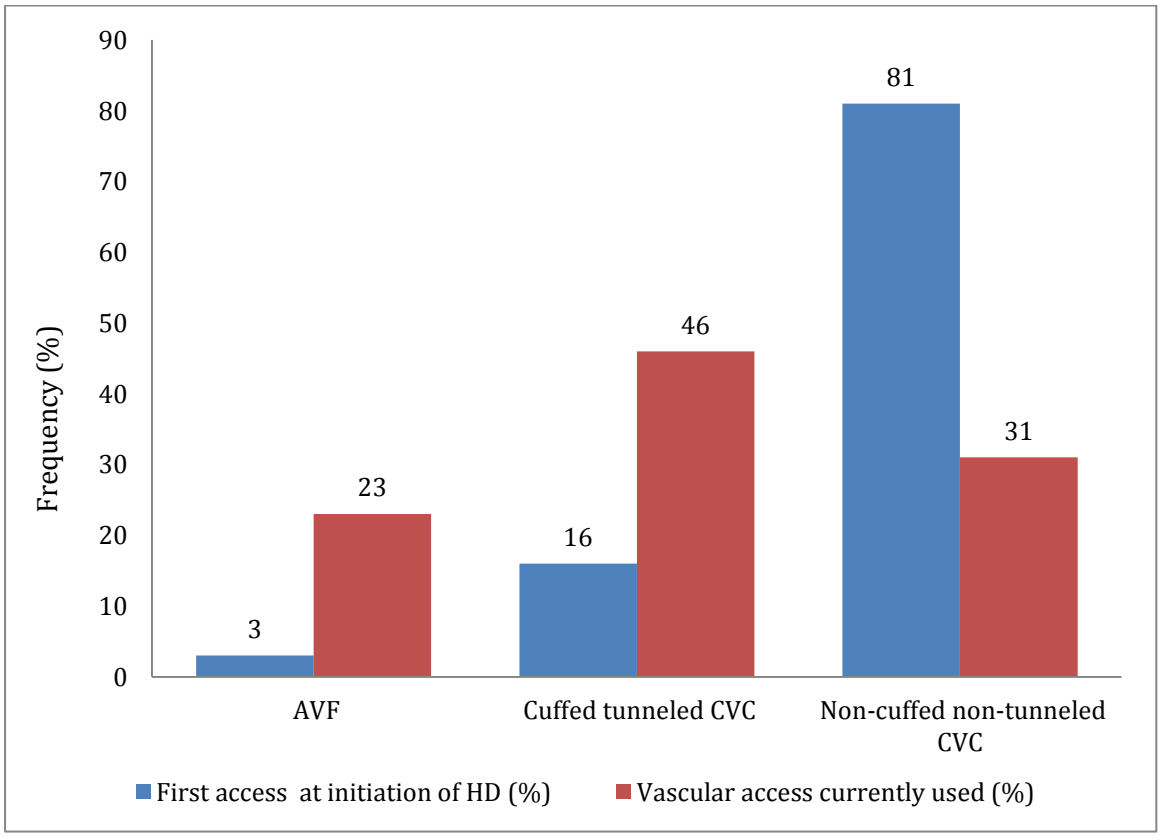

Figure 2.Comparison of vascular access type at initiation versus access type currently used during haemodialysis in the study

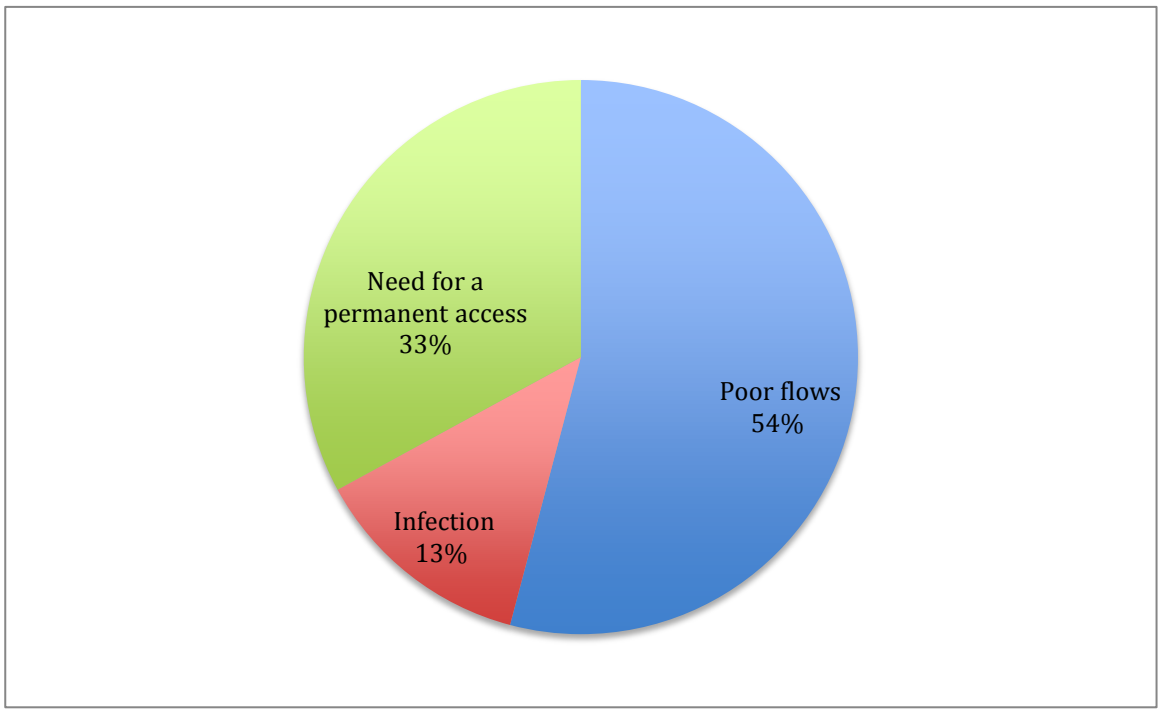

Figure 3.Reason for change of first haemodialysis vascular access in the study patients

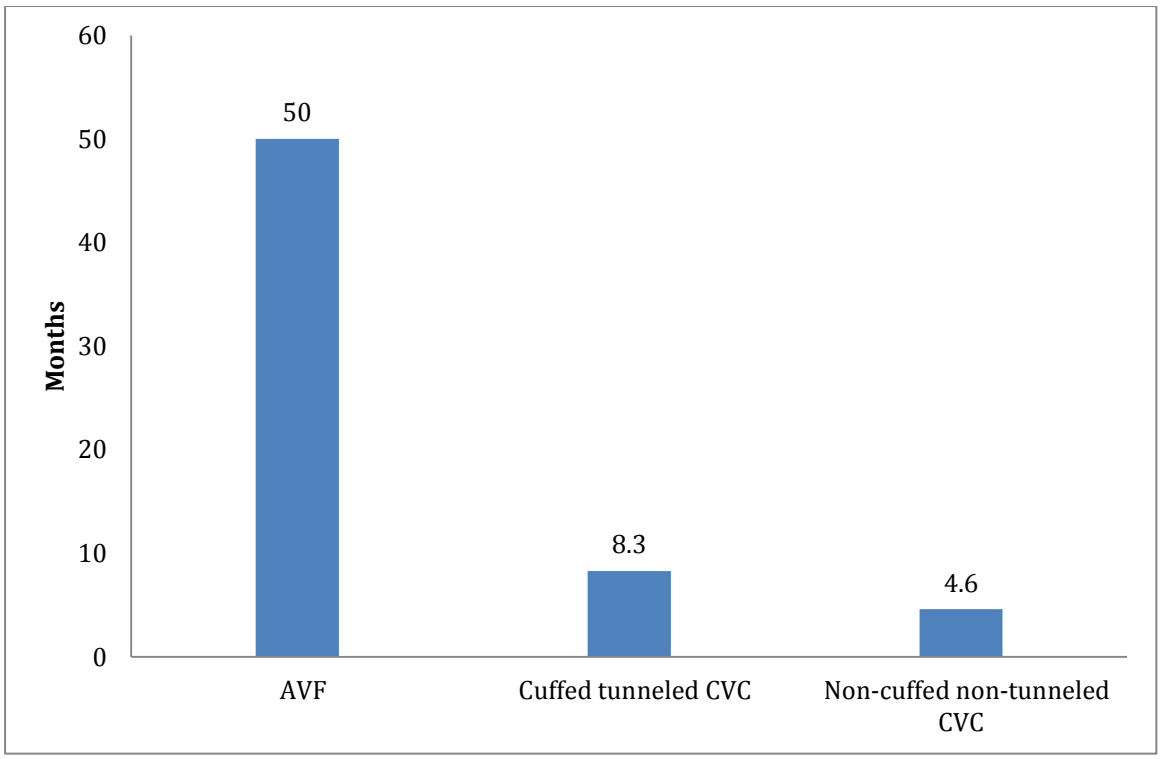

Figure 4.Mean duration in months of vascular access used in the study patients

4.3.2 Dialysis characteristics

A large proportion of patients, 128 (85.2%) dialyzed twice a week. All dialysis sessions were scheduled for 240 min; the mean blood volume processed was 76.0L. The sustained peak BFRs achieved for the group ranged from 180 to 480 ml/min with the recorded mean BFR, URR and Kt/V for the dialysis sessions for the group was 311.5 ml/min, 69.8% and 1.5 respectively. The dialysis session variables of the study population are described in Table 3.

