CLINICAL OUTCOMES ASSOCIATED WITH INTRADIALYTIC FOOD INGESTION IN PATIENTS UNDERGOING HIGH VOLUME ONLINE HAEMODIAFILTRATION

By

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In the

Department of Biomedical and Clinical Technology
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Durban University of Technology
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Supervisors: **Mr M E Memela**
Prof J K Adam

This study was carried out at Fresenius Medical Care dialysis Centers in KZN, North Coast region. The study represents original work done by the author and has not been submitted in any form to another University. In cases where use of the work by others, it has been duly acknowledged in the text.

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Abstract

Introduction: The quality of haemodialysis (HD) treatment received by chronic renal failure patients is important for their overall well-being. Adequate HD improves patients quality of life, minimizes disease complications and hospitalizations. Dialysis inadequacy over a prolonged period exacerbates pre-existing conditions, increases morbidity and mortality, deteriorates patients health leading to a poor quality of life. Mitigating factors that may contribute to dialysis inadequacy is important for optimizing patient care and achieving good clinical outcomes. Dialysis centres often provide meals for patients while receiving their treatment. The aim of the study was to evaluate whether intradialytic food intake may affect dialysis adequacy in patients undergoing online haemodiafiltration (OL-HDF). In the present study Single- pool Kt/V and urea reduction ratio (URR) were the measurements of molecular clearance utilized to measure dialysis adequacy.

Methodology: The study was conducted at Fresenius medical care dialysis clinics on adult patients undergoing OL-HDF treatment. Consent was obtained from the patients. Adequacy of dialysis was assessed using SpKt/V and URR. Patients underwent sampling of pre-dialysis and post-dialysis urea for the calculation of URR and SpKt/V was obtained from OCM® feature on the 5008s haemodialysis machine. The sampling was done on two consecutive mid-week treatments with and without food ingestion. The principal investigator also recorded MAP at 30 minute intervals for the assessment of post-prandial hypotension and pre- and post-Hgt for blood glucose stability during sessions with and without food ingestion.

Results: Fifty-two adult chronic renal failure patients were enrolled into the study. Twenty-four were males and twenty 28 females. The two groups of participants included the AV-Fistula group which consisted of 38 participants (73.1%) and the Permanent catheter group 14 participants (26.9 %). The total sample was made of African, Indians and Whites. There were 21 Africans, 30 Indians and 1 White.

The age distribution for AV-Fistula group was 55.29±8.45years (Mean±SD) and for Permanent catheter group was 56.86±10.35years. The mean URR with food ingestion 70.9±9.93 ($p = 0.918$) and without food ingestion 70.9±7.41 ($p = 0.508$). The mean spKt/V with food ingestion was 1.26±0.29 ($p = 0.599$) and without food ingestion 1.26±0.30 ($p = 0.788$). During sessions without food ingestion 13.5% of the patients were recorded to have hypotensive episodes and 86.5% did not experience hypotensive episodes. During sessions with food ingestion 38.5% patients were recorded to experience hypotensive episodes and 61.5% did not experience hypotensive episodes. There was a significant difference in the number of patients who did not have a hypotensive episode compared to those who did ($p < 0.001$). There wereno participants classified with hypoglycaemia as all of the minimum values were greater than 4.0mmol/L. The Mean±SD with food ingestion pre-dialysis was 9.12±4.93, post-dialysis 8.39±2.56. The Mean±SD without food ingestion pre-dialysis was 9.39±4.38 and post-dialysis was 7.22±2.26.

Discussion: The spKt/V and URR values for both the AV-Fistula and Permanent catheter groups were in optimal range as recommended by the KDOQI guidelines. There was no significant difference in the spKt/V and URR values achieved from the OL-HDF sessions with and without intradialytic food ingestion. Intradialytic food ingestion did not negatively impact dialysis adequacy, although it was noted that during sessions of food ingestion more patients did experience post-prandial hypotension as compared to without food ingestion and post-dialysis blood glucose levels were lower during sessions without food ingestion as compared to with food ingestion, there was no significant difference in these variables.

Conclusion: Intradialytic food ingestion is recommended for patients undergoing OL-HDF treatment. Patients that suffer severe malnutrition and low albumin levels should be considered to be treated with OL-HDF treatment and intradialytic feeding should introduced. This may contribute in an increase in quality of life in patients with CKD.

Acknowledgement

I would like to take this opportunity to acknowledge the people that played an important role throughout my journey.

I give thanks to God for the protection and ability to complete the research successfully.

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I Thank You

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List of abbreviations

ABBREVIATION	DESCRIPTION
CRF	Chronic renal failure
CKD	Chronic kidney disease
ESRD	End stage renal disease
HD	Haemodialysis
HDF	Haemodiafiltration
OL-HDF	Online- Haemodiafiltration
PD	Peritoneal dialysis
SpKt/V	Single-pool Kt/V
URR	Urea reduction ratio
KDOQI	Kidney disease outcomes quality initiative
MAP	Mean arterial pressure
RAAS	Renin angiotensin aldesterone system
CRRT	Continuous renal replacement therapy
UF	Ultrafiltration
GFR	Glomerular filtration rate
PTH	Parathyroid hormone
ESA	Erythropoetin stimulating hormone
BRA	British renal association
CSN	Canadian society of nephrology
BUN	Blood urea nitrogen
NCDS	National cooperative dialysis study
OCM	Online clearance monitoring
AVF	Arteriovenous fistula
AVG	Arteriovenous graft
CVC	Central venous catheter
QB	Blood flow rate
QD	Dialysate flow rate
CVD	Cardiovascular disease
DRA	Dialysis related amyloidosis
CKD-MBD	Chronic kidney disease- Mineral bone disorder
IDH	Intradialytic hypotension
BP	Blood pressure
GI	Gastrointestinal
MHD	Maintenance haemodialysis
FMC	Fresenius Medical Care
HGT	Haemogluco-test
IDWG	Intradialytic weight gain
SST	Serum separating tube
IFI	Intradialytic food ingestion
HVHDF	High volume haemodiafiltraion
Ml	Milliliter
Mmol	Millimole
MW	Molecular weight
Da	Dalton
KoA	Dialyser mass transfer urea coefficient
Ca^{2+}	Calcium ion
Na	Sodium

Mg	Magnesium
Cl^-	Chloride ion
K^+	Potassium
HCO3	Bicarbonate
NaHCO3	Sodium bicarbonate

CHAPTER ONE

INTRODUCTION

Kidney failure results in blood toxicity and disruption of homeostasis of the body; it may be classified as either acute renal failure which is reversible or chronic renal failure (CRF) which is irreversible. Hypertensive and diabetic nephropathy are common causes of CRF (Van Buren and Toto, 2011). Patients diagnosed with CRF are treated with haemodialysis (HD), haemodiafiltration (HDF), peritoneal dialysis (PD) or kidney transplant. Nephrologists prescribe the type of dialysis therapy that best matches the patient's needs. In 2014 the South African renal registry reported that 71.8% of CRF patients were treated with conventional HD (Davids *et al*. 2014).

The objective of dialysis is to remove toxins and excess fluid from blood via a semi-permeable membrane; how effectively this is done is referred to as adequacy of HD. Adequate HD improves patient survival, quality of life, biochemical outcomes, minimizes disease complications and hospitalizations (Adas *et al*. 2014). The renal association defines adequacy as a global concept which includes clinical assessment of well-being, the impact on the patient's life and measures of the molecular clearance by the dialysis process (The renal association, 2002). Measurements of molecular clearance generally utilises single-pool Kt/V (spKt/V) and urea reduction ratio (URR). Single-pool Kt/V was developed by Frank Gotch and John Sargent in the 1970's as a way for measuring adequacy of dialysis. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend a minimum spKt/V of 1.2 with a target value of 1.4 and a URR greater than 65%. Values obtained below these targets may indicate inadequate dialysis. Dialysis inadequacy over a prolonged period exacerbates pre-existing conditions, e.g., dialysis related amyloidosis, hyperkalaemia, may lead to an increase in hospitalizations, deterioration on the patient's health and poor quality of life.

Maduell *et al*. (2013) demonstrated that high-efficiency post dilution online haemodiafiltration (OL-HDF) increases clearance of middle to large molecules by combining diffusive and convective transport which improves dialysis adequacy and reduces all-cause mortality compared to conventional HD. During a dialysis session it is common for patients to experience dialysis related complications, e.g., dialysis disequilibrium, intradialytic hypotension, hypertension,

muscle cramps, and hypoglycaemia (Himmelfarb, 2005). It is important for these complications to be managed appropriately in order to maintain and optimise dialysis adequacy. The long duration of the treatment results in patients becoming restless, hungry and tired. As a method of improving compliance, satisfaction and comforting patients many dialysis centres provide a complimentary meal for patients while receiving their treatment. Food intake during HD increases the risk of complications such as hypotension, nausea, and vomiting (Borzou *et al*. 2016).The effects of intradialytic food ingestion has been documented for patients undergoing HD, however, no such study has been conducted on the effects of intradialytic food ingestion in patients undergoing High volume OL-HDF.

The aim of the present study was to evaluate whether intradialytic food intake may affect dialysis adequacy in patients undergoing OL-HDF. The rationale for the study was to improve dialysis adequacy, lower morbidity and mortality rates and increase quality of life in CKD patients. The objectives were to determine adequacy of OL-HDF by pre-dialysis and post-dialysis urea blood sampling in patients withand without food ingestion, compare the adequacy of treatment between patients, i.e., with and without food ingestion during OL-HDF, and to determine the effects of food ingestion on blood glucose levels and mean arterial pressure (MAP) in patients with and without food ingestion.

The present study utilized spKt/V and URR to investigate the effect of intradialytic food ingestion in CKD patients undergoing OL- HDF. A comparison was made on the outcomes of spKt/V and URR in treatments with and without food ingestion, the incident of post-prandial hypotension and the effect of foodingestion on blood glucose. The study was conducted at two Fresenius medical care dialysis units on the North coast of KwaZulu- Natal, i.e., Victoria and Stanger Kidney & dialysis centres. Permission was granted by Fresenius Medical Care South Africa (Pty) Ltd, after ethical approval was obtained from the Durban University of Technology research and ethics committee (Appendix 3). Informed consent was obtained from all participants enrolled to the study.

CHAPTER TWO
STUDY BACKGROUND AND LITERATURE REVIEW

2.1 STUDY BACKGROUND

2.1.1 Introduction

In order for the cells of the body to function effectively, it needs a stable environment. It must be able to maintain the level of the body's substances in a relatively constant number to achieve homeostasis (Mcphee and Hammer, 2010). The kidney as a major excretory organ is crucial in maintaining an optimal internal environment for homeostasis.

The large blood supply to the kidney enables it to serve important functions, including filtration and excretion of metabolic waste products such as urea, regulation of necessary electrolytes, acid-base balance and stimulation of red bloodcell production which carry oxygen throughout the body. They also serve to regulate blood pressure via the renin-angiotensin-aldosterone system (RAAS), have hormonal functions via calcitriol and vitamin D activation and control the reabsorption of water and maintain intravascular volume (Daugirdas, 2007). When the kidney fails to perform it's function, the internal environment of the body changes drastically, such that the cells will no longer function adequately resulting in uraemic syndrome (rnspeak, 2010).

Patients diagnosed with end stage renal disease (ESRD) may undergo continuous renal replacement therapy (CRRT) as part of an initiative to increase quality of life and decrease morbidity and mortality by effective uraemic toxin clearance and ultrafiltration (UF).

Recent studies have proven OL-HDF to be one of the leading therapies for ESRD providing haemodynamic stability in terms of fewer hypotensive episodes due to the advantages of volume substitution. It also provides an increase in adequacy of treatment by the ability of improved removal of lower and higher molecular weight solutes e.g., (urea, creatinine), overall producing an excellent spKt/V (Canaud *et al*.

2006). All-cause hospitalizations were reported to be lower in patients assigned to OL-HDF. High-efficiency post-dilution OL-HDF reduces all-cause mortality compared to conventional HD (Maduell *et al*. 2013). Dialysis patients are often offered a light meal while receiving their treatment. In keeping with the main objective of dialysis treatment, to achieve optimum clearance with minimal complications, it has been noted that patients may experience complications after food ingestion (Eggers, 2000). Post-prandial hypotension is common, of which may result in intradialytic complications thus lowering the targeted spKt/ V and URR.

2.1.2 Physiology of end stage renal disease

Patients with ESRD show a constellation of signs, symptoms and laboratory abnormalities. These reflect the long standing and progressive nature of their renal impairment. The most common causes of ESRD are Diabetes Mellitus, Hypertension and Glomerulonephritis (Mcphee and Hammer, 2010).

The irreversible loss of nephrons is characterised by chronic injury of the kidneys. An increase in glomerular filtration pressure causes hypertension of the individual nephron resulting in a greater functional burden on fewer nephrons. Residual renal function becomes inadequate and progression to uraemia begins.Up to 50% of the nephrons can be lost without any evidence of functional impairment. When glomerular filtration rate (GFR) is further reduced leaving only about 20% of initial renal capacity some degree of azotemia is observed (Mcphee and Hammer, 2010). During this steady state the levels of waste products are not high enough to result in toxicity. Patients remain asymptomatic, but progress to ESRD. At this level of GFR any slight added stresses, e.g., infection, dehydration,or nephro-toxic drugs may contribute to a uraemic state (Mcphee and Hammer, 2010).

The pathogenisis of ESRD derives from the toxic levels of retained products normally excreted by the kidneys, e.g., nitrogen-containing products of protein metabolism. Normal products such as hormones are present in increased amounts, and loss of normal products of the kidney (e.g., loss of erythropoietin) can be observed. Excretory failure also results in fluid shifts with increased intracellular sodium and water, and decreased intracellular potassium (Mcphee and Hammer, 2010).

All individuals with a GFR <60 ml/min/1.73 m^2 for 3 months are classified as having ESRD, irrespective of the presence or absence of kidney damage. The reduction in kidney function to this level or lower represents loss of half or more of the adult level of normal kidney function. This may be associated with a number of complications such as the development of cardiovascular disease (National Kidney Foundation, 2000).

Normal human kidney and diseased kidney.

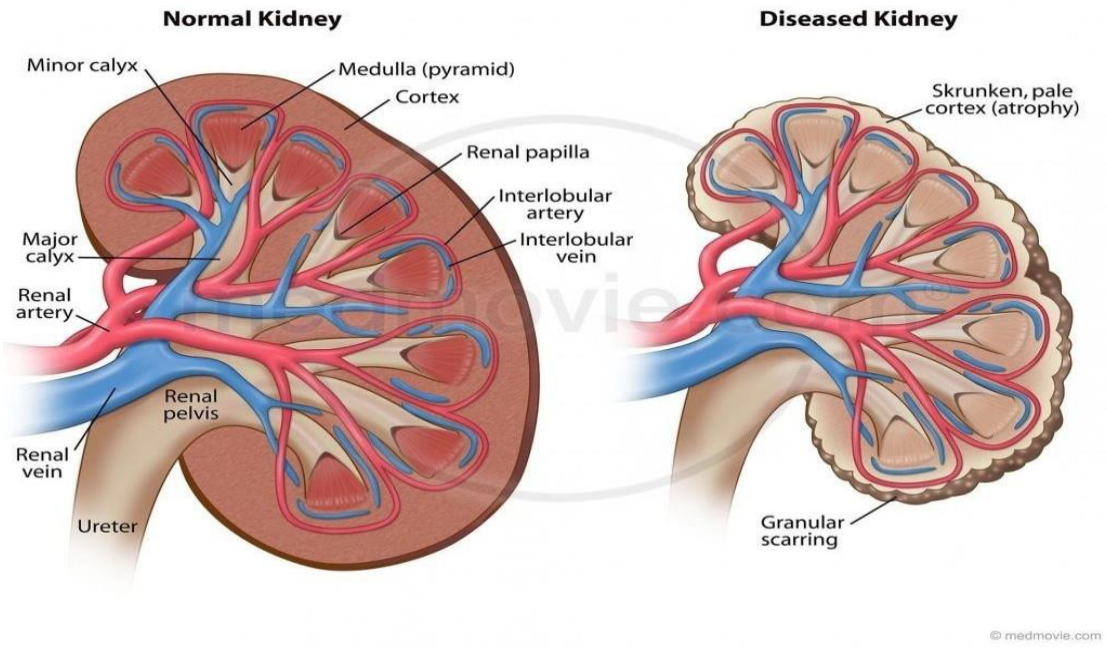

Figure 1: Normal and diseased human kidney, 2010. (Available: http://www.striveforgoodhealth.com)

2.1.3 Clinical Manifestations of CKD

2.1.3.1 Sodium balance and volume status

Patients with ESRD typically have some degree of sodium and water excess, reflecting loss of renal route of salt and water excretion. A moderate degree of sodium and excess water may occur without objective signs of extracelluar fluid; however, continued excess sodium ingestion contributes to congestive heart failure, ascites,

Peripheral oedema and weight gain. Excessive fluid ingestion contributes to hyponatremia. End stage renal disease patients are advised to restrict sodium and fluid intake, adjustments to volume status can be made through the use of diuretics for those patients that produce urine, or through dialysis (Mcphee and Hammer, 2010).

2.1.3.2 Hyperkalemia

Hyperkalemia is an accumulation of potassium in the blood with a range of symptoms including malaise and potentially fatal cardiac arrhythmias (Figure 2). It is a serious problem for patients with ESRD, especially in patients with a GFR less than 5 mL/min (Arora, 2017). Hyperkalemia usually does not develop until GFR falls to less than 20–25 ml/min/1.73 m^2, at which point the kidneys have decreased ability to excrete potassium (Arora, 2017). HD provides a substantially higher potassium clearance (removal of 50-80 mmol of K^+ in a 4-h session) than continuous forms of RRT (Ricci *et al*. 2009).