Table 2. Characteristics of haemodialysis in the study patients

Session Variables	N =150
Weight after dialysis (Kg)*	57.4 (33 – 96)
Number of dialysis sessions a week (%)**	
i. Once a week	12.0
ii. Twice a week	85.2
iii. Irregular	2.7
Urea blood level before dialysis*	27.1 (7.8 – 58)
Urea blood level after dialysis*	8.1 (2.1 – 31)
Urea reduction ratio (%)*	69.8 (29.6 – 87.8)
Kt/V*	1.5 (0.4 – 2.5)
Peak blood flow rate (ml/min)*	368.3 (180 – 480)
Mean blood flow (ml/min)*	311.5 (175 – 373.3)
Total volume of blood processed (L)*	76.0 (42.0 - 89.6)
Ultrafiltration volume (L)*	2.3 (0.4 – 5.0)
Total dialysis session duration	Standard time of 240 minutes

* Mean (Max-Min)

** No patient had dialysis sessions more than twice a week

4.3.3 Vascular access blood flow rates, URR and Kt/V

Adequate blood flow rates as defined by a mean blood flow rate above 300 mL/min was achieved by 87.5 % , 81.7 % and 47.5% of patients using arterio-venous fistula, cuffed tunnelled CVC and non-cuffed non-tunnelled CVC respectively as shown in figure 5. Overall, patients with arterio-venous fistula achieved higher blood flow rates and better urea clearance. The differences in achieved averages among the three modalities of vascular accesses were significant as shown in Table 3. These fistulae were equally demonstrated to have good flow velocities on Doppler ultrasonography as 72% of them had blood flows above 500 mL/min as shown in figure 6.

Mean blood flow of < 250 mL/min was associated with poor dialysis dose as 87% of patients had urea reduction ratios of < 65% as shown in figure 7. On the contrary, only 15.1% of patients with a mean blood flow rate above 300 mL/min had a URR less than 65%.

The complications observed among patients with AVF on Doppler ultrasound are as described in figure 8 and included: Anastomotic stenosis in 6 patients (20.6%) of which in 4 patients (13.7%), the stenoses were haemodynamically significant. All 4 patients had stenosis of between 58% and 75% on the venous side of the anastomosis. Increased flow rates were seen in 6 patients (18.8%) of whom one patient presented with steal syndrome and two had venous hypertension. Venous aneurysms were the most common complications seen accounting for 46.9%.

The results of bivariate analysis at 0.05 level of significance using the pearson's correlation coefficient is as shown in table 3 below. There was a significant association of mean blood flow rate and Kt/V (P=0.000)

Table 3.Correlations between Kt/V, Mean blood flow rate, post dialysis weight and vascular access type in the study population

	Age in years	Kt/V	Mean blood flow rate for vascular access (ml/min)	Patient's weight after dialysis (kg)	Type of vascular access currently used
Age in years Pearson correlation Sig	1	-.293** .000	-.062 .449	.453** .000	-.126 .123
Kt/V Pearson correlation Sig	-.293** .000	1	.366** .000	-.367** .000	-.184** .024
Mean blood flow rate for vascular access (ml/min) Pearson correlation Sig	-.062 .449	. 366** .000	1	.147 .073	-.392** .000
Patient's weight after dialysis (kg) Pearson correlation Sig	.453** .000	-.367** .000	.147 .073		-.048 .559
Type of vascular access currently used Pearson correlation Sig	.419** .000	-.349** .000	-.392** .000	-.048 .559	1

**Correlation is significant at the 0.05 level (2-tailed).

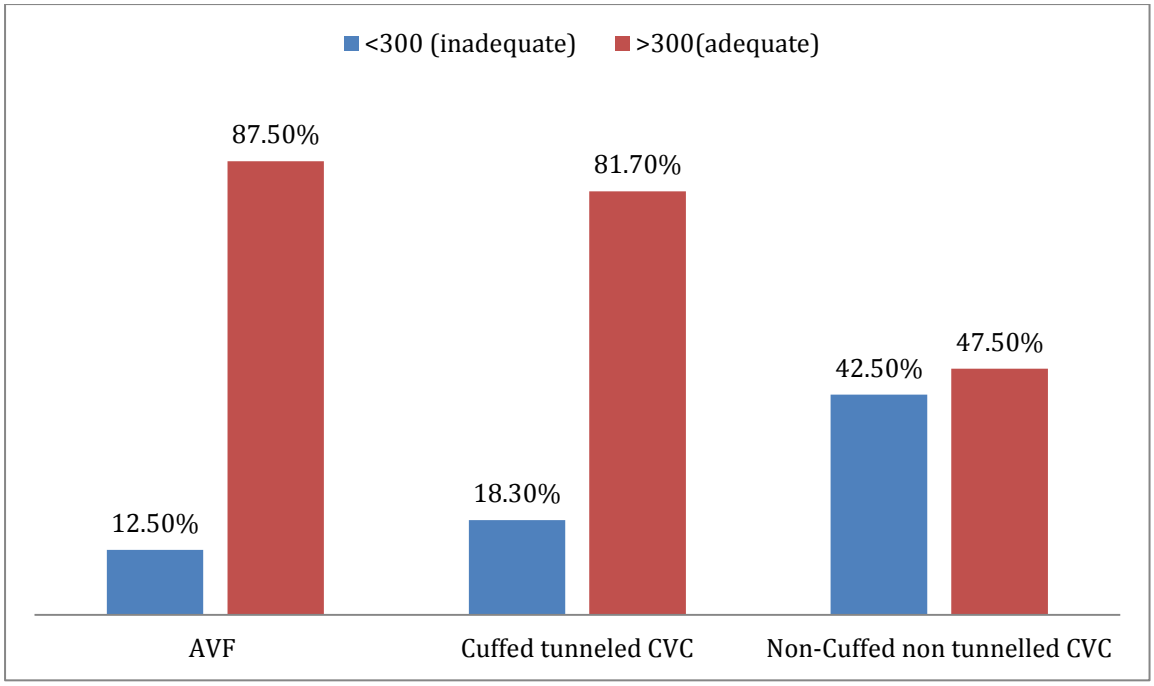

Figure 5.Adequacy of mean blood flow rates for the various vascular access types of the study patients

Table 4.Comparison of the various types of vascular access based on mean blood flow rates, URR and Kt/V in the study patients

	Arterio-venous fistula	**Cuffed tunneled CVC**	**Non-cuffed non-tunneled CVC**	**P Value****
*MBF (mL/min)	330.1	316.9	290.7	0.000
*MPF (mL/min)	399.2	376.4	336.3	0.000
Mean Kt/V	1.6	1.5	1.4	0.000
Mean URR	70.9	70.9	67.2	0.000

*MBF, Mean blood flow; MPF, mean peak flow

** P value for between vascular access types

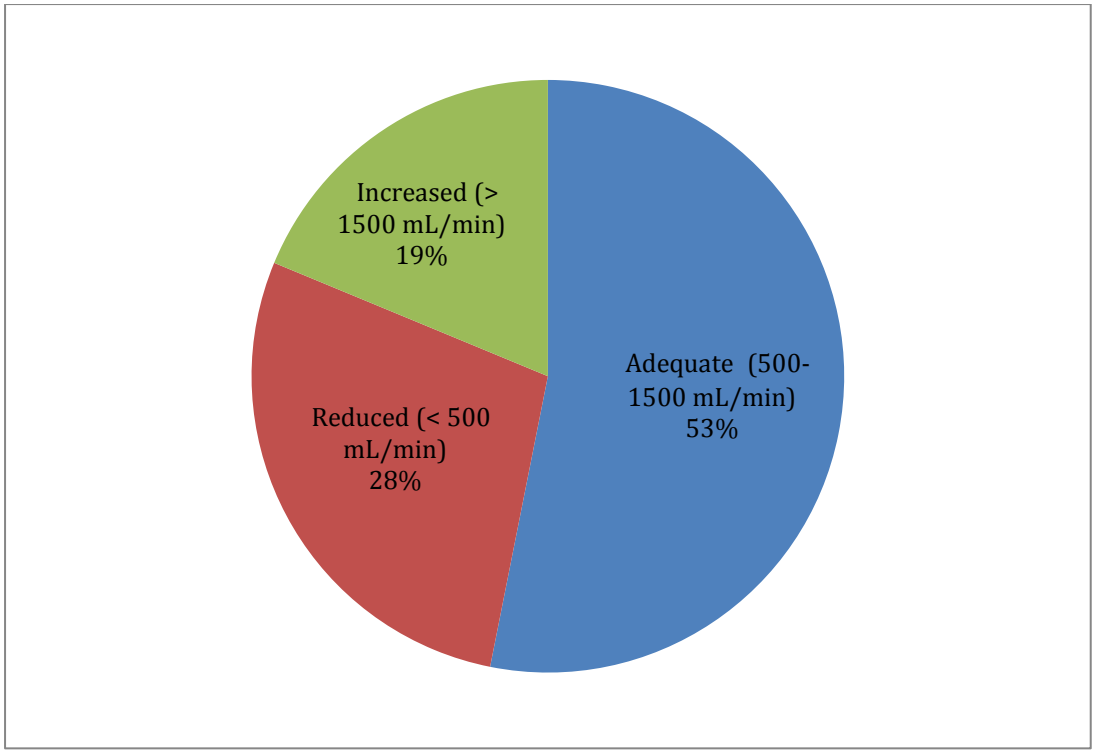

Figure 6. Blood flow rates in patients with arterio-venous fistula as assessed by Doppler ultrasound in the study (N=34)

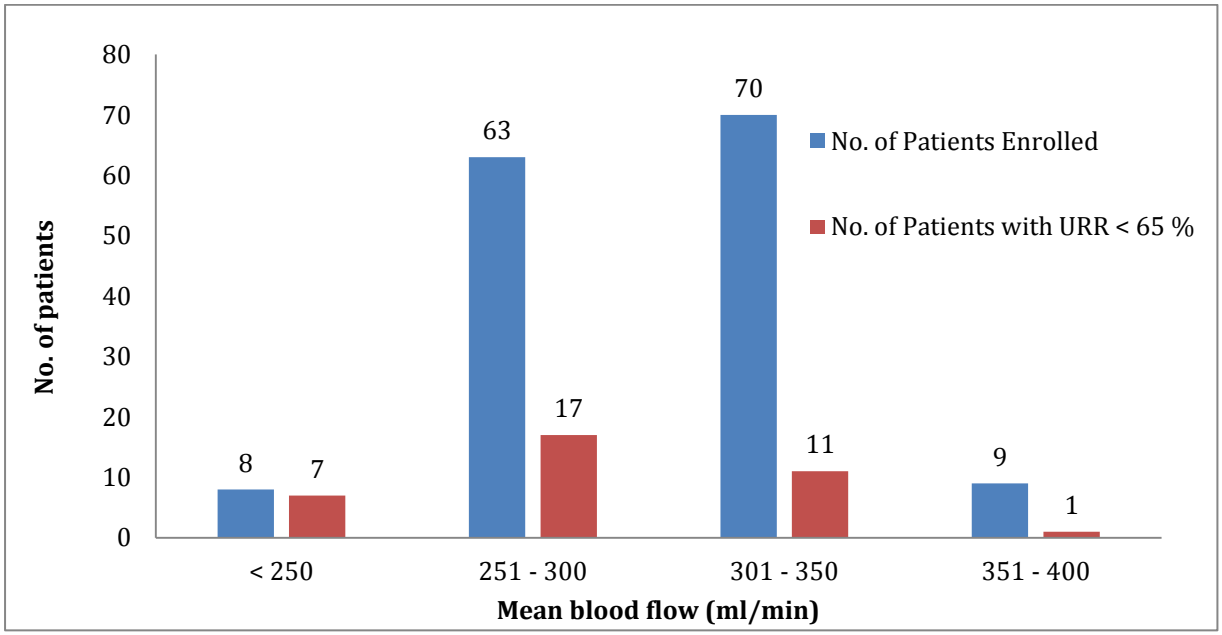

Figure 7.Comparison of mean blood flow rates among patients with URR < 65%

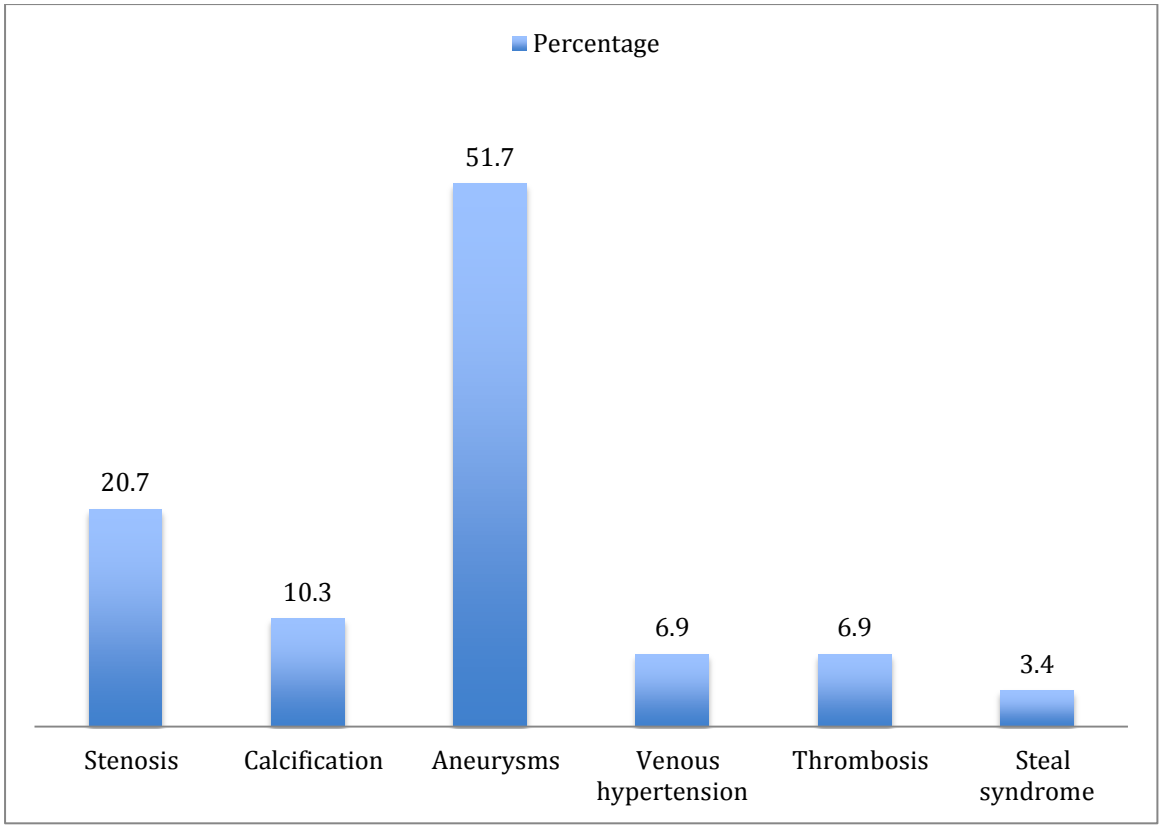

Figure 8.Complications of arterio-venous fistula as demonstrated by Doppler ultrasound in the study (N = 29)

CHAPTER FIVE: DISCUSSION

A good functioning vascular access is the cornerstone of intermittent haemodialysis, this was a cross sectional study evaluating the vascular access performance of haemodialysis patients at the KNH. Our study population was young with a mean age of 43.2 years similar to what has been reported in previous studies at The Kenyatta National Hospital (22,83). Forty seven percent of patients were less than 40 years of age. We recruited a mixed population of acute kidney injury (AKI) and CKD patients giving us a male to female ratio of 1:1.