An ECG reading for Hyperkalemia

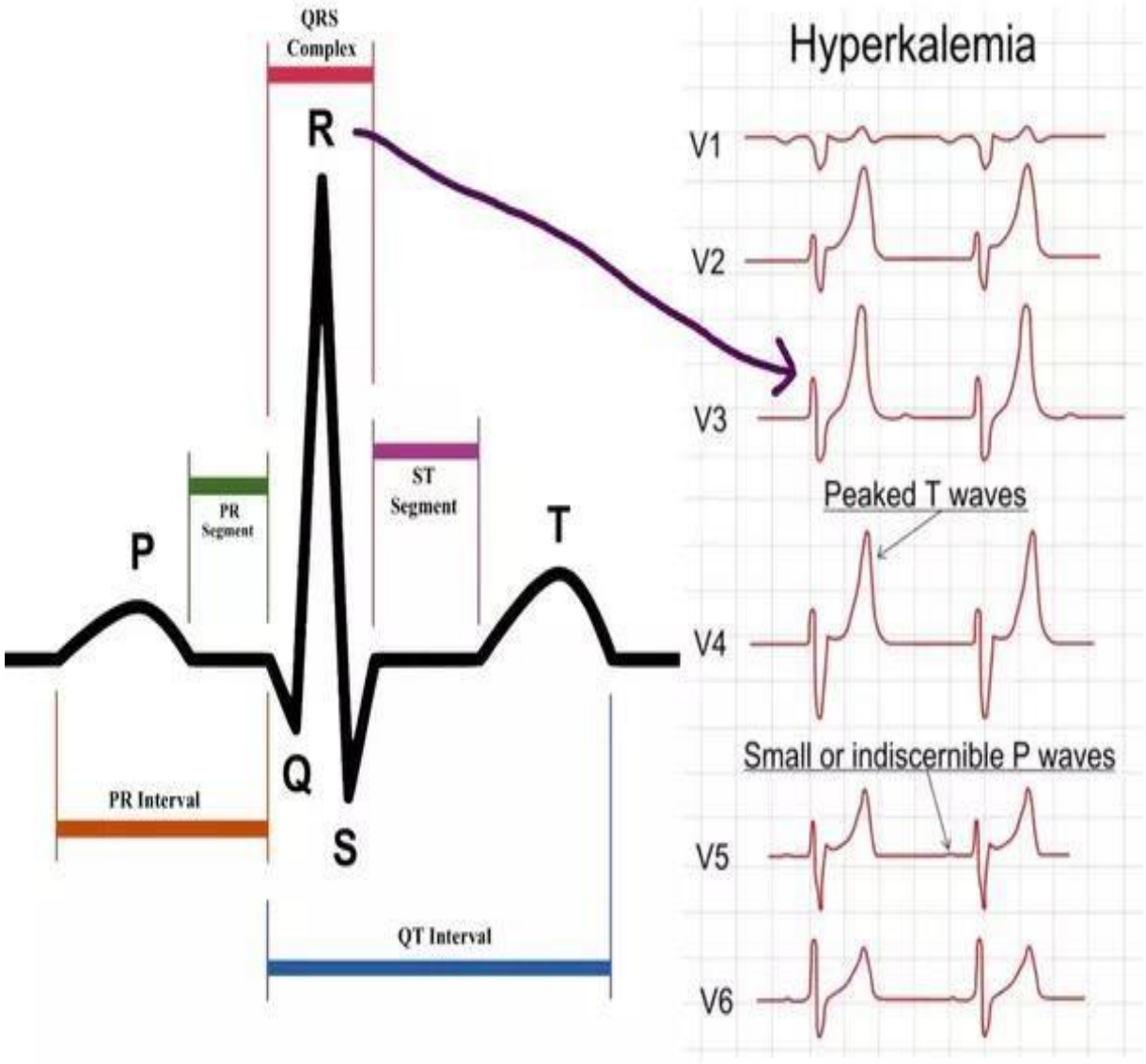

Figure 2: ECG Hyperkalemia, 2016. (Available: https://www.quora.com)

2.1.3.3 Metabolic acidosis

The diminished capacity to excrete acid and generate base in ESRD results in metabolic acidosis. In most cases when the GFR is above 20mL/min only moderate acidosis develops before re-establishment of a new steady state of buffer production and consumption. The fall in blood pH in these individuals can usually be corrected with 20-30mmol of sodium bicarbonate by mouth daily (Mcphee and Hammer, 2010).

2.1.3.4 Bone and Mineral

Several disorders of phosphate, calcium and bone metabolism are observed in ESRD as a result of a complex series of events. The key factors in the pathogenesis of these disorders include diminished absorption of calcium in the gut, overproduction of PTH, disordered vitamin D metabolism, and chronic metabolic acidosis. All of these factors contribute to enhance bone re-absorption. Hypophosphatemia and hypomagnesaemia can occur through overuse of phosphate binders and magnesium containing antacids, although hyperphosphatemia is more common. Hyperphosphatemia contributes to the development of hypocalcaemia and thus serves as an additional trigger for secondary hyperparathyroidism, elevating blood PTH levels. The elevated blood PTH further depletes bone calcium and contributes to osteomalacia of CKD (Mcphee and Hammer, 2010).

Early diagnosis and treatment of the underlying cause and institution of secondary preventive measures is imperative in patients. Diagnosing and treating the pathologic manifestations of CKD (Table 1) and timely planning for long term renal replacement therapy may slow, or possibly halt, progression of the disease (Arora, 2017). Co-morbid conditions example Hypertension and Diabetes mellitus worsen during the progression of CKD and are often treated under pre-renal care in order to preserve the remaining kidney function and prolong the onset of ESRD (Arora, 2017).
Table 1 displays common clinical manifestations of CKD which are treated as pre-renal (Arora, 2017).

Table 1: Clinical manifestations of CKD treated as pre-renal.

Clinical Manifestation	Treatment
Anaemia	When the haemoglobin level is below 10 g/dL, treat with erythropoietin-stimulating agents (ESAs), which include epoetin alfa and darbepoetin alfa after iron saturation and ferritin levels are at acceptable levels.
Hyperphosphatemia	Treated with dietary phosphate binders and dietary phosphate restriction.
Hypocalcaemia	Treated with calcium supplements with or without calcitriol.
Hyperparathyroidism	Treated with calcitriol or vitamin D analogues or calcimimetics.
Volume overload	Treated with loop diuretics or ultrafiltration.
Metabolic acidosis	Treated with oral alkali supplementation.
Uremic manifestations	Treated with long-term renal replacement therapy (haemodialysis, peritoneal dialysis, or renal transplantation).

2.1.4 Indications for renal replacement therapy

- Severe metabolic acidosis
- Hyperkalemia
- Pericarditis
- Encephalopathy
- Intractable volume overload
- Peripheral neuropathy
- Intractable gastrointestinal symptoms
- In asymptomatic patients, a GFR of 5-9mL/min/1.73 m^2 irrespective of the cause of the CKD or the presence or absence of other co-morbidities (Lameire and Van Biesen, 2010).

2.1.5 Treatment for ESRD

Dialysis was first introduced in 1854 when Thomas Graham of Gaslow presented the principle of solute transport across a semi-permeable membrane (Graham, 1854). There are two main types of dialysis, haemodialysis and peritoneal dialysis. They remove waste and excess water from the blood in different ways (Pendse, Singh and Zawada, 2008).

2.1.5.1 Haemodialysis

Haemodialysis is the most common type of renal replacement therapy. Standard HD uses the principle of diffusion to remove waste products from blood. Diffusion is the movement of solutes from a higher concentration to lower concentration across a semi-permeable membrane (Mosby's dictionary of medicine, 2006).

Haemodialysis is an extracorporeal process of removing wastes and water by circulating blood outside the body through the dialyser containing a semi- permeable membrane (Pendse, Singh and Zawada, 2008). The blood flows in one direction and the dialysate flows in the opposite direction. The counter-current flow of the blood and dialysate maximizes the concentration gradient of solutes between the blood and dialysate, promoting the removal of urea and creatinine from blood. The concentrations of solutes example potassium are undesirably high in the blood, but low in the dialysate solution, the replacement of dialysate ensures that the concentration of undesired solutes are low on the blood compartment of the membrane. The dialysate has levels of minerals like potassium and calcium that are similar to their natural concentration in healthy blood (Pendse, Singh and Zawada, 2008).

The process of HD

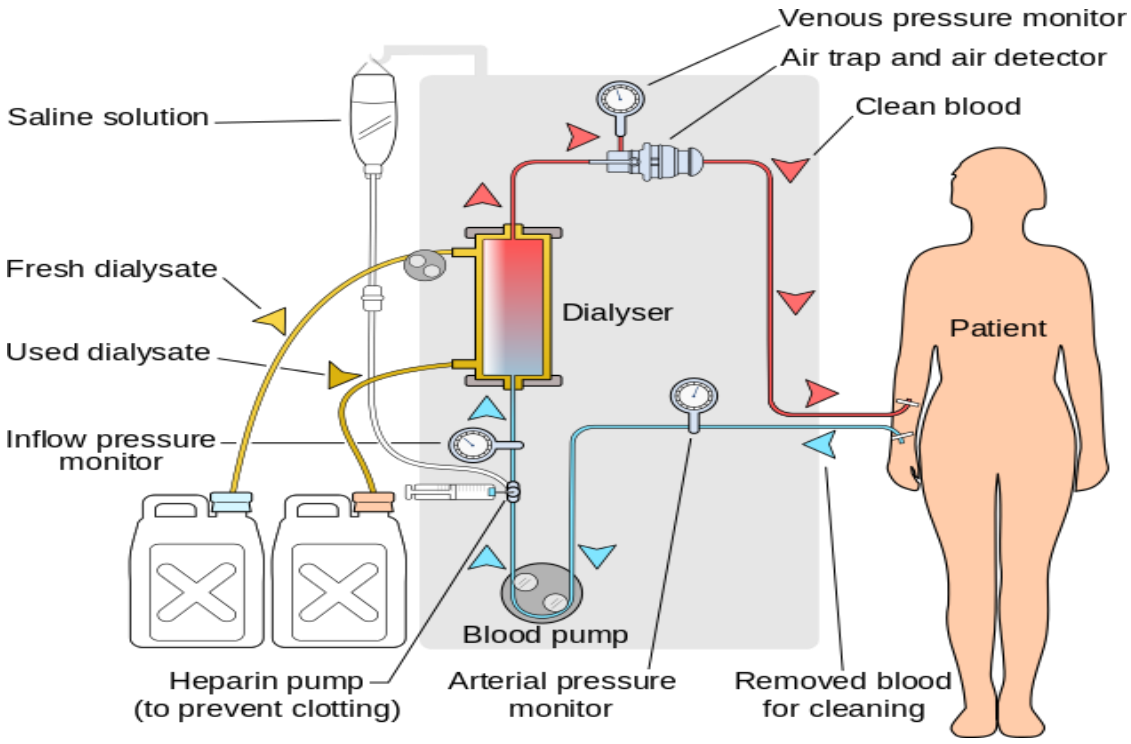

Figure 3: Haemodialysis schematic (Haemodialysis schematic, 2008)

2.1.5.2 Haemodiafiltration

Haemodiafiltration (HDF) unlike HD uses the principle of convection in addition to diffusion to remove waste products from the blood. Convection is the removal of waste products and water from the blood by infusing large amounts of dialysate to the water and toxins once they reach the dialyser. During HDF the dialysis machine can remove more water safely from the body than standard HD (Fresenius medical care, 2016). The dialysate that is infused in large volumes ± 21 litres per session does not stay in the body, it is automatically removed by the dialyser via a negative pressure. In order for the full benefits of HDF to be achieved, the amount of water exchanged should be maximized hence the approach of High volume HDF (HVHDF). High volume HDF is the only treatment that comes closest to the function of a normal kidney (Fresenius medical care, 2016). It is simple, safe, effective and cost effective, eliminates larger molecules, more tolerable, stable and a more comfortable treatment (Fresenius medical care, 2016).

The process of HDF.

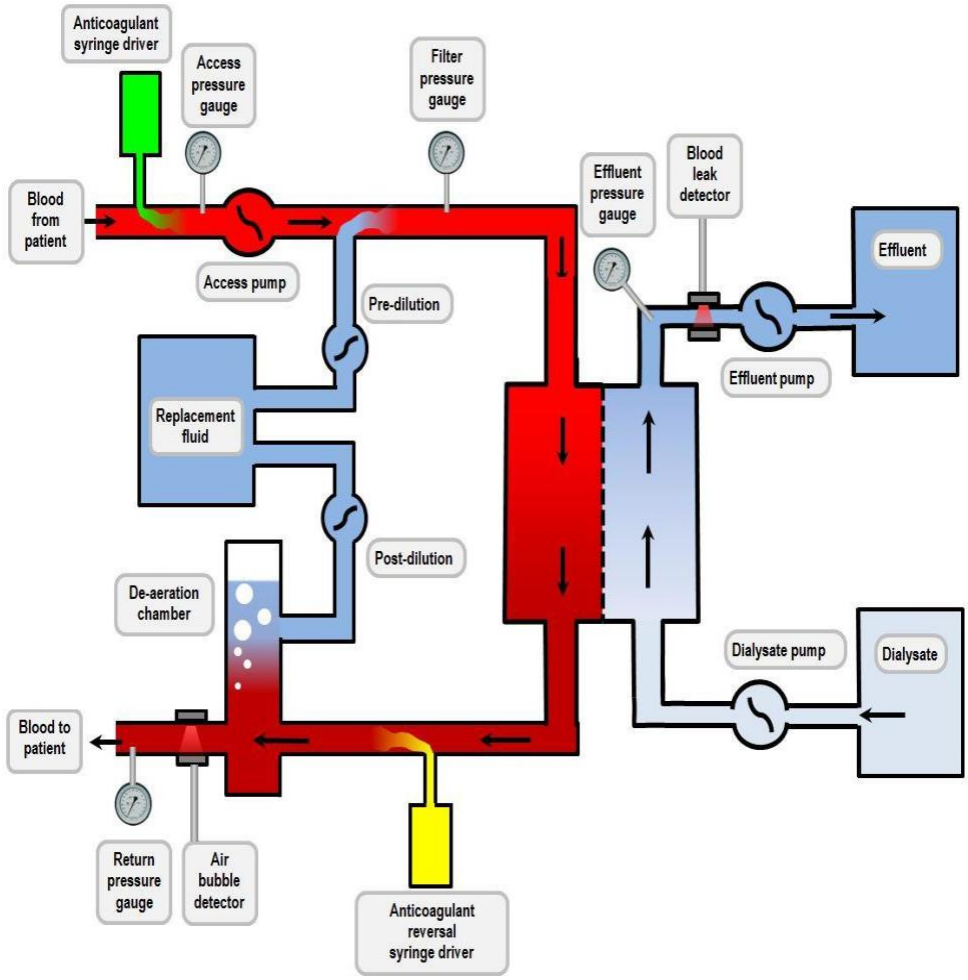

Figure 4: Haemodiafiltration schematic (Yartsev, 2013)

High volume HDF is dose related, the higher the substitution flow rate, the more effective the toxin clearance, achieving the mean delivered total convective volume of 23 litres per session should therefore be the target for every HDF treatment (Fresenius medical care, 2016).

2.1.5.2.1 Advantages of HVHDF according to Fresenius medical care, (2016):

- HVHDF has much improved clearance of toxins
- There is a significant decrease in complications
- Increases the patients appetite
- Reduced risk of dialysis related amyloidosis

- Less tissue and organ inflammation
- Improved anaemia control, resulting in decrease use of ESA.
- Increased removal of phosphate, resulting in decreased need for phosphate binders
- Increased removal of beta 2 microglobulins
- Less fatigue, headache and nausea
- Reduced risk for hypotension during dialysis
- Higher spKt/V resulting in improved outcome of dialysis
- Decreased hospitalizations.

The use of online fluid injected by the machine into blood ensures a more stable and gentle dialysis that is highly effective. The FX Cordiax® (Fresenius medical care, Germany) HDF dialyser which is especially designed for this state of the art treatment has scientifically calculated fibers and pores to ensure absolute purity of blood (Fresenius medical care, 2016).

The FX-class® dialyzer by Fresenius Medical Care

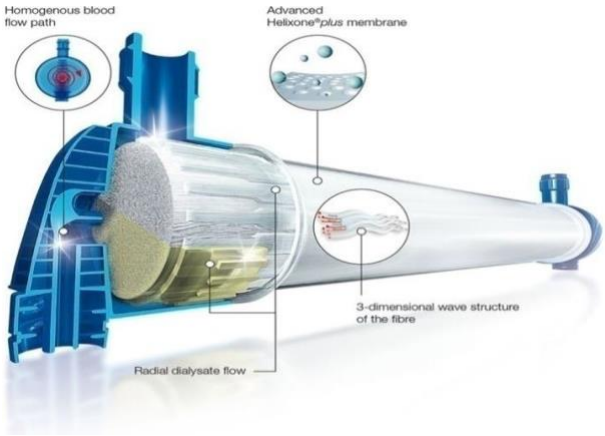

Figure: 5 FX-class® Dialyzer design, 2016. (Available: www.freseniusmedicalcare.co.za)

A study conducted by Tiranathanagul *et al.* (2009) demonstrated a decrease in the incidence of intradialytic undesired events, including hypotension. An apparent increase in appetite and an improvement in overall wellbeing were recorded by most patients after switching to OL-HDF. Dry weight, body mass index, and normalized protein nitrogen appearance, which represent nutritional status, showed a significant improvement while still maintaining a satisfactory albumin level. The adequacy in

terms of URR significantly increased. Serum pre-dialysis b2-microglobulin levels were reduced. The patient's lipid profile was well controlled, and the mean C-reactive protein value was still maintained in the normal range as an indicator for low inflammatory state.

Fresenius Medical Cares 5008s Cordiax HD machine

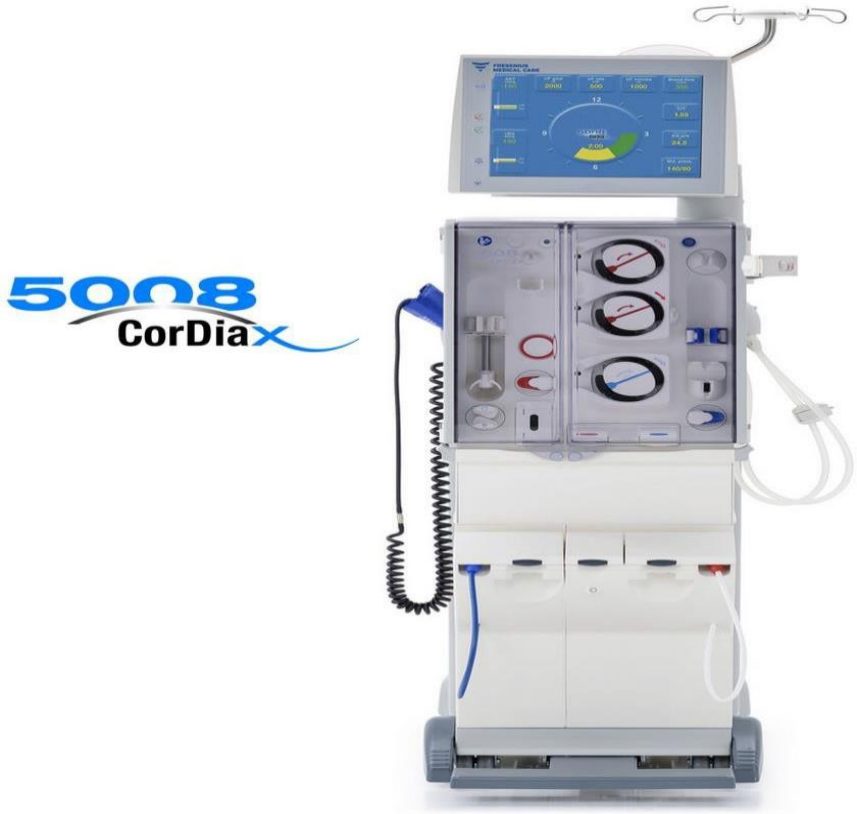

Figure 6: Fresenius Medical Care 5008s Cordiax haemodialysis machine, 2016. Available: https://www.freseniusmedicalcare.com.

2.1.6 MANAGEMENT OF DIALYSIS ADEQUACY

Some may define adequacy of dialysis as a determination made by clinical assessment of patient well-being. Experience has taught, however, how inadequate dialysis may be overlooked by strictly adhering to clinical criteria; although the inverse is equally true (Lazarus and Hakim, 1965). Inadequate therapy can remain unrecognized when therapeutic decisions are exclusively based on clinical parameters (Raja, 1978). Clinical symptoms, patient's satisfaction with life, left ventricle hypertrophy, nervous conduction power, mineral metabolism, blood pressure, volume control of body fluids and urea clearance can be indicated as useful tools in dialysis adequacy measurement. Whereas, blood urea concentration is easily measurable and is distributed equallyin the whole body, so it seems that urea clearance is the best indicator for dialysis quality measurement (Hojjat, 2009).

2.1.6.1 Methods of measuring adequacy

Dialysis adequacy is measured using spKt/V and URR in which blood urea nitrogen (BUN) is measured before and after HD (Daugirdas & Schneditz, 1995; Nafar *et al*. 2008). SpKt/V where K is the total (dialyzer plus residual renal function) urea clearance (mL/mm), t is the duration of the dialysis treatment (minutes) and V is the patient's urea volume of distribution or total body water volume (ml). British Renal Association (BRA) and Canadian Society of Nephrology (CSN) recommended a Kt/V of 1.2 for three times dialysis per week and URR of more than 65% (Kerr *et al*. 2005). URR is calculated as 1 minus the ratio of the post-dialysis over the pre-dialysis BUN expressed as a percentage. Several investigators have shown a correspondence between spKt/V and URR (National Kidney Foundation, 2000).

The National Cooperative Dialysis Study (NCDS) established that a higher dialysis dose resulted in reduced morbidity (Lowrie *et al.* 1981). Observational studies have suggested that urea clearance below a single-pool Kt/V of 1.2 or URR of 65% three times per week is associated with increased mortality (Collins *et al.* 1994).

2.1.6.2 Online clearance monitoring

Online Clearance Monitoring (OCM®) is a standard feature of the Fresenius Medical Care 5008 therapy system that provides an automatic intradialytic measurement of the effective *in-vivo* urea clearance, the total cleared blood water volume, the delivered dose of dialysis (Kt/V) and the plasma sodium concentration of the patient. OCM® makes it possible to easily monitor these essential parameters without additional costs during regular OL- HDF in either pre- or post-dilution mode or during standard HD. OCM® helps physicians and nursing staff to ensure and document on a regular basis that the RRT meets the recommended quality standards without the need for additional laboratory tests or expenses (Online Clearance Monitoring, 2007).

In searching for an alternative, a substance was considered which is present in large quantities in the dialysis fluid and where changes in concentrations can be measured by a sensor installed within the dialysis machine namely ionised sodium. Sodium ions represent the largest proportion of freely mobile electrolytes in the dialysis fluid and their concentration essentially determines the total conductivity of the dialysate. Although the small, positively charged sodium ion differs from the non-charged and larger urea molecule, both particles exhibit comparable in-*vitro* and *in- vivo* diffusion characteristics across a synthetic dialysis membrane, i.e., their specific diffusion coefficient is almost identical at 37°C. Urea as postulated above has a diffusion profile similar to that of the sodium ion, urea clearance can be determined irrespective of the actual concentration of urea in the blood. Steil *et al.* (1993) were able to demonstrate that the dialysance is directly proportional to urea clearance. They showed how closely measured ionic clearance correlates with measured urea clearance (Online Clearance Monitoring, 2007).

The online clearance monitoring system on the 5008s Cordiax machine.

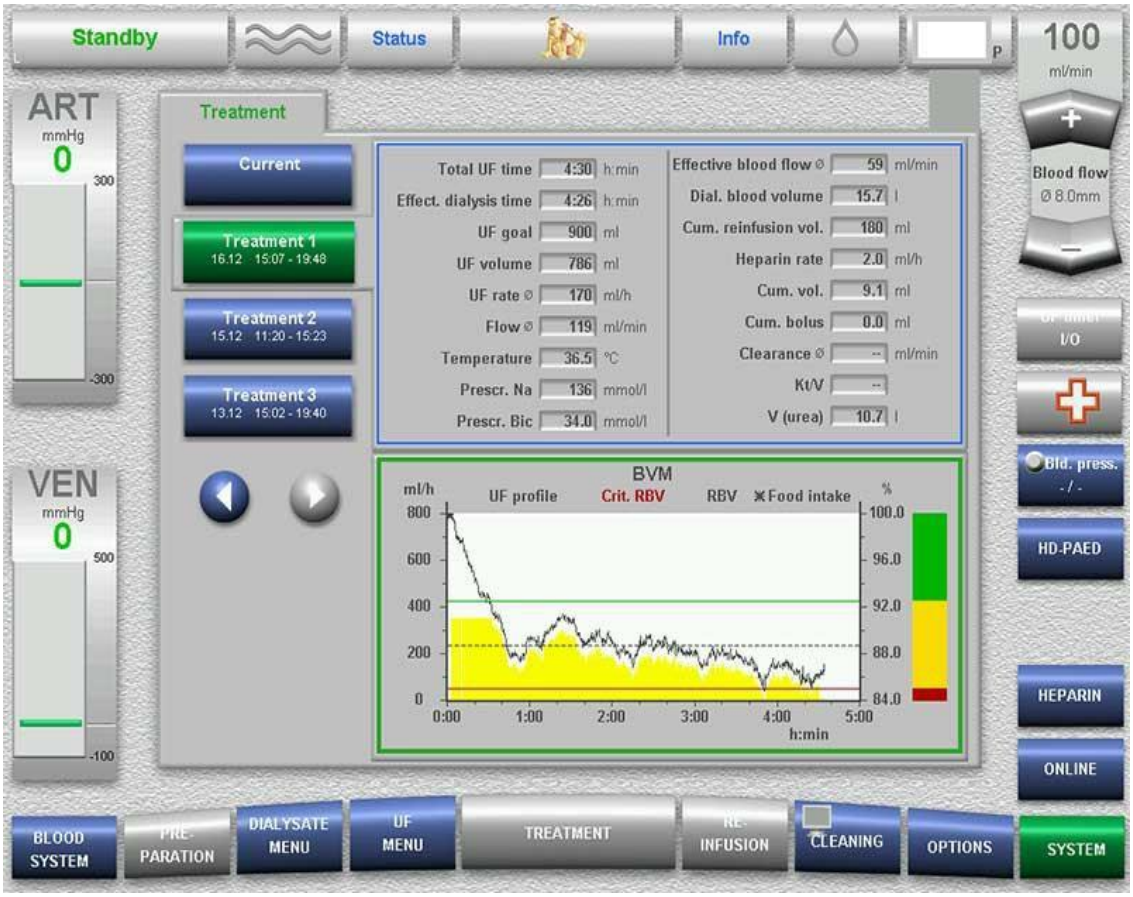

Figure 7: OCM feature on the 5008s Cordiax machine, 2016.
(Available:https://www.freseniusmedicalcare.com)

To ensure that patients are receiving the prescribed urea clearance, the clinician must regularly monitor and measure the dose delivered. Urea clearance should be measured at least every 8 weeks (Jindal *et al*. 2006). Less frequent dialysis may be acceptable for brief periods in patients with greater levels of residualrenal function, or those in whom the primary indication for dialysis is control of extracellular fluid volume rather than solute clearance (Jindal *et al*. 2006).

Uraemic toxins are preferentially classified according to the physicochemical characteristics affecting their clearance during dialysis, which is the main therapeutic option for their removal. Traditionally, this subdivision focuses on three types of molecules: the small water-soluble compounds molecular weight (MW <500Da), the larger middle molecules (MW>500 Da) and the protein-bound compounds (Vanholder *et al*. 2003). Middle molecules are intangible compounds with a MW

between 300 and 5,000 Daltons (Choots *et al.* 1984). Middle molecular peaks are prominent in severe uraemia (Urst *et al*. 1976).

There are many factors that can affect dialysis adequacy; such as the type of vascular access, type of dialyser, device used, dose of treatment, and route of erythropoietin stimulation agents used (Shahdadi, 2015).

2.1.6.3 Vascular access

There are three types of vascular access. Arteriovenous-fistula (AVF), Arteriovenous-graft (AVG) which is made of synthetic and bovine blood vessel, and central venous catheter (CVC) (Bay *et al*. 1998; Hakim & Himmelfarb, 2009). According KDOQI guidelines, the ideal vascular access should have three characteristics:

- Adequate blood flow for dialysis
- Long life span
- Have few side effects (e.g., infection, stenosis, and thrombosis) (Levin & Rocco, 2006; Sarani *et al*. 2015; Arbabisarjou & Mahnaz, 2013).

The AVF meets all these conditions. The CVC, unlike AVF has a high prevalence of infection, high costs, and associated with increased morbidity and mortality (Combe. *et al*. 2000; Hoen *et al.* 1995; Lee *et al*. 2002). Therefore, AVF is the recommended vascular conduit for HD by the Canadian and American kidney associations (Levin & Rocco, 2006). CVC is still continued to be used as a bridge of vascular access in most centres (Fadrowski, *et al*. 2009; Hayes et al. 2012). Since AVF needs time to mature to be used for HD, CVC are still being used for emergent HD in patients (Levin & Rocco, 2006). CVC is also used in people with diabetes, the elderly or patients with vascular diseases. It has also been used for patients with heart failure, patients who are waiting for kidney transplant and those who referred to the Nephrologists late (Levin & Rocco, 2006; Poredos, Kek, & Verhovec, 1997; Wasse *et al*. 2007).

Some studies have shown mixed results for the associations of vascular access with HD adequacy (Arbabisarjou *et al.* 2016). In a study conducted by Shahdadi (2015), 76.7% of patients being dialyzed via AVF and 23.3% of patients used central venous catheters (CVC). There was no statistical significant difference between dialysis

adequacy, vascular access type, device used for HD and the filter used for HD (Shahdadi, 2015). Health promotion behaviours such as regular exercise, adequate sleep, avoiding alcohol and tobacco use, proper nutrition, avoidance of obesity, medical care and avoidance of stress are advised (Arbabisarjou *et a*l. 2016).

The anatomy of an AV- Fistula

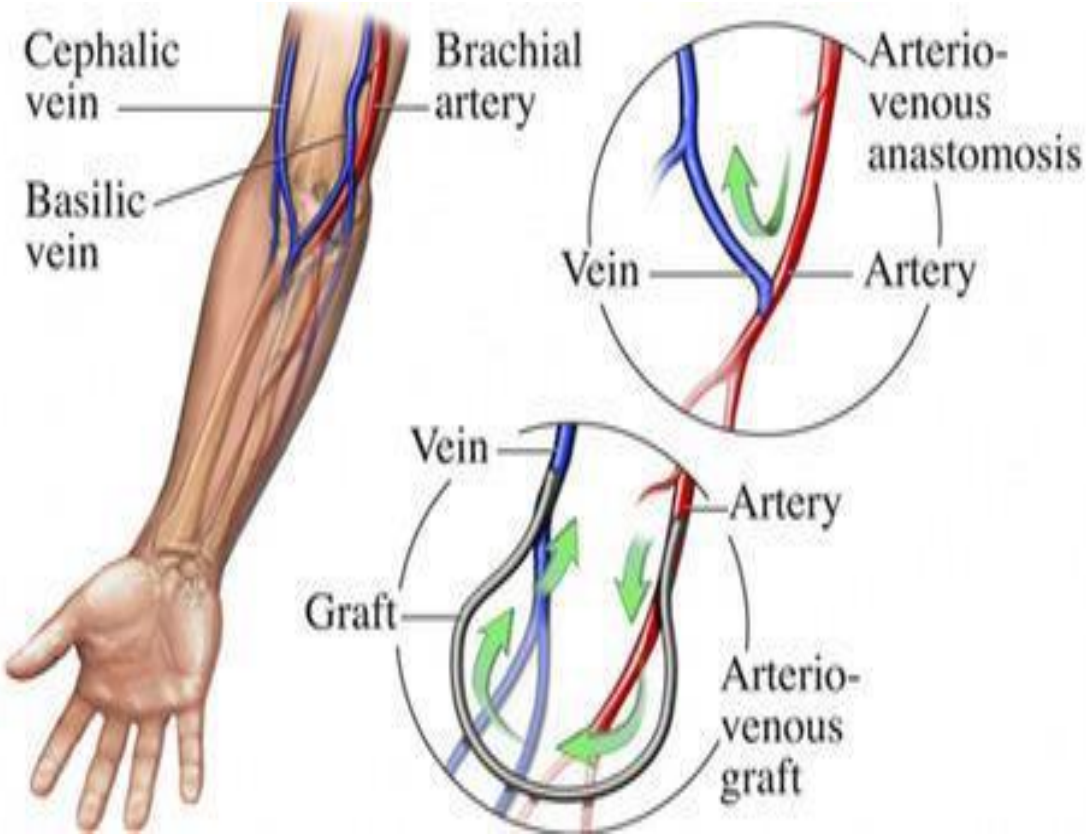

Figure 8: Arteriovenous-Fistula (Vascular-surgeon/surgeries,1996)

The position and structure of a central venous catheter

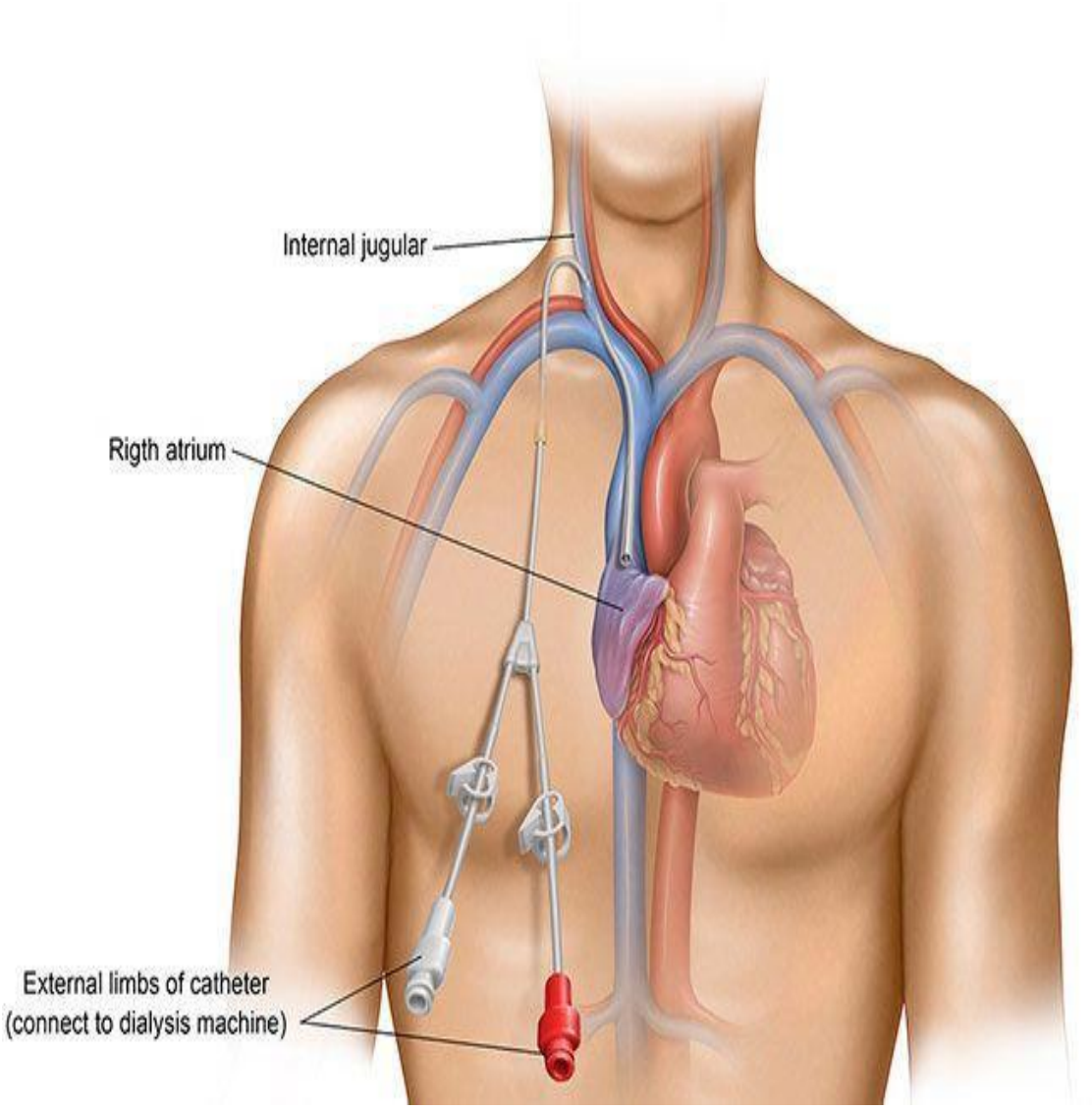

Figure 9: Central venous catheter (The Kidney Foundation of Canada, 2010)

2.1.6.4 Blood flow rate

Increase blood flow rate (Qb) through the dialyser depends primarily on the rate of Qb through the dialyser. No matter how good a dialyser is, how well it works depends primarily on moving blood through it. In many patients, a good rate is difficult to achieve because of vascular access problems. If a patient's Qb is good, further improvements in clearance can be obtained by using a big dialyser (dialysers with KoA values greater than 700mL/min) or, in some cases,by increasing the flow rate for dialysis solution (National Kidney Foundation, 2001).