Glomerular disease was a presumed cause of renal disease in 33.3% of the patients (n=50). Hypertension was a common presentation in many patients but its presence would be a consequence of the renal disease and unlikely to be an underlying cause. Majority of the study participants (76%) had been on haemodialysis for less than 2 years and only a smaller proportion (14%) had been on haemodialysis for more than 4 years.

There has been a shift in vascular access creation and usage at the KNH since the late 1980's where largely arterio-venous shunts (67%) and arterio-venous fistula (24%) were the predominant types of vascular access used for haemodialysis (84). Central venous catheter (CVC) usage has been on the increase over the last two decades (22). A large proportion (77.3%) of patients in our study were using CVCs for haemodialysis.

The arterio-venous fistula and the cuffed tunnelled CVC were in use in 22.7% and 46.7% of patients respectively. The cuffed tunnelled CVC has become an acceptable form of long term vascular access for haemodialysis particularly in the setting where arterio-venous fistula or grafts have not been created (6). The CVC usage in our study population was far in excess of the NKF-DOQI recommendations that CVCs be used in less than 10% of prevalent haemodialysis patients (8). This can be explained by the late presentation of patients to the nephrologist to allow for adequate access planning as has been demonstrated in a study carried out at the Kenyatta national hospital renal clinic that 43.3% of patients with chronic kidney disease first presented to a nephrologist at clinical stage 4 and 5 disease (85).

The overall mean blood flow rate was adequate at 311.5 mL/min and mean peak blood flow achieved was 368.3 mL/min. A mean blood flow rate of < 300 mL/min occurred in 25.3% of patients and this was majorly driven by the non-cuffed non tunneled CVC. Poor delivered dialysis dose as determined by URR < 65% and Kt/V < 1.2 occurred in 24% and 20.7% of

patients respectively. Almost all patients (87.5%) with mean blood flow rate < 250 mL/min had poor delivered dialysis dose. This may necessitate measures such as use of thrombolytics to improve blood flows or change of vascular access to ensure adequate dialysis.

In a multicenter study in Iran that recruited 4004 patients, the mean blood flow rate achieved was 242.9 +/- 39.2 mL/min, the percentage of patients with Kt/V < 1.2 and URR < 65% were 56.7% and 65.2% respectively (86). This emphasizes the contribution of low MBF to poor delivered dialysis dose. Of the 52.7% of patients in our study who had adequate mean blood flow rates (MBF > 301 mL/min), 15.1% had poor delivered dialysis dose. This serves as a reminder that other patient variables other than mean blood flow such as age, pre dialysis weight, time on dialysis and percentage access recirculation play a role in the delivered dialysis dose (15,87), and in our study we demonstrated significant associations with the patient variables.

The study also revealed a tendency for better performance for AVF access with a mean blood flow rate of 330.1mL/min and mean Kt/V of 1.6 as compared to cuffed tunneled haemodialysis that achieved a mean blood flow rate of 316 mL/min and Kt/V of 1.5. Similar findings were demonstrated by Canaud et al in a prospective 2 phase study where MBF for AVF versus cuffed tunneled CVC were 340 mL/min and 316 mL/min respectively with a higher Kt/V for AVF at 1.45 (88).

Moist et al in a study done in Canada among 259 patients with tunneled cuffed haemodialysis catheters, the mean blood flow rate achieved was 352.1 mL/min (15). The proportion of patients with URR < 65% was at 10.5% compared to 18% in our study population. The better catheter performance measures can be due to the routine monthly vascular access blood flow and dialysis dose measurements, as was the practice in Canada.

Majority of our vascular accesses (74.7%) achieved the minimum recommended mean blood flow rates (at least 300 mL/min) for HD (8). Non-cuffed non-tunneled CVC performed poorly as only 47.5% achieved a mean blood flow of above 300 mL/min. This compared to arterio-venous fistula and tunneled cuffed CVC where 87.5% and 81.7% respectively achieved a mean blood flow above 300 mL/min. Poor performance of the non-cuffed non-tunneled CVCs may be attributed to their geometrical design, stiffer material and position in the venous system hence some intrinsic functional limitation (88).

Our population is unique in that 85.2% of patients underwent twice-weekly haemodialysis; the remainder dialyzed for less than twice a week. Reason to pursue twice a week or less HD is mainly economical. Dialysis sessions lasted a standard time of 4 hours for all patients. The recommendations that a minimum target Kt/V of 1.2 mL/min or URR of at least 65% (67) are based on patients dialyzing for 4 hours three times a week. Therefore, based on the urea kinetics of thrice-weekly HD the recommended dosing for twice-weekly HD should be an equivalent Kt/V of 2 or more per session (70). This can only be achieved for a majority of our patients by lengthening the treatment times (89) and in a few patients by increasing the mean blood flow rate within the acceptable arterial and venous pressure limits to approach the peak blood flow rates.

Arterio-venous vascular access assessment by Doppler ultrasound in our study population revealed adequate flows in a majority of the patients (53.1%). The percentage of stenosis in our study was 20.7%. This figure is low compared to results seen in other studies at 46% and 64% (90,91). The thrombotic events in other studies ranged between 17 to 25% (92). The higher prevalence in the other studies may be explained by the recruitment of patients with already dysfunctional access during haemodialysis. Our sample size was relatively small. Two of our patients lost their AVF due to thrombosis, which is the most serious complication of Arterio-venous fistula access.

A thrombosed AVF is easily diagnosed on physical examination. It is confirmed by the absence of blood flows and visualization of a hypoechoic clot within the vessel lumen on color Doppler ultrasound scans.

The stenotic lesions were located on the venous side of the anastomosis in six patients; two patients had additional long segment stenotic lesions in the efferent vein. Aneurysms although were much more common at 46.9%, they did not interfere with the hemodynamics of the AVF. Aneurysms are usually caused by repetitive trauma from large bore needling. Intervention in such cases would be for cosmetic purposes or in instances where there is overlying skin necrosis with risk of rupture (93).

In our study we also demonstrated that a high mean blood flow rate was associated with a high delivered dialysis dose (Kt/V and URR). A high Kt/V and URR were equally associated with younger age and low body weight.

5.1 CONCLUSION

This study demonstrates that 74.7% of vascular access in use for haemodialysis at the KNH renal unit delivered adequate blood flow rates. Tunneled cuffed haemodialysis CVCs offered adequate blood flows and achieved good delivered dose of dialysis that were comparable to arterio-venous fistula. The non-tunneled non-cuffed CVCs delivered poor blood flow rates and dialysis dose and were in use for longer than the recommended duration of two weeks. On the whole, arterio-venous fistula access had better blood flow rates and delivered dialysis dose, however there is need to have routine surveillance by measuring blood flow rates and delivered dialysis dose. Interventional procedures need also to be made affordable to prevent access loss.

5.2 RECOMMENDATIONS

1. Establishment of a vascular access surveillance protocol that includes; monthly assessment of vascular access blood flow rates, Doppler ultrasound assessment of AVF surveillance as well as delivered dialysis dose monitoring.
2. Initiation of long term haemodialysis dialysis using a cuffed tunneled CVC as awaiting AVF creation.
3. Increase uptake of arterio-venous fistula access for haemodialysis through close collaboration between vascular surgeons and nephrologists

5.3 LIMITATIONS

1. Haemodialysis vascular access recirculation was not measured, this may have contributed to lower delivered dialysis dose despite seemingly good blood flow rates.
2. Blood flow measures and delivered dialysis dose were all done in a single session of dialysis.

REFERENCES

1. Jha V, Garcia G, Iseki K, *et al*. Chronic kidney disease: Global dimension and perspectives. The Lancet. 2013;382(9888):260–272.

2. Eggers PW. Has the incidence of end-stage renal disease in the USA and other countries stabilized? Current Opinion in Nephrology and Hypertension. 2011;20(3):241-245.

3. Arogundade FA, Barsoum RS. CKD prevention in Sub-Saharan Africa: a call for governmental, nongovernmental, and community support. American Journal of Kidney Diseases. 2008;51(3):515–523.

4. South African renal registry annual report 2012. Available from: http://www.sa-renalsociety.org/Registry.asp

5. Liyanage T, Ninomiya T, Jha V, *et al*. Worldwide access to treatment for end-stage kidney disease: a systematic review. Lancet. 2015;385(9981):1975–1982.

6. U.S. Renal Data System: Chapter 12: International comparisons. In: USRDS 2012 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, Bethesda, MD, National Institute of Diabetes.