2.1.6.5 Dialysate flow

Increasing the dialysate flow (Qd) for dialysis solution from the usual 500mL/min to 600 or 800mL/min. A good Qd for adult patients is 350mL/min and higher. Few centres are even using two dialyzers at the same time to increase clearance in larger than average patients. However, the rate of Qb through the dialyser is key, and a good vascular access is crucial to make sure a patient is getting good clearance (National Kidney Foundation, 2001).

2.1.6.6 Frequency and duration

Another way to improve clearance is to increase duration of treatment. Dialysis should be delivered at least 3 times per week and the total duration should be at least 12 hours per week, unless supported by significant renal function. Patients that present with haemodynamic or cardiovascular instability remain hypertensive despite maximum possible fluid removal, impaired phosphate control, malnourished, and anuric patients should be reviewed for an increase in duration and frequency of HD treatment (National Kidney Foundation, 2000).

2.1.6.7 Flux and convection

The mass transfer-area coefficient of the dialyser is referred to as KoA. In effect, it is the maximum attainable clearance of a given dialyser at infinite blood and dialyser flow rates (Leypoldt *et al*. 1997). Solute transport is mainly by diffusion, and essentially of small compounds, except when dialysis time or pore size is increased (Vanholder *et al*. 1934). The use of synthetic high-flux membranes should be considered to delay long-term complications of HD therapy. Specific indications include:

- To reduce dialysis-related amyloidosis
- To improve control of hyperphosphatemia
- To reduce the increased cardiovascular risk
- To improve control of anaemia

  (National Kidney Foundation, 2000).

In order to exploit the high permeability of high-flux membranes, OL-HDF or haemofiltration (HF) should be considered. The exchange volumes should be as high as possible, in consideration of safety (National Kidney Foundation, 2000).

2.1.6.8 Anticoagulation

The use of anticoagulation during HD is recommended to prevent clotting of the extracorporeal circuit. Thus preventing inhibition of the patient to reach their optimum clearance, due to obstructions within the dialyser and circuit (Renal urology news, 2017).

2.1.6.9 Ultrafiltraion

Ultrafiltration (UF) adds extra solute flux to diffusion, so that elimination is increased by a quantity that does not match UF rate (Gupta *et al.* 1984). Its negative impact on diffusive clearance was first recognized in coil dialyzers (Husted *et al*. 1976), but appeared later to be present for all types of dialysers and should always be considered for the calculation of Qb based clearances (Sprenger *et al.* 1985).

2.2. LITERATURE REVIEW

2.2.1 Importance of dialysis adequacy

Dialysis treatment may cause severe restriction on patient activity, financial stress, sexual disorders, low self-esteem, loss of energy and independence. It may also have a tremendous impact on the individual and his/her family (Collins *et al*. 2013). Secondary factors, such as race, voluntary withdrawal, age, and various diseases (mainly diabetes mellitus and cardiovascular disease) interfere with survival on dialysis (Parfrey *et al.* 1989). Kjellstrand *et al.* (1990) suggested that there is an increase in morbidity and mortality when dialysis is started late. Medical researchers have always been attracted to promotion of dialysis quality due to the fact that it is one of the most determining factors in quality of life, disability and mortality in ESRD patients (Rambod, 2008; Jindal *et al.* 2006).

Adequate dialysis means enough treatment to help patients live long and well. Inadequate dialysis may result in symptoms of pedal oedema, cardiovascular complications, bone and mineral disorders, and dialysis related amyloidosis. Enhancing the quality of dialysis is the main factor for reducing these complications and mortality rate in patients with ESRD (Hojjat, 2009). High-adequacy dialysis may ameliorate uraemic side effects such as malnutrition, fluid overload, and bleeding, and therefore mitigate these complications (Shahdadi *et al.* 2015). Keshaviah and Collins (1988) claim that morbidity linearly declines as spKt/V increases, and that there is no optimum spKt/V.

More than nine thousand patients suffer from renal failure in South Africa and more than 1 million patients require life time dialysis in the world. The number of patients suffering from ESRD passed 2 million patients in year 2006 in the world and with a 6% annual growth, it stood above the world's population growth. The renal society of South Africa reported in 2015, of the 10 360 patients on RRT, 13.4% had a functioning renal transplant. Of the 8 969 patients on dialysis, 16.1% were on PD and 83.9% on HD. Most of the transplant and PD patients are in the public sector, the private sector has much lower proportions of patients on these RRT modalities (Davids *et al*. 2017).

2.2.2 Complications of inadequate dialysis

When estimating adequacy, clinical signs of under-dialysis should never be ignored. Toxicity or under-dialysis ultimately causes illness. Hospitalization rate is an indication of dialysis inadequacy (Lowin *et al*. 1981; Carlson *et al.* 1984). Uraemia is accompanied by cardiovascular, nervous, muscular, gastrointestinal, metabolic, dermal and haematologic complications (Hojjat, 2009). Progressive CKD and under-dialysis may result in exacerbation of heart disease, mineral and bone disease, amyloidosis, nerve damage, pericarditis, hyperkalemia, and hyperphosphatemia (Hojjat, 2009).

2.2.2.1. Cardiovascular complications

Cardiovascular disease (CVD) is the major cause of death in ESRD patients on regular HD. Patients on HD are more likely to suffer CVD than the general population. Atherosclerosis is present in most if not all long-term dialysis patients. Coronary heart disease is one of the leading causes of death in HD patients, （Levey *et al*. 1998). Diagnosis of CVD in chronic dialysis patients require coronary artery bypass surgery that has more than three times increase in mortality rate in ESRD patients than general population.

2.2.2.2. Dialysis- related Amyloidosis

Dialysis-related amyloidosis (DRA) is a serious complication of long-term dialysis therapy and is characterized by the deposition of amyloid fibrils, principally composed of βeta 2 microglobulins (β2M) (Dialysis related amyloidosis, 2016).
DRA can lead to, arthritis-like pain, joint damage, bone cysts that can lead to fracture, and carpal tunnel syndrome (Dialysis related amyloidosis, 2016).

Prevention of DRA includes:
1) Choose a treatment that removes more $ß_2$m. High flux dialyser removes more $ß_2$m.
2) Use ultrapure water for HD (Dialysis related amyloidosis, 2016).

Bones cysts due to DRA.

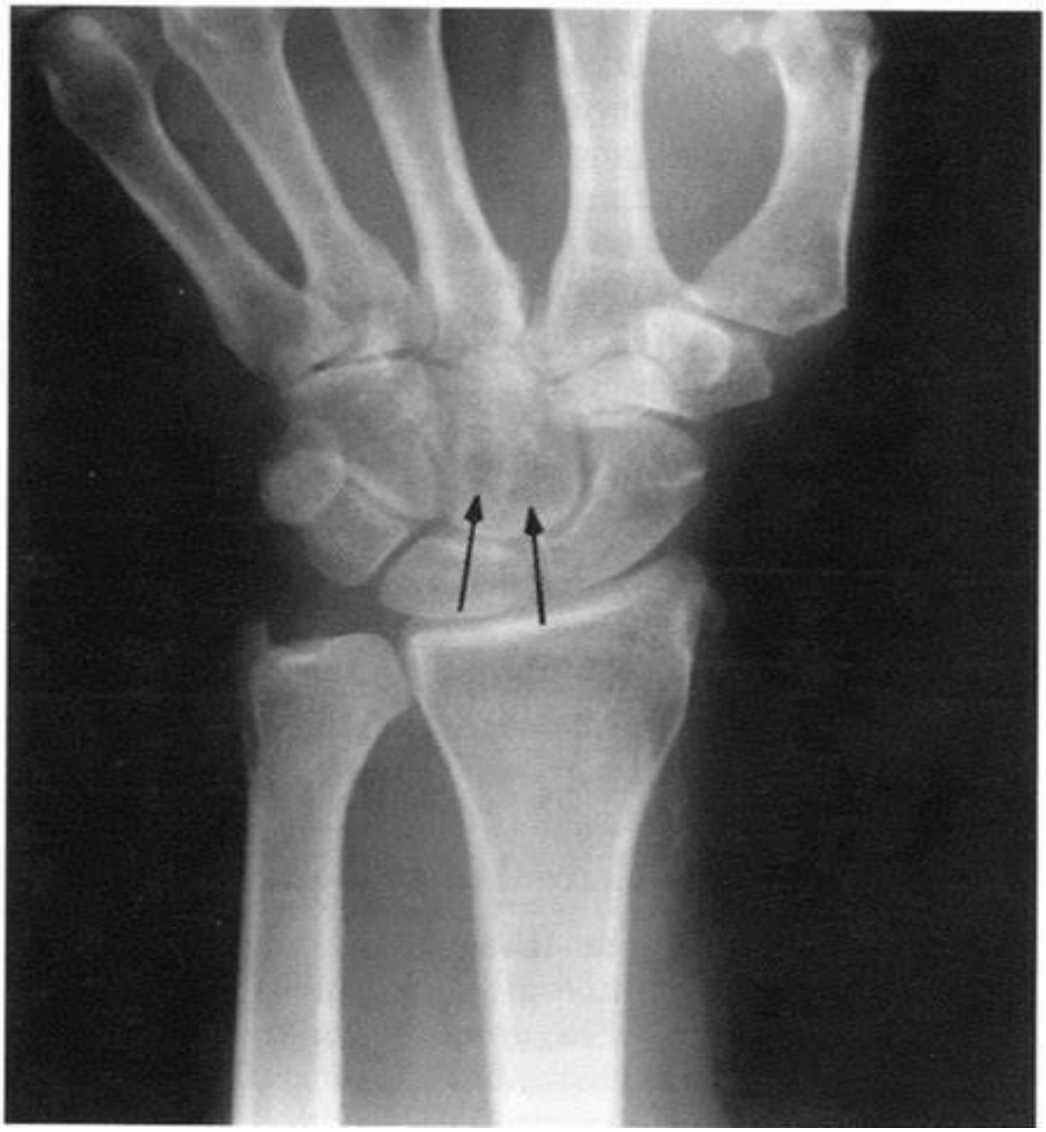

Figure: 10 Bone cysts, 2010. Available: http://intranet.com

2.2.2.3. Neuropathy

Nerve damage (neuropathy) can change sensation, causing pain, numbness, burning, or tingling. From 60% to 100% of people on dialysis have same degree of nerve damage. Research shows that neuropathy mainly happens when the GFR is

less than 12ml/min. Therefore adequate dialysis assists in the prevention of neuropathy (Mansouri *et al*. 2001)

The effects of neuropathy.

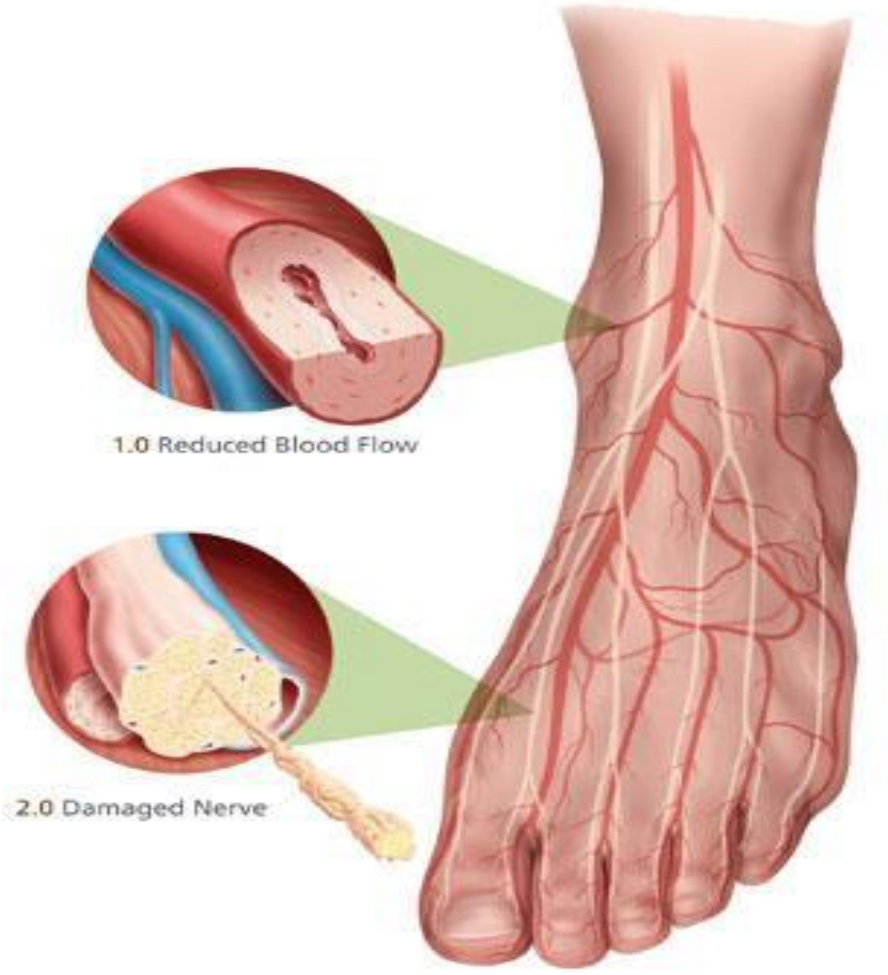

Figure 11: Neuropathy, 2014. Available : https://drdandrapacz.wordpress.com

2.2.2.4. Dialysis-associated pericarditis

Pericarditis is occasionally observed in patients on maintenance HD or PD (Rutsky *et al.* 1987). At least two factors may contribute to this problem: inadequate dialysis (i.e., the patient has uraemic pericarditis) and/or fluid overload (Lundin, 1990). It has been suggested that the two forms of uraemic pericarditis in renal failure can be distinguished by the type (serous versus haemorrhagic) of effusion

that is present, but there is significant overlap. Pathologic examination of the pericardium typically shows adhesions between the pericardial membranes, which are thicker than normal.The clinical features of pericarditis in renal failure are similar to those observed with other causes. Most patients complain of fever and pleuritic chest pain, the intensity ofwhich is quite variable (Alpert, 2003). The pain is characteristically worse in the recumbent position. A pericardial rub is generally audible, but is frequently transient. Signs of cardiac tamponade may be seen, particularly in patients with rapid pericardialfluid accumulation. However, the high prevalence of autonomic impairment in this patient population may hinder the normally observed rise in heart rate (Gunukula and Spodick, 2001). Moreover, some patients with uremic pericarditis present without symptoms or suggestive findings (chest pain or pericardial rub) on physical examination (Banerjee and Davenport, 2006).

2.2.2.5 Hyperphosphatemia

Observational studies have determined hyperphosphatemia to be a cardiovascular risk factor in CKD. Mechanistic studies have elucidated that hyperphosphatemia is a direct stimulus to vascular calcification, which is one cause of morbid cardiovascular events contributing to the excess mortality of CKD (Hruska, 2008). Prevention and correction of hyperphosphatemia is a major goal of chronic kidney disease - mineral and bone disorder (CKD–MBD) management, achievable through avoidance of a positive phosphate balance. To this aim, optimal dialysis removal, careful use of phosphate binders, and dietary phosphate control are needed to optimize the control of phosphate balance in dialysis patients. Using a mixed diffusive–convective haemodialysis techniques and increasing the number and/or the duration of dialysis techniques are all measures able to enhance phosphorus mass removal through dialysis (Cupisti *et al*. 2013).

2.2.3 Intradialytic Complications

According to Bregman *et al* (1994) acute complications commonly occur during routine HD treatments, these include intradialytic hypotension (IDH) occurring in 25 to 55 percent of treatments, cramps 5 to 20 percent, and headaches 5 percent of

treatments. Another common complication during HD is gastrointestinal (GI) symptoms (Borzou *et al.* 2016). Nausea and vomiting as GI symptoms occur in more than 10% of HD patients (Lacson *et al*. 2012). Most of its occurrences are associated with IDH (Daugirdas *et al.* 2007).

2.2.3.1. Blood Pressure

Blood pressure (BP) varies significantly in HD patients depending upon the time taken. The target pre-dialysis BP is <140mmHg/90mmHg (Healthline, 2005). A decrease in systolic BP more than 20 mmHg can be an indication of hypotension (Stefánsson *et al.* 2014). This is usually associated with symptoms of dizziness, headache, weakness, nausea, vomiting, muscle cramps, and fatigue(Zolfaghari *et al*. 2015).

Mean arterial pressure (MAP) is another indicator for hypotension. Normal MAP ranges between 70 mmHg and 100 mmHg. A MAP in this range indicates that there is enough consistent pressure in the arteries to deliver blood throughout the body. A high MAP is greater than 100 mmHg, and a reading below 60 mmHg is usually considered as a low MAP (Healthline, 2005).

2.2.3.2. Intradialytic Hypotension

Many factors may contribute to hypotension during HD. The main factor in IDH is the reduction of circulating blood volume followed by high UF and sodium uptake (Gil *et al.* 2016). A high incidence of hypotension could lead to HD insufficiency (Song *et al*. 2005).

Eating during HD has remained a topic of debate for many years within the field of nephrology. It is restricted in some countries and encouraged in many others. Surprisingly, very little research has assessed many of the proposed risks of eating during dialysis.

Providing nutrition during HD has been shown to be effective in improving whole body protein balance. Intradialytic feeding is heavy restricted in the United States primarily

because of concerns that eating during HD may exacerbate hypotensive events during the treatment. Additionally reducing dialysis adequacy and exacerbation of GI symptoms (Brandon *et al*. 2015).

The KDOQI guidelines recommend an increased caloric and protein intake (35 kcal/kg/day respectively) for maintenance haemodialysis (MHD) patient's (National Kidney Foundation, 2000). These elevated intakes maybe difficult for patients to reach, because of a variety of barriers including dietary restrictions, anorexia and socioeconomic limitations (Sehgal *et al*. 1998).

Food intake leads to displacement and shift in peripheral blood circulation to visceral blood circulation, so that the blood flow rises during the digestion of food in the villi and adjacent areas of intestinal mucosa. Particularly, digestion of fats and carbohydrates could lead to intestinal hyperaemia. Food ingestion causes an increase in heart rate thus increasing cardiac output and reducing systemic vascular resistance hence venous return is reduced and blood is accumulated in the viscera. Heart filling and cardiac output are decreased leading to hypotension (Guyton *et al*. 2006).

Sherman *et al*. (1988) demonstrated that food ingestion during HD is associated with a fall in blood pressure. The effect of eating on blood pressure during HD was examined in nine non-diabetic ESRD patients. A standard meal was given during 62 of 125 dialysis treatments in a prospectively controlled study, mean blood pressure fell significantly faster 45 minutes post-prandial in the fed treatments compared with equivalent times in the fasting treatments. In this period symptomatic hypotension occurred 13 times in 5 patients fed during dialysis compared with 2 episodes in one patient while fasting.

Barakat *et al.* (1993) further examined the mechanism behind haemodynamic adaptations to food ingestion. To accomplish this, they maximized hypovolemic stress by distributing UF over only the first 2 hours of treatment and feeding a standard meal after the first hour. They found eating caused a significant reduction in MAP as a result of reduced systemic vascular resistance and lack of increase in cardiac output. These findings supported a previous hypothesis that the drop in BP as a result of intradialytic feeding was the result of increased blood flow to the digestive system, lowering of peripheral resistance, and lack of cardiac compensation (Daugirdas, 1991).

IDH may be either symptomatic or asymptomatic. Symptomatic IDH may occur as an abrupt fall in BP. It is a major concern because it is both uncomfortable and dangerous for MHD patients. More often symptomatic hypotension requires the UF rate to be decreased or very rarely the treatment to be terminated altogether (Kistler *et al*. 2015). Interventions to treat symptomatic IDH include administration of 0.9% sodium chloride solution, which increase the osmolarity of the blood and expand plasma volume.

These interventions, however, cause significant thirst between treatments, contributing to high interdialytic fluid gains that further increase the risk of IDH in the subsequent HD treatment (Lai *et al.* 2012). Chronic fluid overload during the interdialytic period and hypotension during treatment are believed to contribute to a gradual impairment of cardiac function (Xu *et al.* 2013). These factors may contribute to the strong relationship between IDH and poor outcomes in MHD patients (Shoji *et al.* 2004).

In a study conducted by Maggiore *et al*. (1982), hypotensive episodes were more frequent in patients who were treated predominantly with high-flux HD compared with those who were treated predominantly with HDF. During HDF ultrafiltration exceeds the desired fluid loss in the patient and replacement fluid must be administered to achieve the target fluid balance, which in turn promotes haemodynamic stability in patients.

2.2.3.3. Prevention of IDH

In order to prevent IDH the following should be considered:

- Reduce intradialytic weight gain (dietary and treatment compliance)
- Avoid anti-hypertensive medication on the morning of the dialysis day
- Avoid missing dialysis and stay the entire dialysis time for treatment
- Avoid eating during dialysis (Intradialytic complications, 2006).

2.2.3.4. Patient related factors contributing to hypotension

Other factors contributing to hypotension include:

- Decreased cardiac reserve (diastolic or systolic dysfunction)
- Impaired venous compliance
- Autonomic dysfunction (diabetes, uraemia)
- Arrhythmias
- Anaemia
- Drug therapy (vasodilators and calcium channel blockers)
- Eating during treatment (increased splanchnic blood flow)
- Too low target weight estimation (Intradialytic complications, 2006)

2.2.3.5. Intradialytic food ingestion

The advantages and disadvantages of intradialytic nutrition are illustrated on table 2 (Sehgal et al. 1998).

Table 2: Proposed advantages and disadvantages of intradialytic food ingestion

Proposed Advantages	Proposed Disadvantages
Reduced mortality	Post-prandial hypotension
Improved nutritional status	Reduction in dialysis adequacy
Patient adherence and satisfaction	Gastrointestinal symptoms
Educational opportunity	Hygiene
Improved blood glucose control	Increased staff burden
Provide more appropriate food choices	Financial constraints
Reduced inflammation	Aspiration

Allowing patients to eat or consume supplements during HD treatment may be an effective strategy to increase intake on treatment days and improve nutritional status (Kalantar-Zadeh *et al.* 2011). Providing supplements high in protein during HD treatment has been shown to improve net protein balance during a single dialysis session (Pupim *et al*. 2006; Ikizler *et al*. 2002; Veeneman *et al.* 2003). This practice

may be especially beneficial in patients with morning treatments, as past research indicates that MHD patients may be in a severe catabolic state after an overnight fast (Nakaya *et al*. 2011). Additionally, intradialytic supplementation programs have been shown to improve nutritional reserve (Dong *et al*. 2011) and biochemical indicators such as serum albumin and pre-albumin (Caglar *et al.* 2002).

A reduction in treatment efficiency with solute removal is a proposed consequence arising from eating during treatment. Poor adequacy of HD has been reported to be associated with CVD, the main determinant of mortality in patients (Lacson *et al*. 1999). Two main mechanisms have been proposed to explain why intradialytic food consumption may reduce the efficiency of HD treatment. The first is that symptoms of hypotension often cause physical discomfort during treatment resulting in skipping and shortening of dialysis treatment which has shown to reduce solutes removed by dialysis and increase risk of inadequate dialysis (Gordon *et al.* 2003) The second mechanism proposes a reduction in solute removal because of sequestration of blood in the digestive tract, minimizing the blood available to be dialyzed and reducing the concentration gradient between the blood and dialysate (San Juan Miguelsanz *et al*. 2001).

Several studies have examined the influence of eating before or during HD on treatment efficiency. Singri *et al*. (2004) compared the efficiency of a single dialysis treatment after a 3 hour fast to that of a meal 2 hours before the start of dialysis in 42 dialysis patients. The meals were variable, but all contained at least 0.4 g of protein per kilogram of body weight. They found that efficiency as measured by URR and spKt/V was not reduced as a result of eating a meal before the start of the treatment. These findings may be expected given that eating before the start of HD is unlikely to lead to the circulatory changes or early termination hypothesized to contribute to a reduction in treatment efficiency.

San Juan Miguelsanz *et al.* (2001) found that intradialytic food consumption led to a significant change in the spKt/V value in 14 HD patients. Patients were assessed during standard dialysis in which they were allowed to eat, followed by restricting intradialytic food intake the following week. Efficiency was reduced in the treatment in which patients ate.

Using different methodology Muller-Deile *et al*. (2014) further examined the effect of eating during HD on treatment efficiency. They continually monitored treatment efficiency by both ultraviolet (UV) absorbance and dialysate collection. Efficiency, as measured by UV absorbance, was transiently influenced by eating. Potential explanations for the transient reduction in efficiency with UV absorbance include increasing solute appearance because of rapid absorption or release from other compartments. The combination of results from these studies suggest that observed reductions in measurements of efficiency may be the result of increased appearance rather than reduced clearance, and the clinical significance of these reductions may be limited. This argument is furthered by recent evidence from Kistler *et al.* (2015) suggesting that reduced treatment efficiency is not commonly experienced by practitioners who allow patients to eat during treatment.

In a study conducted by Kara and Aclkel (2009) twenty-five patients were enrolled in the study. The first stage involved patients given a standard meal after the first hour of treatment. The same study group underwent treatment without food 1 week later. Pre-dialysis and post-dialysis blood samples were drawn to assess spKt/V and URR. The results demonstrated that although URR and spKt/V values obtained from the HD sessions with and without food were in optimal range, according to recommendations of the KDOQI guidelines. Food consumption during HD caused a decrease in URR and spKt/V. However they analyzed the effects of food ingestion 1 h after treatment was started in HD patients. Eating at different periods of treatment may have different effects on HD adequacy. The study power was 98% for URR and 88% for spKt/V. The study power was found to be acceptable (>80%) for both values. There was a gradual decreasing trend in MAP values and increasing trend in heart rate in both sessions. The session with food intake showed a faster decrease in the MAP value after 2 hours and the value was lower than the other treatment at the end of the session. In contrast, the heart rate increased faster after the first hour in the same session and the value was higher than the session with no food intake at the end of the treatment. There was a statistically significant difference between the HD sessions regarding the MAP ($F = 32.663$; $P < 0.001$) and heart rate values ($F = 18.399$; $P < 0.001$). All dialysis treatments were tolerated without symptomatic hypotension.

In the present study the OCM feature was used to assess spKt/V and BUN sampling for the calculation of URR. Both these methods of adequacy are currently being utilized at Fresenius Medical Care and will be discussed fully in chapter 3.

CHAPTER THREE

MATERIALS AND METHODS

3.1. Study design

This quantitative prospective observational study was conducted at Fresenius medical care dialysis clinics in the North coast of KwaZulu-Natal, South Africa. The study was performed at Fresenius medical care dialysis clinics offering High-volume online HDF treatment for patients diagnosed with ESRD. The main aim of the study was to evaluate whether intradialytic food intake may affect dialysis adequacy in patients undergoing high volume online HDF treatment, to assess the incidence of post-prandial hypotension and the effects of food ingestion on blood glucose levels intra-dialysis. The study was approved by the Faculty of Health Sciences Research committee at the Durban University of Technology. The consent was obtained directly from the patients that were eligible for enrolment into the study. Permission to conduct the study was obtained from the Operations Manager at Fresenius Medical Care Pty, Ltd, South Africa.

3.1.1 Sample

Fifty four (n=54) chronic renal failure patients currently dialyzing at Fresenius Medical Care's Stanger and Victoria Kidney & Dialysis Centres were enrolled in the study. This sample size was acceptable to achieve a study power of 98%. All patients dialysing at the respective clinics were screened for eligibility to be enrolled into the study. Patients were included in the study if they were between the ages of 18 and 65 years. They must be prescribed for High-volume online HDF (Post-dilution) treatment, having an intradialytic weight gain of not more than 4 litres. They must also have a good dialysis access that obtains blood flow (Qb) rates of greater than or equal to 300ml/min. The exclusion criteria consisted of patients that were prescribed standard HD, PD or slow efficiency dialysis. Patients with a poor dialysis access (Qb ≤ 200mL/min).Those with acute renal failure, patients that are less than 3 months on dialysis, and have an intradialytic weight gain of more than 4 litres as they are prone to IDH, therefore, unable to achieve spKt/V due to fluid overload (Daugirdas, 2001).

3.1.2. Patient Consent

All patients enrolled in the study were fully orientated. The principal investigator provided a letter of information and consent to all participants. The details of the study were discussed in full to each participant prior to him/her signing the consent form. The data collection process only commenced once informed consent was received.

3.2 Materials/Equipment

3.2.1.1 5008s cordiax dialysis machine

Haemodiafiltration and OCM® were performed using Fresenius medical care's 5008s machine with the following components:

- A single use FX cordiax® dialyser (Fresenius Medical care, Germany) with biocompatible helixone membrane.
- A standard solution of bicarbonate dialysate (AC-F 213/4) with a mixing ratio of 1:44 was used for all participants. Composed of 1 part acid concentrate, 1.575 parts, (8.4%) bicarbonate concentrate and 42.425 parts purified water. The final composition after mixing: Na+138mmol/l, K+ 2.0mmol/l, Ca++1.50mmol/l, Mg++0.5mmol/l, Cl-109.0mmol/l, HCO3 -32.0mmol/l, CH3COO-3.0mmol/l and Glucose 1.0g/l.
- FMC bibag 650g (Fresenius medical care, Germany), composed of Sodium bicarbonate powder (NaHCO3).
- Fresenius medical care's arterio-venous blood lines (AV lines).
- Consumables, i.e., connection packs, syringes, sodium chloride solution 0.9%, etc.

Fresenius medical care currently uses the OCM® feature on the 5008s Cordiax HD machine for calculation of spKt/V. To achieve the objective of developing a low cost method of monitoring clearance. It was necessary to move away from the cost-intensive concept of enzymatic urea analysis (Online Clearance Monitoring, 2007). Since sodium ions represent the largest proportion of freely mobile electrolytes in the dialysis fluid and their concentration essentially determines the total conductivity of the dialysis fluid. Both sodium ions and urea molecules exhibit comparable diffusive

characteristics across a semi-permeable membrane. It is, therefore, technically possible to determine the diffusion profile of sodium ions across the dialysis membrane and thus calculate the dialysance or ionic clearance. On the basis of the dialysance of sodium ions, the “diffusibility” of urea through the membrane (permeability) and thus urea clearance can be determined (Steil *et al*. 1993).

In a validation study conducted by Kuhlmann *et al.* (2001), they produced clinical evidence that dialysance also correlates with urea clearance *in-vivo*, and that it can be determined accurately within a very low analytical error range of only ±5% by the OCM® (Fresenius medical care, Germany) (Steil *et al.* 1993).

3.2.1.2. Seca Scale®

The Seca scale® (Seca, Germany) was used to weigh the participants pre and post dialysis. Intradialytic weight gain and UF goal was determined using the patient’s pre-dialysis weight. Calibration of the device was completed prior to the commencement of the study. The device was stored in the treatment room at all times.

3.2.2. Sampling devices

Pre-dialysis and post-dialysis blood sampling was done using:

- Two serum separating blood tubes (Figure 12)
- Two 21G hypodermic needles
- Two 5 ml luerslip single use syringes

After each shift the laboratory was contacted telephonically for sample collection and testing. All the blood samples were processed in the same laboratory.

Concentrations of BUN were determined by routine clinical laboratory methods as follows:

- The samples were received and registered at the laboratory.
- The samples were then spun in a centrifuge machine over 10 minutes at a speed of 4000rpm.

- The blood samples were then loaded for urea analysis in the Siemens Dimension EXL 200® (Siemens Healthcare GmbH, Germany) chemistry system with the relevant reagent.
- The samples were then analysed for a period of approximately 5 minutes.
- The result was then printed, transmitted and flagged for review.

Figure 12: Two serum separation tubes (https://www.medisave.co.uk, 2019)

3.2.3. Monitoring devices

Blood pressure and MAP were monitored using the automatic blood pressuring monitoring feature on the 5008s machine. Haemo-gluco test was performed using the Accucheck active® glucose monitor (Roche, South Africa) and test strips.

The devices were locked within the treatment room throughout the study. The treatment room was monitored by 24 hour surveillance. All monitoring devices were serviced and calibrated prior to commencement of the study. Random quality checks were done using the Welch allyn vital signs monitor® (Welch allyn, USA).

3.3. Procedure

At Fresenius medical care dialysis clinics the OCM® feature is used to routinely monitor patients spKt/V on every treatment received. Pre-dialysis urea is done

quarterly throughout the year with the exception of medical aid requirements. Hgt is monitored for diabetic patients only twice during the treatment (Pre-dialysis and Post-dialysis), and blood pressure is measured at 30 minute intervals during the treatment which includes the MAP reading. Patients that met the inclusion criteria were well informed of the procedures regarding the study and they were only enrolled once the informed consent form was completed. All parameters were measured on consecutive mid-week dialysis sessions for both aspects (i.e., Mid-week session with intradialytic food intake, and the week following Mid-week session without intradialytic food intake).