7. Hakim RM, Breyer J, Ismail N, *et al*. Effects of dose of dialysis on morbidity and mortality. American Journal of Kidney Diseases. 1994;23:661–669.

8. National Kidney Foundation. K/DOQI Clinical practice guidelines for vascular access. American Journal of Kidney Diseases. 2006;48 Suppl 1:S248–S273.

9. National Kidney Foundation. K/DOQI Clinical practice guidelines for vascular access. American Journal of Kidney Diseases. 2006;48 Suppl 1:S176–S247.

10. Held PJ, Port FK, Wolfe RA, *et al*. The dose of hemodialysis and patient mortality. Kidney International. 1996;50(2):550–556.

11. Lowrie EG, Laird NM, Parker TF, *et al*. Effect of the hemodialysis prescription of patient morbidity: report from the National Cooperative Dialysis Study. The New England journal of medicine. 1981;305:1176-1181.

12. Gotch FA, Sargent JA. A mechanistic analysis of the National Cooperative Dialysis Study (NCDS). Kidney International. 1985;28(3):526–534.

13. Owen WF, Lew NL, Liu Y, *et al*. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. New England Journal of Medicine. 1993;329:1001–1006.

14. Lindsay RM, Spanner E. Adequacy of haemodialysis in the elderly. Geriatric Nephrology and Urology. 1997;7(3):147–156.

15. L. M. Moist. Relationship between Blood Flow in Central Venous Catheters and Hemodialysis Adequacy. Clinical Journal of the American Society of Nephrology. 2006;1(5):965–971.

16. Schwab SJ. Hemodialysis vascular access: the Achilles' heel remains. Kidney International. 2007;72:665–666.

17. Pantelias K, Grapsa E. Vascular access today. World Journal of Nephrology. 2012;1(3):69–78.

18. Brescia MJ, Cimino JE, Appel K, *et al*. Chronic Hemodialysis Using Venipuncture and a Surgically Created Arteriovenous Fistula. New England Journal of Medicine.1966;275(20):1089–1092.

19. Santoro A, Canova C, Freyrie A, *et al*. Vascular access for hemodialysis. Journal of Nephrology. 2006;19(3):259–264.

20. Polkinghorne KR, McDonald SP, Atkins RC, *et al*. Epidemiology of vascular access in the Australian hemodialysis population. Kidney International. 2003;64(5):1893–1902.

21. Ethier J, Mendelssohn DC, Elder SJ, *et al*. Vascular access use and outcomes: An international perspective from the dialysis outcomes and practice patterns study. Nephrology Dialysis and Transplant. 2008;23(10):3219–3226.

22. Shosi Rishad. The Adequacy of haemodialysis in end stage renal disease at KNH. MMed Dissertation, Dept of CMT, UoN, 2003.

23. Chan MR. Hemodialysis central venous catheter dysfunction. Seminars in Dialysis. 2008;21(6):516–521.

24. Griffiths RI, Newsome BB, Block G, *et al*. Patterns of Hemodialysis Catheter Dysfunction Defined According to National Kidney Foundation Guidelines As Blood Flow <300 mL/min. International Journal of Nephrology. 2011;2011:1-7.

25. Moss AH, Vasilakis C, Holley JL, *et al*. Use of a silicone dual-lumen catheter with a Dacron cuff as a long-term vascular access for hemodialysis patients. American Journal of Kidney Diseases. 1990;16(3):211–215.

26. Gibson SP, Mosquera D. Five years experience with the Quinton Permcath for vascular access. Nephrology Dialysis and Transplant. 1991;6(4):269–274.

27. Dinwiddie LC. Managing catheter dysfunction for better patient outcomes: a team approach. Nephrology Nurses Journal. 2004;31(6):653–660.

28. Janne d'Othée B, Tham JC, Sheiman RG. Restoration of patency in failing tunneled hemodialysis catheters: a comparison of catheter exchange, exchange and balloon disruption of the fibrin sheath, and femoral stripping. Journal of Vascular and Interventional Radiology. 2006;17(6):1011–1015.

29. Moureau N, Poole S, Murdock MA, *et al*. Central venous catheters in home infusion care: outcomes analysis in 50,470 patients. Journal of Vascular and Interventional Radiology. 2002;13(10):1009–1016.

30. Weijmer M, van den Dorpel M, Van de Ven P, *et al*. Randomized, clinical trial comparison of trisodium citrate 30% and heparin as catheter-locking solution in hemodialysis patients. Journal of American Society of Nephrology. 2005;16(9):2769–2777.

31. Vats HS. Complications of Catheters : Tunneled and Nontunneled. Advvances in Chronic Kidney Disease. 2012;19(3):188–194.

32. Virchow R. Cellular pathology as based upon physiological and pathological histology. Philadelphia: J.B. lippincott; 1863.

33. Suojanen JN, Brophy DP, Nasser I. Thrombus on indwelling central venous catheters: the histopathology of "Fibrin sheaths". Cardiovascular and Interventional Radiology. 2000;23(3):194–197.

34. Vaudaux P, Pittet D, Haeberli A, *et al*. Fibronectin is more active than fibrin or fibrinogen in promoting Staphylococcus aureus adherence to inserted intravascular catheters. Journal of Infectious Disease. 1993;167(3):633–641.

35. Mehall JR, Saltzman DA, Jackson RJ, *et al*. Fibrin sheath enhances central venous catheter infection. Critical Care Medicine. 2002;30(4):908–912.

36. Faintuch S, Salazar GM. Malfunction of dialysis catheters: management of fibrin sheath and related problems. Techniques in Vascular and Interventional Radiology. 2008;11(3):195–200.

37. Roy-Chaudhury P, Sukhatme VP, Cheung AK. Hemodialysis vascular access dysfunction: a cellular and molecular viewpoint. Journal of American Society of Nephrology. 2006;17(4):1112–1127.

38. Beathard GA. The treatment of vascular access graft dysfunction: a nephrologist's view and experience. Advances in Renal Replacement Therapy. 1994;1(2):131–147.

39. Windus DW. Permanent vascular access: a nephrologist's view. American Journal of Kidney Diseases. 1993;21(5):457–471.

40. Fan PY, Schwab SJ. Vascular access: concepts for the 1990s. Journal of the American Society of Nephrology. 1992;3(1):1–11.

41. Weiss MF, Scivittaro V, Anderson JM. Oxidative stress and increased expression of growth factors in lesions of failed hemodialysis access. American Journal of Kidney Diseases. 2001;37(5):970–980.

42. Stracke S, Konner K, Köstlin I, *et al*. Increased expression of TGF-beta1 and IGF-I in inflammatory stenotic lesions of hemodialysis fistulas. Kidney International. 2002;61(3):1011–1019.

43. Rekhter MD, Gordon D. Active proliferation of different cell types, including lymphocytes, in human atherosclerotic plaques. American Journal of Pathology. 1995;147(3):668–677.

44. Roy-Chaudhury P, Kelly BS, Miller MA, *et al*. Venous neointimal hyperplasia in polytetrafluoroethylene dialysis grafts. Kidney International. 2001;59(6):2325–2334.

45. Paszkowiak JJ, Dardik A. Arterial wall shear stress: observations from the bench to the bedside. Vascular and Endovascular Surgery.2003;37(1):47–57.

46. Remuzzi A, Ene-Iordache B, Mosconi L, *et al*. Radial artery wall shear stress evaluation in patients with arteriovenous fistula for hemodialysis access. Biorheology. 2003;40(1-3):423–430.

47. Miller PE, Tolwani A, Luscy CP, *et al*. Predictors of adequacy of arteriovenous fistulas in hemodialysis patients. Kidney International. 1999;56(1):275–280.

48. Mezzano D, Pais EO, Aranda E, *et al*. Inflammation, not hyperhomocysteinemia, is related to oxidative stress and hemostatic and endothelial dysfunction in uremia. Kidney International. 2001;60(5):1844–1850.

49. Roy-Chaudhury P, Kelly BS, Zhang J, *et al*. Hemodialysis vascular access dysfunction: from pathophysiology to novel therapies. Blood Purification. 2003;21(1):99–110.

50. Himmelfarb J, Couper L. Dipyridamole inhibits PDGF- and bFGF-induced vascular smooth muscle cell proliferation. Kidney International. 1997;52(6):1671–1677.

51. Vachharajani TJ, Carolina N. Diagnosis of Arteriovenous Fistula Dysfunction. Seminars in Dialysis. 2012;25(4):445–450.