3.3.1. Patient preparation and measurement

Initially an invite was handed out to all patients undergoing chronic HD treatment for voluntary participation in the study. The following steps were taken to prepare the patient for the procedure:

a) Patients that met the inclusion criteria and indicated interest in voluntary participation were then informed of the study procedures and consent required by the principal investigator. Consent was obtained well in advance to commencing data collection.

b) Prior to the commencement of sampling patients were made aware of their participating days a week in advance.

c) Clinical staff was also trained on sampling techniques and were made aware of the allocated sampling days for each patient as well as the variables being measured, i.e., OCM Kt/V, MAP, Hgt, Pre-dialysis urea and post- dialysis urea.

d) The principal investigator assigned codes for each patient sample (e.g., the first patient sampled was coded as P1IFI – indicating patient one intradialytic food ingestion and P1NIFI – indicating patient one no intradialytic food ingestion, patient 2 will then be coded with P2IFI and P2NIFI. The same group of participants underwent treatment with and without food ingestion.

e) The date of the testing and patients South African ID number was also recorded on the data sheet in case there was a need for review.

f) The blood forms were completed in full and SS tubes labelled and pre-packaged together with a 5ml syringe and a 21G hypodermic needle ready for use. These consumables were set up at the end of the day for the following day. Data record sheets were also readily available for use.

g) On the day of sampling as a routine procedure patients were accompanied into the clinic and weighed by staff in order to establish IDWG. Patients were to remove any items that may interfere with the accuracy of weight measurement, e.g., jacket, wallet or mobile phone that may add extra weight. The patient's dry weight was pre-determined using Fresenius medical care's body composition monitor (BCM®) for establishment of a dry weight together with the prescribed dry weight from the treating nephrologist. The current weight was subtracted from the dry weight and an UF volume was determined.

h) Patients were escorted to their station and left to rest for 5 minutes in semi fowler's position before the first automatic blood pressure was done for the assessment of MAP. The automatic blood pressure monitor used was a feature of the Fresenius medical care's 5008s machine and is able to detect systolic blood pressure, diastolic blood pressure, mean arterial pressure and pulse rate. The machine was activated to cycle an automatic blood pressure for the patient every 30 minutes.

i) Together with all other compulsory parameters set up of the OCM® feature on the Fresenius medical care 5008s machine for the calculation of spKt/V was done. Parameters that were critical to enter were haematocrit, volume-urea, the patient's age, pre-dialysis weight, height and gender and selection of treatment mode (HDF- Post dilution). This was double checked for each participant by the principal investigator to ensure accuracy.

j) Patients were then prepared for connection to the HD machine following Fresenius medical care's good dialysis care instructions procedure for connection via CVC or connection via AVF. Prior to connection of the patient to the HD machine, pre-dialysis blood sampling was done.

k) For patients with CVC blood samples were drawn immediately after 5mls of the heparin lock were removed, a plain 5mL single use syringe was connected to the CVC lumen and the catheter was then flushed 5 times before the blood sample was drawn, thereafter a normal saline flush was done, 4.5mL of the

blood sample was then inserted into a fully labelled SS blood tube using a 21g hypodermic needle for sampling of pre-dialysis urea and the remainder was used to test pre-dialysis hgt.

l) For patients with an AVF, preparation was done according to Fresenius medical care's good dialysis instructions, the pre-dialysis blood sample was then drawn from the arterial needle cannulated, 5ml of blood was withdrawn directly from the site, 4.5mL was added to a fully labelled SS blood tube using a 21g hypodermic needle and the remainder for testing pre-dialysis hgt.

m) MAP was measured in 30 minute intervals using the automatic function of Fresenius medical care's 5008s dialysis machine.

n) Post-dialysis blood sampling procedure commenced when the patient reached an effective treatment time of 3 hours and 55 minutes. The KDOQI guidelines for post-dialysis blood sampling were used. During the remaining 5 minutes of the treatment the blood flow rate was decreased to 100mL/min, and dialysate flow rate is stopped on the dialysis machine. This technique is used to prevent dilution of recirculated blood. Once the 5 minutes lapsed the patient reached an effective treatment time of 4 hours the blood pump was stopped and a blood sample of 4.5mLs was then drawn via the arterial port in the arterial blood line. The blood sample was then immediately inserted into a fully labelled SS tube. The remaining blood was used to test post- dialysis hgt.

3.3.2 Procedure with intradialytic food ingestion for patients undergoing OL-HDF

- UF goal included 600mL(360mL of Nacl used to return the patient's blood at the end of the treatment and 240mL for the meal consumed)
- Patients underwent 4 hours of OL-HDF therapy with food ingestion.
- Pre-dialysis blood sampling was done as illustrated above and food ingestion was allowed during the second hour of the treatment only.
- Patients were given a standard meal comprising of 2 slices white bread (755kj per serving) or brown bread (721kj per serving), with either white cheese,

chicken or tuna consisting of 10-20g of protein, together with either a 200mL apple juice or tea with an artificial sweetener.

- Patient's blood pressure readings continued to be monitored at 30 minute intervals and patients were monitored closely for intradialytic complications and interventions.
- As routine patients were continuously monitored for intradialytic complications and interventions, post-dialysis blood sampling for assessment of post-dialysis urea and post-dialysis hgt were done accordingly.

3.3.3 Procedure without intradialytic food ingestion for patients undergoing OL-HDF

- UF goal was adjusted to ensure that only 360mL were added to IDWG for the return of the patient's blood at the end of the treatment using Nacl solution, instead of 600mL as patients weren't consuming meals.
- Pre-dialysis blood sampling done as described above, hgt was monitored closely for incidence of hypoglycaemia pre-dialysis. HD concentrate used was AC-F 213/4, a standard diabetic formula acid mixing ratio 1:44, with a glucose level of 1.0g/l in both sampling sessions.
- Patients underwent 4 hours of OL-HDF therapy with no food ingestion. Blood pressure was monitored at 30 minute intervals, and patients were monitored closely for intradialytic complications and interventions.
- Post-dialysis blood sampling was done for detection of post-urea and post-hgt.

3.4 Data collection

The data was collected by the principal investigator from the 5008s Cordiax machine data exchange panel and the various monitoring devices that were utilised. This was then manually entered into the data sheet during the patient's treatment at their respective dialysis stations over the 4 hour duration of the treatment. The data was later entered onto an excel spread sheet on the laptop by the principal investigator. Hardcopies of the patient's blood results were obtained from the laboratory the next day for the calculation of URR. These were also entered into the data collection sheet for the respective patients and onto the excel spread sheet. Demographic records were collected from the patients file and illustrated in the data sheet.

3.4.1 Data recording with and without intradialytic food ingestion for patients undergoing OL-HDF

The following parameters were recorded directly from the HD machine by the principal investigator

- MAP recorded before the start of the treatment (T0) was monitored every 30 minutes over 4 hours.
- SpKt/V calculated by OCM® was retrieved post dialysis from the monitor of the 5008s dialysis machine.

The pre- and post-dialysis hgt was retrieved from the patient's HD record sheet and recorded on the patient data sheet by the principal investigator. The pre- and post-dialysis urea results were obtained from the laboratory for the calculation of URR done by the principal investigator. The formula for calculation of URR was used, i.e., URR=100 (1- Post-urea/Pre-urea) (Sherman et al. 1995).

3.5 Observational data

The principal investigator recorded all events that occurred during each sampling treatment for each participating patient. Some of the events listed included hypotension, hypertension, hypoglycaemia, continuous lower arterial pressure alarm, successful adjustment with vascular access to maintain Qb, decrease in Qb due to

movement and unsuccessful adjustment to vascular access, vomiting, choking and termination of treatment. The time of the event and inventions were also recorded in the data sheet. An additional line was added to the data sheet to record any other notes.

3.6 Data analysis

Upon completion of data collection, all the data was compiled in the spread sheet using MS excel 2007 and analysed with the assistance of a statistician. The data was analysed using Mann Whitney and chi square tests.

CHAPTER FOUR

RESULTS

This chapter will concentrate on describing the participants, data collected and data analysis. The proposed sample size of (n=52) was obtained with almost all the participants enrolled throughout the study period. The study was conducted at the Stanger and Victoria kidney and dialysis centres using the inclusion criteria. All the data was collected by the principal investigator. The data collected from the responses was analysed with SPSS version 26.0.The graphs, cross tabulations and other figures are used to elaborate on the quantitative data that was collected. Inferential techniques include the use of non-parametric tests which are interpreted using the p-values.

4.1. Participant's biographical distribution

There were 52 participants enrolled into the study as the total sample size. The sample consisted of two groups of participants as indicated in table 3.

Table 3: Sample groups

Groups	Venous Access	Number of Participants	Percent (%)
Group A	AV – Fistula	38	73.1
Group B	Permanent Catheter	14	26.9
	Total	52	100

The two groups of participants included the AV-Fistula group which consisted of 38 participants (73.1%) and the permanent catheter group 14 participants (26.9 %). This was a common distribution within both the dialysis centres.

4.1.1. Gender distribution

The gender distribution for both groups is represented by the bar graph (Figure 13). The total numbers of males were 24 and females were 28 for the entire groups.

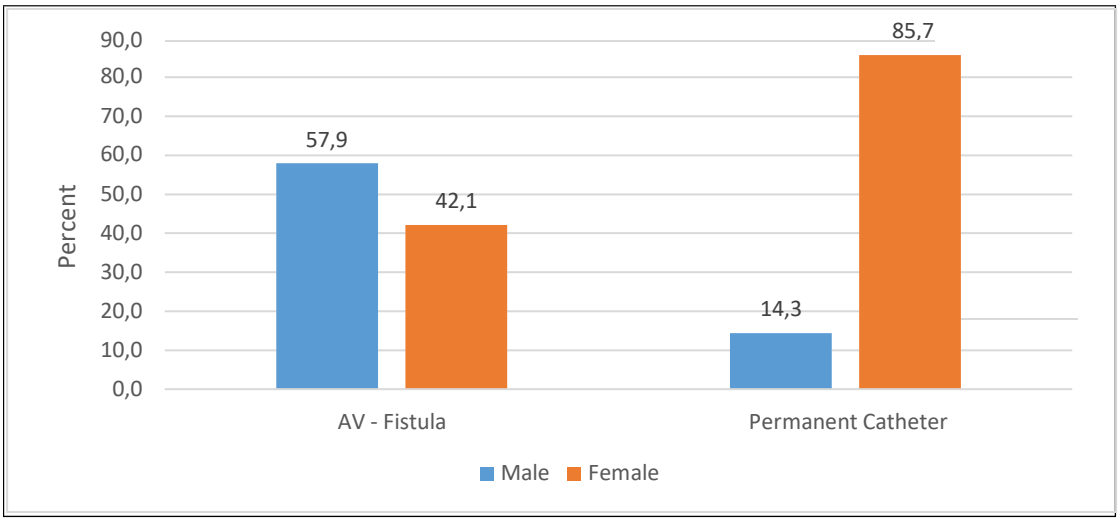

Figure 13: Gender distribution

Overall, the ratio of males to females was approximately 3:2 (57.9%: 42.1%) (p = 0.330) for the AV-Fistula group. The catheter group had approximately 1:6 (14.3%: 85.7%) (p = 0.008).

4.1.2. The racial distribution

The total sample was made of African, Indians and Whites. There were 21 Africans, 30 Indians and 1 White (Table 4).

Table 4: Racial distribution

		Vascular Access		Total
		AV - Fistula	Permanent Catheter	
African	Count	16	5	21
	% within Vascular Access	42.1%	35.7%	40.4%
Indian	Count	21	9	30
	% within Vascular Access	55.3%	64.3%	57.7%
White	Count	1	0	1
	% within Vascular Access	2.6%	0.0%	1.9%
Total	Count	38	14	52
	% within Vascular Access	100.0%	100.0%	100.0%

The AV-Fistula group had Africans, Indians and Whites with 42.1%, 55.3% and 2.6%, respectively. The Permanent catheter group had Africans and Indians and whites with 35.7%, 64.3% respectively. There were more Indian patients, followed by African patients and only one White. The white patient was found only in the AV-Fistula group. This is common as the population around the area is mostly Africans and Indians.

4.1.3. Age distribution

The age distribution for AV-Fistula group was 55.29±8.45years (Mean±SD) and for Permanent Catheter group was 56.86±10.35 years (table 5).The average age for the Catheter group is slightly higher than that for the Fistula group. However, the Mann Whiney test indicates that the difference is not significant (p = 0.326).

Table 5: Age distribution

Vascular Access	N	Mean	Median	Std. Deviation	Minimum	Maximum	Range
AV – Fistula	38	55.29	56.50	8.45	36.00	65.00	29.00
Permanent Catheter	14	56.86	62.00	10.35	34.00	65.00	31.00
Total	52	55.71	60.00	8.92	34.00	65.00	31.00

4.2. Data Analysis

4.2.1. URR

The error plots for URR were represented using figure 14.

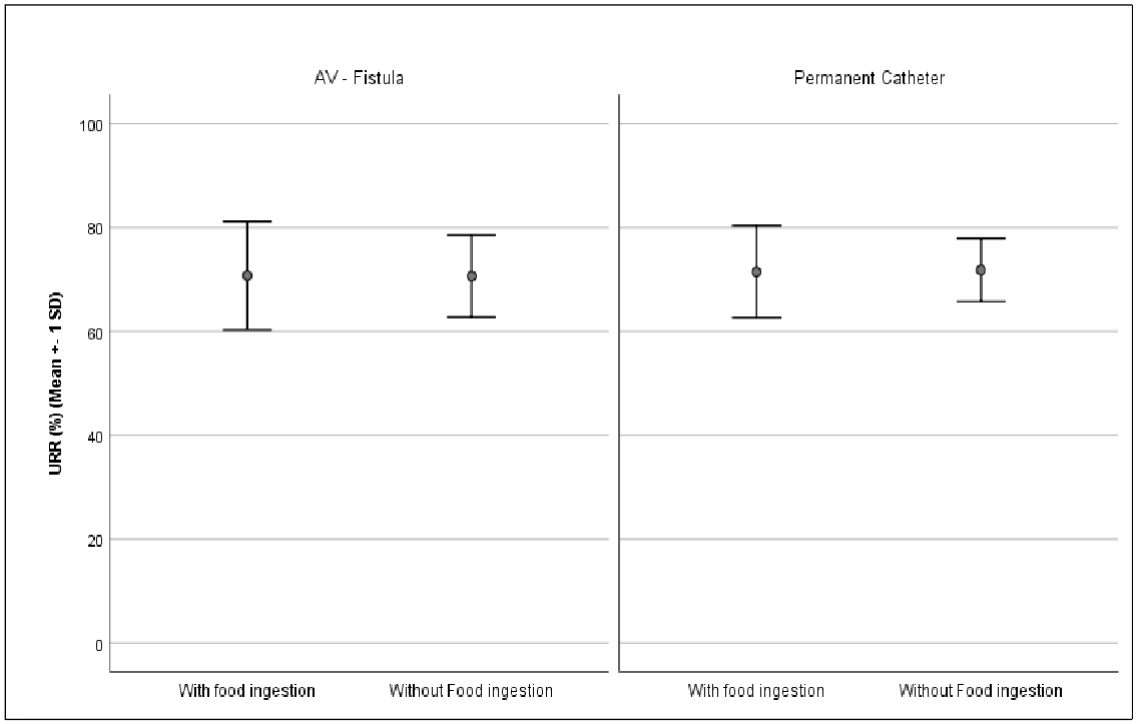

Figure 14: Error plots for URR within AV-Fistula and Permanent catheter groups

4.2.1.1. The URR within the AV-Fistula group

The error plots demonstrate that there was no significant difference between the central URR values that were obtained with intradialytic food ingestion (IFI) and without intradialytic food ingestion (No IFI) ($p = 0.379$).The results show the URR overall average of 70.68%. This overall average is within optimum range (>65%) as recommended by the KDOQI guidelines for adequacy of dialysis.

4.2.1.2. The URR within the Permanent Catheter group

The error plots within the permanent catheter group demonstrated that there was no significant difference between the central URR values with IFI and without IFI ($p = 0.972$). The overall URR average was 71.61%.This indicates that the URR achieved was in optimum range, and dialysis adequacy was achieved in the Permanent Catheter group with and without intradialytic food ingestion.

4.2.1.3 URR comparisons between the AV fistula and Permanent catheter groups

Each variable for URR was compared for the AV-fistula and Permanent catheter group. The results are shown in table 6. The table indicates that there was no significant difference in the URR achieved between the AV-Fistula and Permanent catheter groups. The p value for the group with IFI was p = 0.918 and the group without IFI was p = 0.508.

Table 6: URR comparisons between the AV-Fistula and Permanent catheter groups

	URR % - With food ingestion	URR % - Without Food ingestion
Mann-Whitney U	261.000	234.000
Wilcoxon W	1002.000	975.000
Z	-0.103	-0.662
Asymp. Sig. (2-tailed)	0.918	0.508

The data was also categorised by adequacy of dialysis determined by URR and the results are shown in table 7. The AV-Fistula group had 32 (84.2%) participants out of 38 which were reported to have achieved the optimum URR of >65 % during intradialytic food ingestion. This means that the other 6 (15.8%) participants experienced inadequacy (URR values <65%) when food ingestion occurred.

During the session without IFI 30 (78.9%) out of 38 participants were adequate and 8 (21.1%) had inadequate sessions, not reaching optimal URR level. In the AV-Fistula group, there were more participants that had adequate treatments with IFI as compared to without IFI.

The Permanent catheter group had 10 (71.4%) out of 14 participants with adequate URR during IFI and 4 (28.6%) with inadequate URR. In the sessions without IFI 11

(78.6%) out of 14 participants had inadequate URR and 3 (21.4%) had inadequate URR values achieved without food ingestion (Table7). This indicates that there were more adequate sessions encountered without IFI for the Permanent catheter group as compared to when food was ingested, which is conflicting compared to the AV-Fistula group, which appears to have the opposite result.