52. May RE, Himmelfarb J, Yenicesu M, *et al*. Predictive measures of vascular access thrombosis: a prospective study. Kidney International. 1997;52(6):1656–1662.

53. Bay WH, Henry ML, Lazarus JM, *et al*. Predicting hemodialysis access failure with color flow Doppler ultrasound. American Journal of Nephrology. 1998;18(4):296–304.

54. Basseau F, Grenier N, Trillaud H, *et al*. Volume flow measurement in hemodialysis shunts using time-domain correlation. Journal of Ultrasound in Medicine. 1999;18(3):177–183.

55. Winkler AJ, Wu J. Correction of intrinsic spectral broadening errors in Doppler peak velocity measurements made with phased sector and linear array transducers. Ultrasound in Medicine and Biology. 1995;21(8):1029–1035.

56. Stewart SF. Effects of transducer, velocity, Doppler angle, and instrument settings on the accuracy of color Doppler ultrasound. Ultrasound in Medicine and Biology. 2001;27(4):551–564.

57. Xue JL, Dahl D, Ebben JP, *et al*. The association of initial hemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. American Journal of Kidney Diseases. 2003;42(5):1013–1019.

58. Pastan S, Soucie JM, McClellan WM. Vascular access and increased risk of death among hemodialysis patients. Kidney International. 2002;62(2):620–626.

59. Dhingra RK, Young EW, Hulbert-Shearon TE, *et al*. Type of vascular access and mortality in U.S. hemodialysis patients. Kidney International. 2001;60(4):1443–1451.

60. Lacson E, Lazarus JM, Himmelfarb J, *et al*. Balancing Fistula First with Catheters Last. American Journal of Kidney Diseases. 2007;50(3):379–395.

61. Allon M, Daugirdas J, Depner TA, *et al*. Effect of change in vascular access on patient mortality in hemodialysis patients. American Journal of Kidney Diseases. 2006;47(3):469–477.

62. Astor BC, Eustace J A, Powe NR, *et al*. Type of vascular access and survival among incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study. Journal of the American Society of Nephrology. 2005;16(5):1449–1455.

63. Di Iorio BR, Bellizzi V, Cillo N, *et al*. Vascular access for hemodialysis: the impact on morbidity and mortality. Journal of Nephrology. 2004;17(1):19–25.

64. Rajabi-Jaghargh E, Banerjee RK. Combined functional and anatomical diagnostic endpoints for assessing arteriovenous fistula dysfunction. World Journal of Nephrology. 2015;4(1):6–18.

65. Lok CE, Foley R. Vascular access morbidity and mortality: trends of the last decade. Clinical Journal of the American Society of Nephrology. 2013;8(7):1213–1219.

66. Daugirdas JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: An analysis of error. Journal of the American Society of Nephrology. 1993;18(4):1205–1213.

67. Hemodialysis Adequacy 2006 Work Group. Clinical practice guidelines for hemodialysis adequacy, update 2006. American Journal of Kidney Diseases. 2006;48(Suppl 1):S2-90.

68. Couchoud C, Kooman J, Finne P, *et al*. From registry data collection to international comparisons: examples of haemodialysis duration and frequency. Nephrology Dialysis and Transplantation. 2009;24(1):217–224.

69. Hanson JA, Hulbert-Shearon TE, Ojo AO, *et al*. Prescription of twice-weekly hemodialysis in the USA. American Journal of Nephrology. 1999;19(6):625–633.

70. Panaput T, Thinkhamrop B, Domrongkitchaiporn S, *et al*. Dialysis dose and risk factors for death among ESRD patients treated with twice-weekly hemodialysis: a prospective cohort study. Blood Purification. 2014;38(3-4):253–262.

71. Bouchouareb D, Saveanu A, Bartoli JM, *et al*. A New Approach to Evaluate Vascular Access in HemodialysisPatients. Artificial Organs. 1998;22(7):591–595.

72. Tonelli M. Monitoring and maintenance of arteriovenous fistulae and graft function in haemodialysis patients. Current Opinion in Nephrology and Hypertension. 2004;13(6):655–660.

73. Neyra NR, Ikizler TA, May RE, *et al*. Change in access blood flow over time predicts vascular access thrombosis. Kidney International. 1998;54(5):1714–1719.

74. Al-Ghonaim M, Manns BJ, Hirsch DJ, *et al*. Relation between access blood flow and mortality in chronic hemodialysis patients. Clinical Journal of American Society of Nephrology. 2008;3(2):387–391.

75. Ward RA, Idoux JW, Hamdan H, *et al*. Dialysate flow rate and delivered Kt/Vurea for dialyzers with enhanced dialysate flow distribution. Clinical Journal of the American Society of Nephrology. 2011;6(9):2235–2239.

76. Palmer BF. Dialysis as treatment of End-Stage Renal Disease. Volume 5, Chapter six: The Dialysis Prescription and the Urea Modeling. 1998. illustrated Edition.

77. Chazot C, Jean G. The advantages and challenges of increasing the duration and frequency of maintenance dialysis sessions. Nature Clinical Practice Nephrology. 2009;5(1):34–44.

78. Charra B, Terrat JC, Vanel T, *et al*. Long thrice weekly hemodialysis: the Tassin experience. International Journal of Artificial Organs. 2004;27(4):265–283.

79. Saran R, Bragg-Gresham JL, Levin NW, *et al*. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. Kidney International. 2006;69(7):1222–1228.

80. Lowrie EG, Laird NM, Parker TF, *et al.* Effect of the hemodialysis prescription of patient morbidity: report from the National Cooperative Dialysis Study. New England Journal of Medicine. 1981;305(20):1176–1181.

81. Garabed E, Gerald JB, Alfred K, Cheung, *et al*. Effect of Dialysis Dose and Membrane Flux in Maintenance Hemodialysis. New England Journal of Medicine. 2002;347:2010–2019.

82. Daniel W.W. Biostatistics: A Foundation for Analysis in Health Sciences. 7th ed. New York: John Wiley & Sons; 1999.

83. Soki.K.B. An echocardiographic evaluation of pulmonary pressures in chronic haemodialysis patients at KNH. MMed Dissertation, Dept of CMT, UoN,2015.

84. Ngugi PN, McLigeyo SO, Kayima JK *et al*. Vascular access for haemodialysis. East African Medical Journal. 1991;68(6):442–447.

85. Kinango D. Prevalence and factors associated with late presentation of patients with chronic kidney disease to the nephrologist at the Kenyatta national hospital renal clinic. MMed Dissertation, Dept of CMT, UoN, 2009.

86. Amini M, Aghighi M, Masoudkabir F *et al*. Hemodialysis adequacy and treatment in Iranian patients: a national multicenter study. Iran Journal of Kidney Disease. 2011;5(2):103–109.

87. Depner T a. Hemodialysis adequacy: basic essentials and practical points for the nephrologist in training. Hemodialysis International. 2005;9(3):241–254.

88. Canaud B. Effective flow performances and dialysis doses delivered with permanent catheters: a 24-month comparative study of permanent catheters versus arterio-venous vascular accesses. Nephrology Dialysis in Transplant. 2002;17(7):1286–1292.

89. Bieber B, Qian J, Anand S *et al.* Two-times weekly hemodialysis in China: frequency, associated patient and treatment characteristics and Quality of Life in the China Dialysis Outcomes and Practice Patterns study. Nephrology Dialysis in Transplant. 2014;29(9):1770–1777.

90. Moghazy KM. Value of color Doppler sonography in the assessment of hemodialysis access dysfunction. Saudi Journal of Kidney Disialysis and Transplantation. 2009;20(1):35–43.

91. Pietura R, Janczarek M, Zaluska W *et al*. Colour Doppler ultrasound assessment of well-functioning mature arteriovenous fistulas for haemodialysis access. European Journal of Radiology. 2005;55(1):113–119.

92. Stolic R. Most important chronic complications of arteriovenous fistulas for hemodialysis. Medical Principles and Practice. 2013. p. 220–228.

93. Kumbar L. Complications of Arteriovenous Fistulae : Beyond. Advances in Chronic Kidney Disease. 2012;19(3):195–201.

APPENDICES

APPENDIX I: PATIENT CONSENT EXPLANATION FORM

Information sheet

Research Title: Haemodialysis vascular access function in End Stage Renal Disease patients at Kenyatta National Hospital

I am Dr. Ndinya Florentius, currently studying for a Masters degree in Internal medicine at University of Nairobi. I am conducting a research project to assess the functioning of hemodialysis vascular access of patients undergoing dialysis at the Kenyatta National Hospital for which I request your participation.