Table 7: Adequacy of dialysis determined by group for URR achieved

	AV – Fistula				Permanent Catheter			
	Adequate		Not adequate		Adequate		Not adequate	
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %
With food ingestion	32	84.2%	6	15.8%	10	71.4%	4	28.6%
Without Food ingestion	30	78.9%	8	21.1%	11	78.6%	3	21.4%

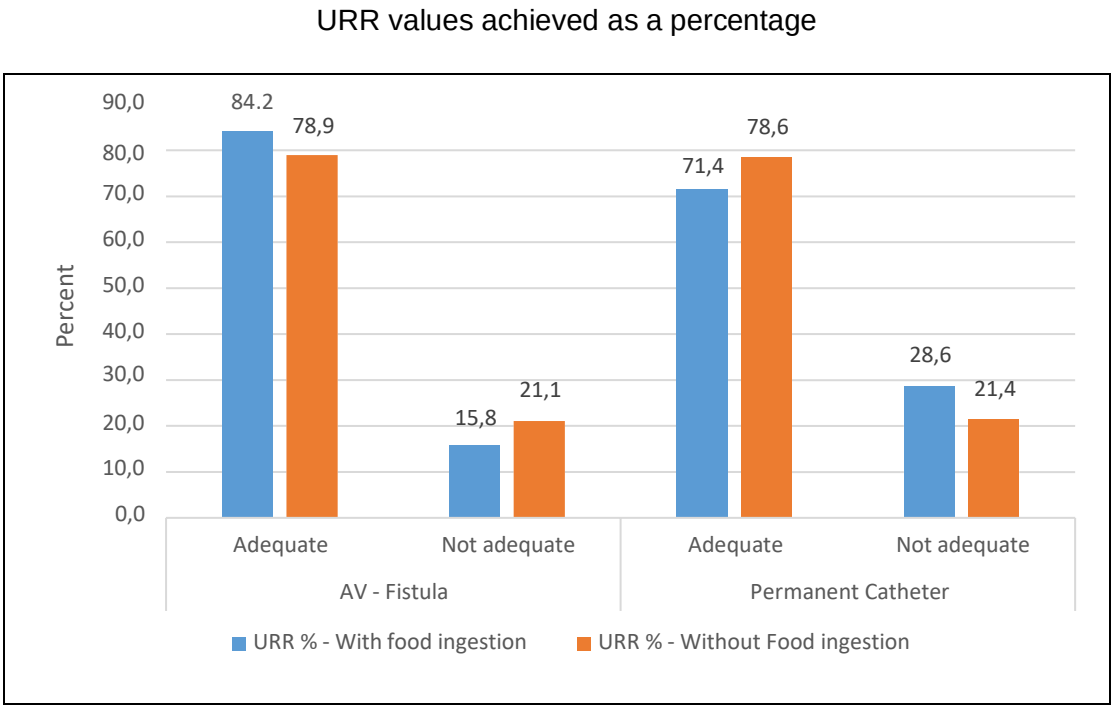

Figure 15: URR outcomes as a percentage

4.2.1.4 Chi square test for URR

A chi square test (table 8) was done to determine whether the patterns per statement were significantly different per option. The null hypothesis claims that similar numbers of patients were observed across each option for each variable. The alternate states that there is a significant difference.

The significant values (p-values) are less than 0.05 (the level of significance), it implies that the distributions were not similar, i.e., the differences between the number of participants were significant. There were more adequate readings than inadequate readings.

Within the AV-Fistula group, there were significantly more patients with adequate URR values than inadequate values ($p < 0.001$ for each).Within the Permanent catheter group, there was no significant difference in adequacy for with IFI ($p = 0.109$), whilst there was a significant difference in adequacy for without IFI ($p = 0.033$). It appears that the Permanent catheter group experienced more adequate sessions without food ingestion.

Table 8: Chi square test to determine the significance of the URR

	URR % - With food ingestion	URR % - Without Food ingestion
Chi-Square	2.571[b]	4.571[b]
Df	1	1
Asymp. Sig.	0.109	0.033

4.2.2. SpKt/V

The error plots were done to determine the variation in spKt/V for both groups. The figure 16 represents the error plots for spKt/V.

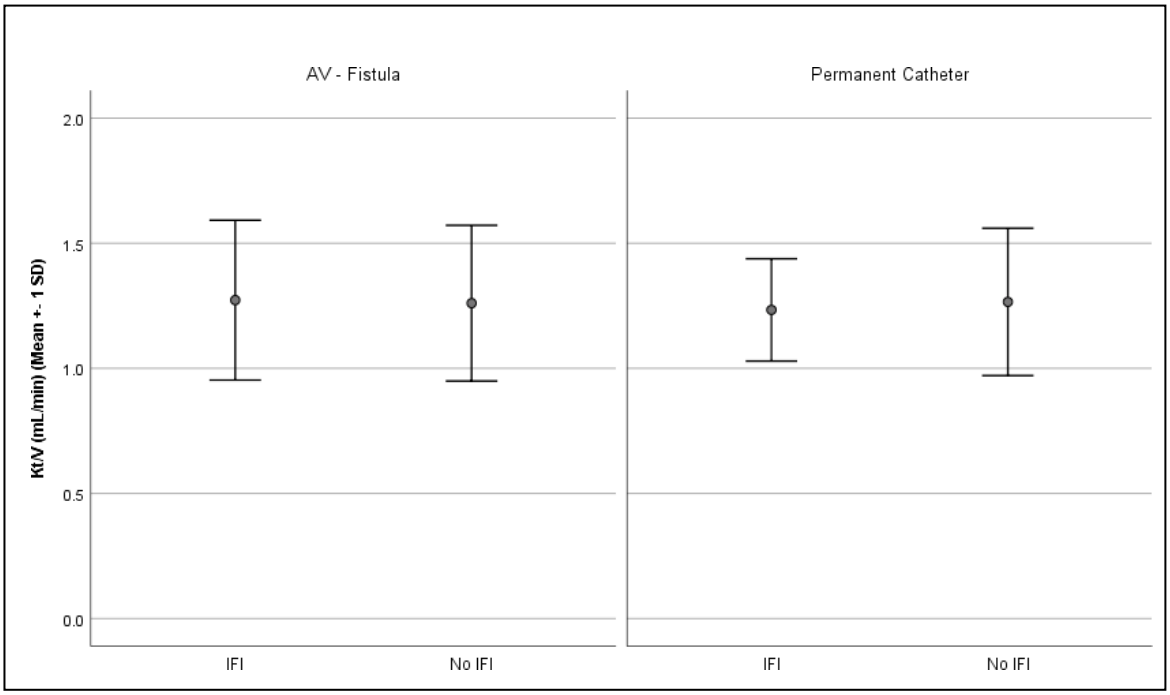

Figure 16: Error plots for spKt/V

4.2.2.1 The spKt/V for the AV-Fistula group

The error plot for the AV-Fistula group indicated that there was no significant difference between the central spKt/V values with food ingestion and without intra-dialytic food ingestion (p = 0.541). The overall average was 1.27. This is within range as recommended by the KDOQQI guidelines (spKt/V >1.2).

4.2.2.2 The spKt/V for the Permanent Catheter group

The error plot indicates that there was no significant difference between the central spKt/V values with intradialytic food ingestion and without food ingestion (p = 0.248). The overall average is 1.25. This is within range as recommended by the KDOQI guidelines.

4.2.2.3 The spKt/V comparisons between the AV -Fistula and Permanent catheter groups

Each variable for spKt/V was compared by group using Mann-Whitney test (table 9). The average spKt/V for with and without intradialytic food ingestion was higher in the AV-Fistula group (1.27) as compared to the Permanent catheter group (1.25). The results indicates that there is no significant difference in the spKt/V between the AV-Fistula and Permanent catheter groups for with food ingestion (p = 0.599) and without food ingestion (p = 0.788).

Table 9: SpKt/V comparison between the AV-Fistula and Permanent catheter groups

	IFI - Kt/V	No IFI spKt/V
Mann-Whitney U	240.500	253.000
Wilcoxon W	345.500	994.000
Z	-0.526	-0.268
Asymp. Sig. (2-tailed)	0.599	0.788

The data was also categorised by adequacy defined by spKt/V (table 10). The AV-Fistula group had 26 (68.4%) out of 38 participants that had adequate spKt/V with intradialytic food ingestion and 12 (31.6%) with inadequate spKt/V readings. For the sessions without food ingestion, the AV-Fistula group had 26 (68.4%) out of 38 participants with an adequate spKt/V and 12 (31.6%) with an inadequate spKt/V. The AV-Fistula group demonstrates the same results for spKt/V in sessions with and without intradialytic food ingestion, indicating that food ingestion had no effect on the spKt/V achieved.

The Permanent catheter group had 9 (64.3%) out of 14 participants with adequate spKt/V with intradialytic food ingestion and 5 (35.7%) with an inadequate spKt/V (Table 10 and figure 17). For the sessions without food ingestion the Permanent catheter group had 8 (57.1%) participants with adequate spKt/V and 6 (42.9%) with inadequate spKt/V. The Permanent catheter group demonstrates that there were

more participants that had adequate spKt/V's with intradialytic food ingestion than without food ingestion (64.3% and 57.1%).

Table 10: Adequacy of dialysis determined by group for spKt/V

	AV – Fistula				Permanent Catheter			
	Adequate		Not adequate		Adequate		Not adequate	
	Count	Row N %	Count	Row N %	Count	Row N %	Count	Row N %
IFI	26	68.4%	12	31.6%	9	64.3%	5	35.7%
No IFI	26	68.4%	12	31.6%	8	57.1%	6	42.9%

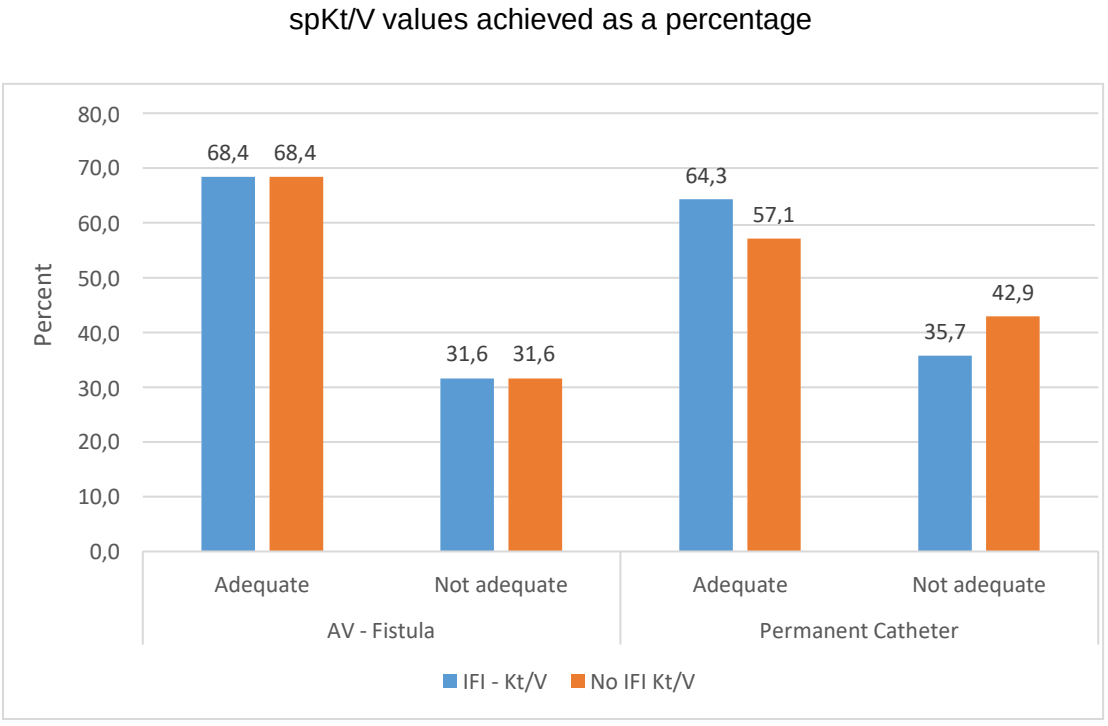

Figure 17: SpKt/V outcomes as a percentage

Overall there were more adequate spKt/V readings than inadequate ones. In the AV-Fistula group there were more adequate sessions with and without intradialytic food ingestion, suggesting that adequacy was not affected by whether or not food ingestion occurred.

The Permanent catheter group overall had more adequate sessions (64.3% and 57.1%) than inadequate ones (35.7% and 42.9%). The adequate sessions prevailed during food ingestion.

4.2.2.4. Chi square test for spKt/V

Each variable for spKt/V per group was also compared using the Chi square test (table 11). Within the AV-Fistula group, there were significantly more participants with adequate spKt/V values than inadequate values (p = 0.023 for each).

Table 11: Chi square test for spKt/V in AV-Fistula participants

	IFI - spKt/V	No IFI spKt/V
Chi-Square	5.158	5.158
Df	1	1
Asymp. Sig.	0.023	0.023

There was no significant difference in adequacy for with food ingestion (p = 0.285), nor for without food ingestion (p = 0.593), within the Permanent catheter group (table 12).

Table 12: Chi square test for spKt/V in Permanent catheter participants

	IFI - spKt/V	No IFI spKt/V
Chi-Square	1.143	.286
Df	1	1
Asymp. Sig.	0.285	0.593

4.2.3 Haemo-glucose test

The error plot was done to determine the variations in Hgt amongst the groups. Figure 18 represents the error plots for Hgt for the AV-Fistula and Permanent catheter groups.

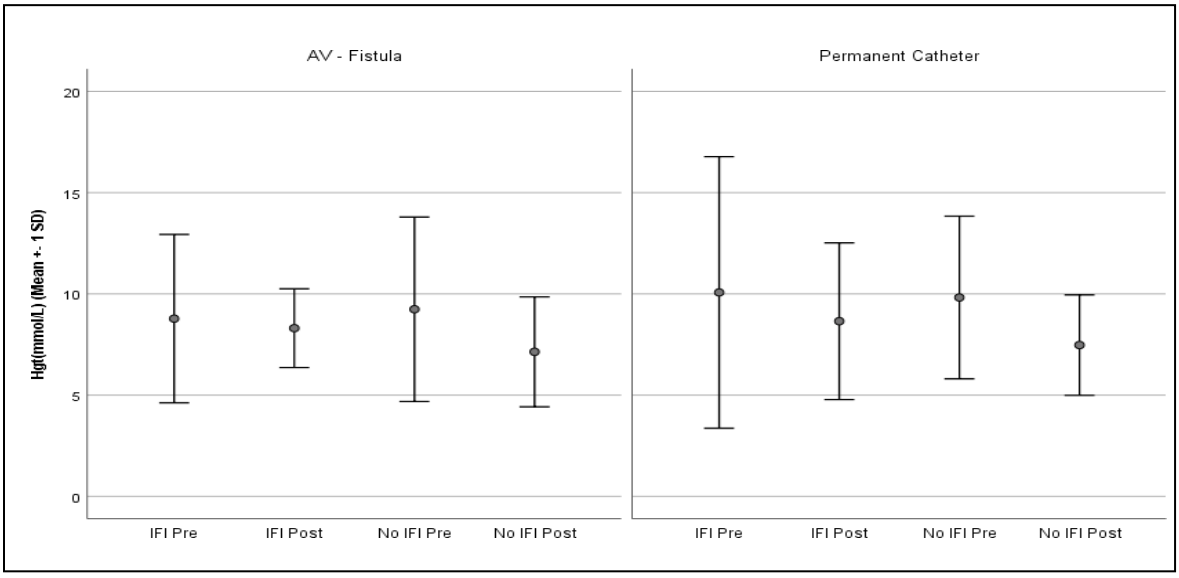

Figure 18 Error plots for Hgt

4.2.3.1 The Hgt for the AV-Fistula group

Table 13: Pre- versus post-Hgt with IFI and without IFI for AV fistula group

	IFI Post Hgt(mmol/L) - IFI Pre Hgt(mmol/L)	No IFI_PostHgt(mmol/L) - No IFI_PreHgt(mmol/L)	No IFI_PreHgt(mmol/L) - IFI Pre Hgt(mmol/L)	No IFI_PostHgt(mmol/L) - IFI Post Hgt(mmol/L)
Z	-.704[d]	-4.419[c]	-1.219[d]	-4.062[c]
Asymp. Sig. (2-tailed)	0.482	0.000	0.223	0.000

The first two columns compared the Pre- versus Post-Hgt for intradialytic food ingestion and No intradialytic food ingestion. It is observed that there was a significant difference between the Pre versus Post for No IFI ($p < 0.001$), but not for IFI ($p =$

0.482). The pre- versus post-without food ingestion is significantly lower than the pre- versus post-with food ingestion. The lack of food consumption caused a decrease in blood glucose levels compared to when food was ingested ($p < 0.001$ versus $p = 0.482$).

The last two columns compared the Pre-Hgt values for intradialytic food ingestion and No intradialytic food ingestion ($p = 0.223$), and for Post-Hgt between IFI and No IFI ($p < 0.001$). That is, there was a significant difference between the No IFI post value and the IFI post value. The Hgt values post-dialysis without food ingestion were significantly lower than those obtained with food ingestion.

4.2.3.2 The Hgt for the Permanent Catheter group

Table 14: Pre- verses post-Hgt with IFI and without IFI for Permanent catheter group.

	IFI Post-Hgt(mmol/L) - IFI Pre-Hgt(mmol/L)	No IFI_Post-Hgt(mmol/L) - No IFI_Pre-Hgt(mmol/L)	No IFI_Pre-Hgt(mmol/L) – IFI-Pre Hgt(mmol/L)	No IFI_Post-Hgt(mmol/L) - IFI Post-Hgt(mmol/L)
Z	-.785[c]	-3.172[c]	-.491[d]	-1.766[c]
Asymp. Sig. (2-tailed)	0.432	0.002	0.624	0.077

It can be observed that there was a significant difference between the Pre- versus Post-Hgt for No IFI ($p = 0.002$), but none for the comparisons for food ingestion ($p > 0.05$). The pre- versus post-Hgt for without food ingestion appears to be lower.