Why have I been invited to take part?

Vascular access (catheter or fistula) is important for the haemodialysis procedure. It should be able to provide an adequate amount of blood flow for you to achieve good dialysis. We intend to assess how much blood flow your access can deliver and if at the end of the dialysis session the treatment was adequate. This information will help us put in place measures that would help us detect early poorly functioning vascular access and intervene to ensure quality dialysis services.

How do I benefit from the study?

The immediate benefits of this study will be to give information on the best type of access and the functioning of your vascular access and as well as the quality of the dialysis session. Participants will have a clinical examination, urea levels before and after the dialysis session and an ultrasound scan for those with fistula done free of charge when they come for their regular dialysis sessions. All of this information will be availed to the patient and relayed to his / her doctor to ensure the patient receives the best care. The patients will however not be compensated with money.

Risks of participation

There are minimal risks involved in clinical assessment and laboratory tests done in this study. Blood sample will be drawn from the dialysis tubing and no direct prick will be made. Only a total of one teaspoon of blood will be drawn from you. The Doppler ultrasound is non-invasive and not painful. These investigations shall be done during your regular dialysis visit though you may have to spend some extra hours in the renal unit after dialysis for the ultrasound to be done.

Do I have to take part?

It is up to you to decide whether or not to take part, taking part is voluntary. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. You will still receive all treatment that you should get even without participating in the study.

What would I have to do?

If you consent for the study, you will be expected to give information about yourself and the illness you have. Your weight and blood pressure will be taken and your vascular access examined. You will also have blood drawn for investigations and if you have a fistula have a Doppler ultrasound done.

Confidentiality

The medical records and data collected for this study will only be accessible to authorized persons. This will minimize accidental disclosure to any unauthorized personnel. Results will only be made available to the patient and his/her primary care provider.

What happens to the information that is collected?

All details that can identify you will be removed before storing the data. The data will then be analyzed to help us build an understanding of the burden of haemodialysis vascular access dysfunction as well as the impact on the dialysis session at the Kenyatta National Hospital and improve on the management of patients undergoing haemodialysis. The data will be destroyed after successful completion of the study.

Thank you for taking the time to read this information sheet.

KIAMBATISHO IFOMU YA MAELEZO KUHUSU UTAFITI HUU

Mada:Njia za kuosha damu {sindano kubwa mishipani kuu au mishipa miundo (fistula)}kwenye wagonjwa wenye magonjwa ya figo katika Hospitali Kuu ya Kenyatta.

Mimi ninaitwa Daktari Florentius Ndinya.Ninasomea shahada ya juu katika matibabu ya watu wazima katika Chuo Kikuu ya Nairobi.Ninafanya utafiti kutambua uwezo wa njia za kuosha damu, kuosha damu ya wagonjwa wenye magonjwa ya figo vyema.Ninaomba ujiunge na utafiti huu.

Je, nimealikwa kwa nini?

Njia zitumiwazo kuosha damu (sindano kubwa mishipani au mishipa miundo),ni muhimu sana ili matibabu ya kuosha damu yafaulu.Njia hizi zinapaswa kutoa kiasi ya kutosha ya damu ili uchafu mwingi kwenye damu iondolowe vyema.Mimi na watafiti wenzangu tunataka kuangalia kiasi ya damu njia yako ya kuoshewa damu inasafirisha kwenye mashini ya kuosha damu. Pia tunataka kutambua kama ufikapo mwisho wa wakati wako kwenye mashini ya kuosha damu,matibabu hiyo itakuwa imeondoa uchafu mwilini wa kutosha.Habari hii itatusaidia kuweka mikakati ya mapema kutambua wagonjwa ambao njia zao za kuosha damu hazifanyi kazi vyema na kuchukua hatua za haraka kuhakikisha matibabu ya kuosha damu inaendelea vyema.

Je, nitanufaika kivipi kwa kujiunga na utafiti huu?

Manufaa ya kuingia utafiti huu yanaanzia kupata mawaidha kuhusu njia bora ya kuoshewa damu. Pia utajua ubora wa njia yako ya kuoshewa damu na hivyo basi,ubora wa matibabu yako ya kuosha damu.Isitoshe,wanaoingia utafiti huu watapimwa miili yao kikamilifu na wapimwe viwango vyao vya urea (uchafu wa mwili) kabla ya kuingia kwenye mashini ya kuosha damu na baada ya kuoshwa damu.Zaidi ya hayo, watu wote wanaotumia mishipa miundo kuosha damu watapigwa picha wakija wakati wao wa kawaida kuoshwa damu.Maelezo, vipimo vyote vya maabara na picha hayalipishwi.Matokeo ya kupimwa na picha yatawasilishwa kwa mgonjwa pamoja na daktari wake ili kuhakikisha wagonjwa wanapata matibabu bora.Wanaojiunga na utafiti huu hawatapewa pesa.

Je ,kuna athari za kujiunga na utafiti?

Athari zilizopo ni kidogo sana na zinatokana na vipimo vya damu vitakavyofanywa kwenye utafiti huu.Damu itakayotumiwa kufanya vipimo itatolewa kwenye mipira inayotoa damu mwilini kutoka njia yako ya kuoshewa damu,mwili wako hautadungwa kutolewa damu.Kiasi ya damu itakayotolewa ni kijiko cha chai pekee yake.Picha ya mishipa sio kama sindano,hamna uchungu wa kudungwa.Vipimo hivi vitafanywa wakati wako wa kawaida wa kuoshwa damu.Wagonjwa wenye mishipa miundo watalazimika kusubiri kidogo baada ya kuoshwa damu ili wapigwe picha.

Je,ni lazima kujiunga na utafiti huu?

La!Uamuzi kuingia utafiti huu ni wako,unaingia kwa hiari yako.Ukiamua kujiunga na utafiti huu, utapewa fomu hii ya maelezo na kusaini kartasi ya makubaliano.Ukiingia utafiti huu,una uhuru wa kutoka wakati wowote bila ya kutupatia sababu zako za kutoka.Baado utaendelea kupata matibabu yako yote ya kawaida hata bila kuendelea na utafiti huu.

Nikitaka kujiunga na utafiti huu,nitahitajika kufanya nini?

Mwanzo,utatupa maelezo kidogo kukuhusu wewe binafsi pamoja na maelezo zaidi kuhusu ugonjwa wako wa figo.Baada ya hapo utapimwa mwili na utatolewa damu ili vipimo zaidi ya maabara yafanywe.Kama unatumia mshipa muundo,itapigwa picha ya kutambua kama inatoa damu sawasawa.

Je,rekodi zangu binafsi na matokeo ya vipimo vyangu yatawekwa siri?

Rekodi zako za matibabu na matokeo yote yatakayojulikana kutoka utafiti huu yataangaliwa na watafiti walioidhinishwa pekee yao.Tunatumaini kwamba kufanya hivi itapunguza uwezekano ya watu nje ya utafiti huu kutambua mambo yako binafsi.Matokeo yatapeanwa kwa mgonjwa binafsi ama kwa mtu yule wa karibu aliyeidhinishwa kupokea matokeo ya matibabu yake.

Habari yote itakayotambuliwa kunihusu mimi na wagonjwa wengine itafanywaje?

Vitambulishi vyako vyote (nambari ya rekodi yako,nambari ya simu na vinginevyo) vitaondolewa kabla ya ripoti yako kuhifadhiwa. Ripoti yako,pamoja na ya wagonjwa wengine, itaangaliwa kwa undani - ili tubaini ni wagonjwa wangapi wenye njia za kuoshea damu ambazo hazifanyi kazi vyema.Pia ripoti yako itatusaidia kujua njia bora za kuboresha matibabu ya kuosha damu ya wagonjwa wa figo katika hospitali kuu ya Kenyatta.Ripoti hizi zote zitatupwa baada ya kumaliza utafiti huu.

Asanta kwa kuchukua muda wako kusoma maelezo haya.

APPENDIX II: PATIENT CONSENT FORM

I, _____, have read and fully understood the explanation given to me regarding this study. All my questions have been answered satisfactorily by the investigators. I hereby consent to participation in this study.

Signed: ---------- Patient

Witness: ---------- (Principal Investigator or Research assistant)

Date: ----------

CONTACTS

For further information, you may contact any of the following:

1. Dr. Ndinya Florentius. (Principal investigator)

P.O Box 19882 – 00100, Nairobi.

Tel: 0722 449056

2. Professor A. N. Guantai,

Chairman of Kenyatta National Hospital/University of Nairobi Ethics and Research Committee,

P.O Box 20723, Nairobi.

Tel 020-2726300, extension 44102.

KIAMBATISHO II: KARATASI YA MAKUBALIANO YA WATU WAZIMA

Mimi,…….. ,nimesoma na kukubaliana na maelezo nimepewa kuhusu utafiti huu.Maswali yangu yote yamejibiwa kwa ukamilifu na Daktari Ndinya na watafiti wenzake.

Nimekubali kuingia utafiti huu.

Sahihi ……. (mgonjwa)

Shahidi ……. (mtafiti mkuu ama msaidizi wake)

Tarehe ……

Wanaohusika:

Kwa maelezo zaidi ,unaombwa uwasiliane na watu wafuatao

1. **Daktari Florentius Ndinya-mtafiti mkuu**
   Sanduku la posta (S.L.P.) 19882-00100
   Simu 0722449056.

2. **Profesa A.N. Guantai**
   Mkurugenzi wa Idhaa ya Uadilifu kwenye utafiti,
   Hospitali Kuu ya Kenyatta,
   S.L.P. 20723,Nairobi
   Simu ya ofisi:020-2726300-ugani 44102

APPENDIX III: PATIENT ASSENT FORM

I, _____, have read and fully understood the explanation given to me regarding this study. All my questions have been answered satisfactorily by the investigators. I hereby assent to participation in this study.

Signed (Patient): _____

Parent / guardian: _____

Witness (PI / Research assistant): _____

Date: _____

CONTACTS:

For further information, you may contact any of the following:

1. Dr. Ndinya Florentius (Principal investigator)

P.O Box 19882 – 00100, Nairobi.

Tel 0722 449056

2. Professor A. N. Guantai,

Chairman of Kenyatta National Hospital/University of Nairobi Ethics and Research Committee,

P.O Box 20723, Nairobi.

Tel 020-2726300, extension 44102.

KIAMBATISHO III: FOMU YA MAKUBALIANO KWA WATOTO/WASIOWEZA KUPEANA RUHUSA WENYEWE

Mimi ,…….. ,nimesoma na kuelewamaelezo niliyopewa kuhusu utafiti huu.Maswali yanhgu yote yamejibiwa kikamilifu na watafiti.Ninakubali kwa niaba ya mgonjwa ninayesimamia kujiunga na utafiti huu

Sahihi (Mgonjwa): ……..

Mzazi / Mlezi : ……

Shahidi : …….. (mtafiti mkuu/mtafiti mkuu)

Tarehe : ……. Wanaohusika:

Kwa maelezo zaidi ,unaombwa uwasiliane na watu wafuatao

1. **Daktari Florentius Ndinya-mtafiti mkuu**
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APPENDIX IV: METHOD FOR PRE-DIALYSIS BUN SAMPLING

Samples will be drawn by the PI or a trained assistant under aseptic technique before initiation of haemodialysis to avoid reflecting the impact of dialysis on the sample as well as dilution from saline and heparin.

When using an arteriovenous fistula

1. Blood sample is obtained from the arterial needle prior to connecting the arterial blood tubing or flushing the needle. Ensure there is no saline and/or heparin in the arterial needle and tubing prior to drawing the sample for BUN measurement.

When using a venous catheter

1. A 5ml syringe is used to draw the heparin lock solution plus blood to the total volume of the syringe, this is to be discarded
2. With a new syringe a sample for BUN measurement will be withdrawn

Haemodialysis will be completed as per KNH renal unit protocol

APPENDIX V: POST DIALYSIS BUN SAMPLING.

Recommended method is the slow flow method

1. At the completion of haemodialysis, the PI or a trained assistant will turn off the dialysate flow and decrease the ultra filtration rate (UFR) to 50ml/hr, to the lowest transmembrane pressure (TMP)/UFR setting, or off.

2. The blood flow will be decreased to 100ml/min for 15 seconds. To prevent pump shut off as the blood flow is reduced it may be necessary to manually adjust the venous pressure limits downward.

3. With the blood pump still running at 100ml/min blood for BUN sampling will be drawn at the arterial port closest to the patient.

4. The blood pump will then be stopped and the patient disconnection done as per KNH renal protocol.

APPENDIX VI: CASE REPORT FORM.

STUDY ID NO. …….. DATE…….

SECTION I: DEMOGRAPHICS.

1. Age (years)……
2. Gender Male ☐ Female ☐
3. Cause of kidney disease?
   a)Hypertension b)Obstructive uropathy
   c)Diabetes d)Glomerulopathy e)Others (specify)…….
4. Duration of haemodialysis?
   a)< 6 months b) 6 – 12 months c)1 – 2 years d) 2 – 5 years e) > 5 years
5. Type of vascular access currently used
   a)AV fistula b)Permanent catheter c) Temporary catheter
6. Site of vascular access currently used (for patients with CVC)
   a) subclavian vein b) internal jugular c) femoral
7. Duration of current vascular access used.
   a)< 6 months b) 6 – 12 months c)1 – 2 years d) 2 – 5 years e) > 5 years
8. Previous vascular access type, site and reason for change of access

Type	*site	#Duration of use	$Reason for change
1.			
2.			
3.			

*Site a) subclavian vein b) internal jugular c) femoral

#Duration of use a)< 6 months b) 6 – 12 months c)1 – 2 d) 2 – 5 years e) > 5 years

$Reason for change of access a) poor flows b) infection c) access not working d) need for a permanent access

SECTION II: CLINICAL PARAMETER.

1. Time of dialysis session (24 hour clock)……
2. Patients weight (Kg) a) Before dialysis …….. b) After dialysis …….
3. Dialyzer type……
4. Number of hemodialysis sessions per week: a) 1 b) 2 c) 3 d) irregular
5. Urea level (mmol/l) a) Before dialysis ……..b) Post Dialysis ……..
6. URR (%) ……
7. Kt/V …….
8. Peak blood flow rate for the vascular access (ml/min) …….
9. Mean blood flow rate for the vascular access (ml/min) ……..
10. Total volume of blood processed (liters) ……
11. Total duration of the dialysis session (minutes)……
12. UF volume(litres)……..

Interpretation of Laboratory results: URR > 65% or Kt/V > 1.2 = adequate dialysis dose

URR < 65% or Kt/V < 1.2 = inadequate dialysis dose

SECTION III: FINDINGS FOR AVF.

1. Site of AVF. a) lower arm ☐
   b) upper arm ☐
2. Flow velocity (m/s) ……..
3. Stenosis a) present b) absent
4. If stenosis present, Percentage (%) …….. Length (mm) ……
5. Calcifications a) present b) absent
6. Aneursysm a) present b) absent

APPENDIX VII: DUMMY TABLES

Table 3: Baseline demographic and clinical characteristics

	Total (n=149)
Demographic characteristics Age (years) Gender (%female) Years of dialysis Inter-dialytic interval Duration per session	
Co-morbid conditions (%) Diabetes Hypertension Congestive cardiac failure Coronary artery disease[#] Peripheral vascular disease[$]	
*Data are mean Standard Deviation. [#] Includes coronary artery bypass surgery, angina, and myocardial infarction [$] Includes limb amputation, absent foot pulses, and symptoms of claudication	

Table 6: CVC , AVF and Dialysis Session Variable

	Total (n = 149)
AVF	
CVC	
Dialysis shift (%) Morning Afternoon Evening	
Dialysis Pre-dialysis weight (kg) Weight loss during dialysis (kg) Blood volume processed (L) Time on dialysis (min) Mean blood flow (ml/min) Mean pre-dialysis Urea Mean post dialysis Urea	

Table 5: URR by mean blood flow (n =149)

Blood flow (ml/min)	% of patients	URR (% ± SD)	% of patients with URR ≤ 65
< 250			
250 to 300			
301 to 350			
351 to 400			
> 400			

APPENDIX VIII: ETHICAL APPROVAL LETTER

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Ref: KNH-ERC/A/424

16th October 2015

Dr. F.O. Ndinya
H58/63001/2013
Dept.of Clinical Med. & Therapeutics
School of Medicine
University of Nairobi

Dear Dr. Ndinya

Research proposal: Haemodialysis vascular access function in dialysis patients at the Kenyatta National Hospital (P532/08/2015)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 16th October 2015 – 15th October 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **http://www.erc.uonbi.ac.ke**

"Protect to Discover"

Yours sincerely,

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