4.2.3.3 Comparisons between the AV-Fistula and Permanent catheter groups

Each variable for Hgt was compared per groups using Mann-Whitney test (table 15).

Table 15: Comparison between AV-Fistula and Permanent catheter group

	IFI Pre-Hgt(mmol/L)	IFI Post-Hgt(mmol/L)	No IFI_Pre-Hgt(mmol/L)	No IFI_Post-Hgt(mmol/L)
Mann-Whitney U	256.000	248.000	240.000	232.500
Wilcoxon W	997.000	353.000	981.000	973.500
Z	-0.206	-0.372	-0.537	-0.692
Asymp. Sig. (2-tailed)	0.837	0.710	0.592	0.489

There was no significant difference between the groups for each of the variables as all of the p-values were greater than 0.05.

The data was also categorised by type and the results are shown in Figure 19.

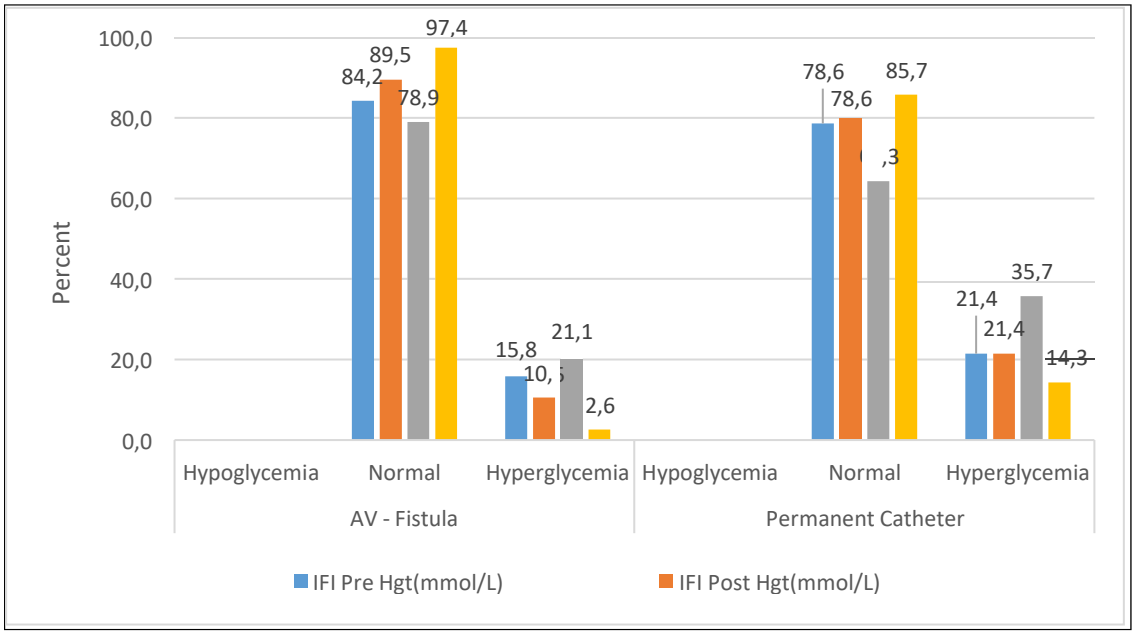

Figure 19: Hgt comparison between AV-Fistula and Permanent catheter groups

Hypoglycaemia is defined as a blood glucose level less than 4.0mmol/L and hyperglycaemia when blood glucose levels are greater than 11mmol/L. The Hgt comparison between AV-Fistula and Permanent catheter groups is also represented in figure 19. There were no participants classified with hypoglycaemia as all of the minimum values were greater than 4.0mmol/L. With food ingestion the AV-Fistula group demonstrated 82.2% pre-Hgt readings to be normal and 15.8% hyperglycaemic. Post-Hgt, 89.5% were normal while 10.5% were hyperglycaemic. Without food ingestion the AV-Fistula group demonstrated 78.9% pre-Hgt readings to be normal and 21.1% hyperglycaemic. Post-Hgt, 97.4% were normal while 2.6% were hyperglycaemic. The AV-Fistula group had the best outcomes for Hgt without food ingestion as 97.4% of participants were reported to have been normal post-dialysis when food was not ingested.

With food ingestion the Permanent catheter group demonstrated 78.6% pre-Hgt readings to be normal while 21.4% were hyperglycaemic. Post-Hgt, 78.6% were normal and 21.4% were hyperglycaemic. Without food ingestion the Permanent catheter group demonstrated 64.3% pre-Hgt readings to be normal and 35.7% hyperglycaemic. Post-Hgt without food ingestion for the Permanent catheter group resulted in 85.7% normal hgt and 14.3% hyperglycaemic. The Permanent catheter group had no change in pre and post-Hgt outcomes with food ingestion, however, without food ingestion more participants experienced normal post-Hgt levels (85.7%) as compared to with food ingestion (78.6%).

Table 16 represents the chi square p-values for the AV-Fistula group. There were significantly more patients with normal than abnormal readings (p=0.000).

Table 16: Chi square p-values for the AV-Fistula group

	IFI Pre Hgt(mmol/L)	IFI Post Hgt(mmol/L)	No IFI_PreHgt(mmol/L)	No IFI_PostHgt(mmol/L)
Chi-Square	17.789[b]	23.684[b]	12.737[b]	34.105[b]
Df	1	1	1	1
Asymp. Sig.	0.000	0.000	0.000	0.000

Table 17 represents the chi square p-values for the Permanent catheter group. For IFI pre-Hgt and IFI post-Hgt (p=0.033). For no IFI pre-Hgt (p=0.285) and for no IFI post-Hgt (p=0.008). There were significantly more patients with normal than abnormal readings.

Table 17: Chi square p-values for the Permanent catheter group

	IFI Pre-Hgt(mmol/L)	IFI Post-Hgt(mmol/L)	No IFI_Pre-Hgt(mmol/L)	No IFI_Post-Hgt(mmol/L)
Chi-Square	4.571[b]	4.571[b]	1.143[b]	7.143[b]
Df	1	1	1	1
Asymp. Sig.	0.033	0.033	0.285	0.008

4.2.4 Mean arterial pressure

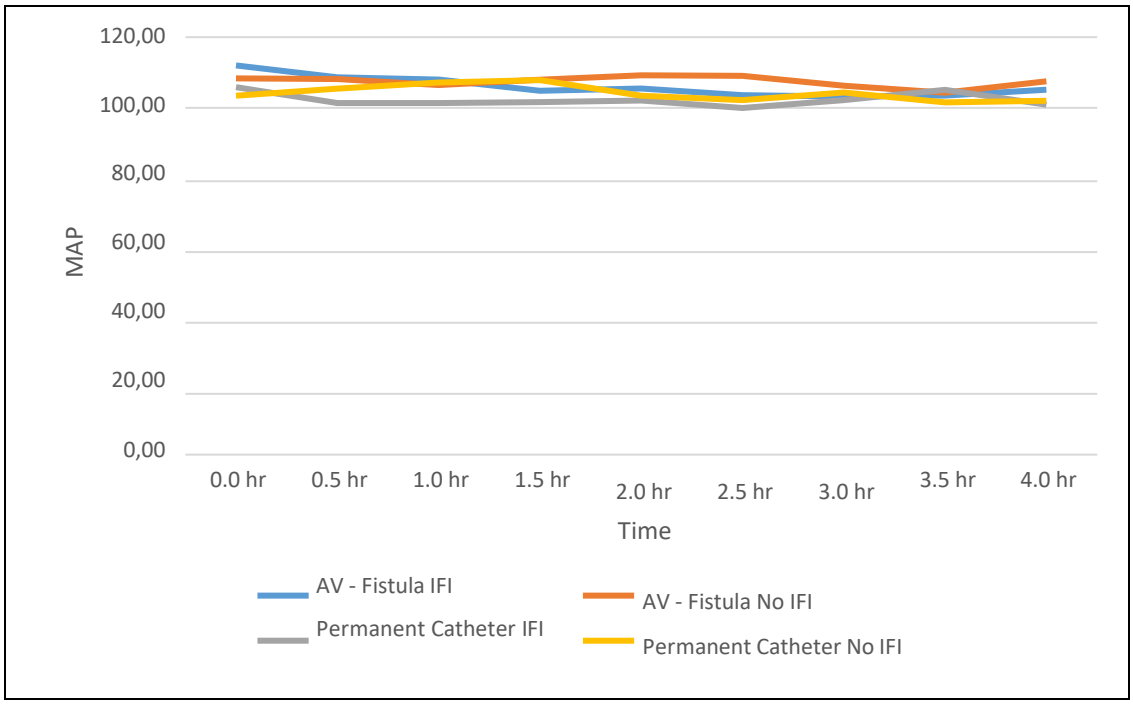

Figure 20: MAP for AV-Fistula and Permanent catheter groups

The Mean±SD for MAP demonstrated for the AV-Fistula group in the time 0.0 hr to 4.0 hr in intervals of 1 hr with IFI was 111.97±22.86, 107.95±20.5, 105.42±19.48, 103.29±20.9 and 105.14±18.80. Without IFI was 108.37±19.45, 106.50±20.20, 109.21±20.85, 106.29±20.94, and 107.53 ± 18.31.

The Permanent catheter group demonstrated Mean±SD for MAP in the time 0.0 hr to 4.0 hr in intervals of 1 hr with IFI was 105.86±13.38, 101.36±11.32, 102.14±15.09, 102,21±20.01, and 100.93±18.66. Without IFI 103.50±15.46, 107.14±15.36, 103.50±19.51, 103.46±18.40, and 102.0±15.93.

The average values for the four data sets seem similar. This was an indication that MAP remained stable for most participants with and without food ingestion. A Wilcoxon test between consecutive time periods showed no significant difference in the average value of MAP recorded , except for the time difference 4.0 hr - 3.5 hr for No IFI for Fistula ($p = 0.030$). For each time period, there was no significant difference between two groups for IFI and No IFI (all $p > 0.05$).

4.2.4.1 Hypotensive episodes experienced per group

A decrease in systolic blood pressure of more than 20 mmHg from the previous reading can be an indication of hypotension (Stefánsson et al. 2014). During sessions without food ingestion 7 (13.5%) were recorded to have hypotensive episodes and 45 (86.5%) did not experience hypotensive episodes (table 18). There was a significant difference in the number of patients who did not have a hypotensive episode compared to those who did ($p < 0.001$).

Table 18: Hypotensive Episode without food ingestion

	Frequency	Percent
Yes	7	13.5
No	45	86.5
Total	52	100.0

During sessions with food ingestion 20 (38.5%) were recorded to experience hypotensive episodes and 32 (61.5%) did not experience hypotensive episodes with food ingestion (table 19).

Table 19: Hypotensive episode with food ingestion

	Frequency	Percent
Yes	20	38.5
No	32	61.5
Total	52	100.0

The Chi square test was done to compare the hypotensive episodes within the groups (table 20). There was no significant difference in the number of patients who did not have a hypotensive episode compared to those who did (p = 0 096).

Table 20: Chi square test

Test Statistics		
	Hypotensive Episode - No IFI	Hypotensive Episode – IFI
Chi-Square	27.769[a]	2.769[a]
Df	1	1
Asymp. Sig.	0.000	0.096
a. 0 cells (0.0%) have expected frequencies less than 5. The minimum expected cell frequency is 26.0.		

The frequency of hypotensive episodes were greater with food ingestion (38.5%) as compared to without food ingestion (13.5%), this is an indication of post-prandial hypotension which may have occurred during food ingestion. There were fewer hypotensive episodes without food ingestion (86.5%) compared to with food ingestion (61.5%).

4.2.5. Effect Size

The differences between IFI and No IFI, or Pre- vs Post-dialysis were determined and used as the dependent variable in the univariate analysis option of the general linear model. Various independent variables and covariates were identified and their effect on the differences was determined.

The effect is measured using the partial eta squared value as indicated in tables 21 to table 24. Partial eta squared gives the effect of the independent variable on the dependent variable.

Table 21: Effect size for URR

Tests of Between-Subjects Effects						
Dependent Variable: URR_IFI_NoIFI_Difference	URR_IFI_NoIFI_Difference					
Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	766.951[a]	8	95,869	1,225	0,308	0,186
Intercept	29,865	1	29,865	0,382	0,540	0,009
Age	0,154	1	0,154	0,002	0,965	0,000
Gender	515,316	1	515,316	6,587	0,014	0,133
Race	266,859	2	133,429	1,706	0,194	0,073
VascularAccess	253,347	1	253,347	3,238	0,079	0,070
Gender * Race	24,472	1	24,472	0,313	0,579	0,007
Gender * VascularAccess	247,143	1	247,143	3,159	0,083	0,068
Race * VascularAccess	137,638	1	137,638	1,759	0,192	0,039
Gender * Race * VascularAccess	0,000	0				0,000
Error	3364,030	43	78,233			
Total	4131,000	52				
Corrected Total	4130,981	51				

4.2.5.1 The difference for URR IFI and No IFI

Race had a medium to large effect on the difference observed for URR (partial eta squared was 0,073). The Indian race had a higher mean value (71.2% with food and 71.1 % without food ingestion). The vascular access had a medium to large effect on the difference for URR. The AV-Fistula group had a higher mean value.

Table 22: Effect size for SpKt/V

Dependent Variable: KtV_IFI_NoIFI_Difference	KtV_IFI_NoIFI_Difference					
Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	.711[a]	8	0,089	1,794	0,105	0,250
Intercept	0,045	1	0,045	0,906	0,347	0,021
Age	0,125	1	0,125	2,513	0,120	0,055
Gender	0,159	1	0,159	3,205	0,080	0,069
Race	0,252	2	0,126	2,547	0,090	0,106
VascularAccess	0,138	1	0,138	2,776	0,103	0,061
Gender * Race	0,018	1	0,018	0,367	0,548	0,008
Gender * VascularAccess	0,090	1	0,090	1,814	0,185	0,040
Race * VascularAccess	0,102	1	0,102	2,063	0,158	0,046
Gender * Race * VascularAccess	0,000	0				0,000
Error	2,131	43	0,050			
Total	2,842	52				
Corrected Total	2,842	51				
a. R Squared = .250 (Adjusted R Squared = .111)						

4.2.5.2 The difference for Kt/V IFI and no IFI

The age had a medium to large effect on the difference observed for spKt/V (partial eta squared was 0.055). Participants between the ages of 60-65 had a higher mean spKt/V. Gender had a medium to large effect on the spKt/V achieved (partial eta squared 0.069). Females had a higher mean spKt/V. Race and vascular access had a medium to large effect on the difference observed for spKt/V (partial eta squared 0.106 and 0.061), African patients and AV-Fistula had a higher mean spKt/V. Gender together with vascular access and race together with vascular access had a small effect on the difference observed for spKt/V (partial eta squared 0.040 and 0.046).

Table 23: The effect size for IFI Hgt

Dependent Variable: Hgt_IFI_Post_Pre_Difference	Hgt_IFI_Post_Pre_Difference					
Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	72.357[a]	8	9,045	0,662	0,722	0,110
Intercept	8,296	1	8,296	0,607	0,440	0,014
Age	16,990	1	16,990	1,243	0,271	0,028
Gender	2,491	1	2,491	0,182	0,672	0,004
Race	1,596	2	0,798	0,058	0,943	0,003
VascularAccess	4,295	1	4,295	0,314	0,578	0,007
Gender * Race	0,246	1	0,246	0,018	0,894	0,000
Gender * VascularAccess	12,997	1	12,997	0,951	0,335	0,022
Race * VascularAccess	0,025	1	0,025	0,002	0,966	0,000
Gender * Race * VascularAccess	0,000	0				0,000
Error	587,645	43	13,666			
Total	687,480	52				
Corrected Total	660,002	51				
a. R Squared = .110 (Adjusted R Squared = -.056)						

4.2.5.3 The difference for Hgt IFI Pre- and post-dialysis

The age together with gender and vascular accesses had a small effect on the difference observed for hgt IFI obtained pre-and post-dialysis. The partial eta squared was 0.028 and 0.022, respectively.

Table 24: The Effect size for No IFI Hgt

Dependent Variable: Hgt_NoIFI_Post_Pre_Difference	Hgt_NoIFI_Post_Pre_Difference					
Source	Type III Sum of Squares	Df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	48.973[a]	8	6,122	0,747	0,650	0,122
Intercept	2,680	1	2,680	0,327	0,570	0,008
Age	0,281	1	0,281	0,034	0,854	0,001
Gender	7,444	1	7,444	0,909	0,346	0,021
Race	16,637	2	8,319	1,016	0,371	0,045
VascularAccess	2,935	1	2,935	0,358	0,553	0,008
Gender * Race	8,595	1	8,595	1,050	0,311	0,024
Gender * VascularAccess	3,569	1	3,569	0,436	0,513	0,010
Race * VascularAccess	0,119	1	0,119	0,015	0,904	0,000
Gender * Race * VascularAccess	0,000	0				0,000
Error	352,158	43	8,190			
Total	645,820	52				
Corrected Total	401,131	51				
a. R Squared = .122 (Adjusted R Squared = -.041)						

4.2.5.4 The difference for hgt no IFI pre- and post-dialysis

The gender and race had a small effect on the difference observed for Hgt no IFI pre- and post-dialysis, the partial eta squared was 0.021 and 0.045, respectively.

CHAPTER FIVE

DISCUSSION

The study prospectively compared spKt/V and URR values with and without food ingestion in adult patients diagnosed with chronic renal failure undergoing OL-HDF therapy in an attempt to define the effect of eating during OL-HDF treatment. The aim of the study was to evaluate whether intradialytic food intake may affect dialysis adequacy in patients undergoing OL- HDF treatment. The objectives were to determine the adequacy of HDF treatment by pre- and post-dialysis blood sampling in patients with and without food ingestion. To compare the adequacy of treatment between patients that is with and without food ingestion during HDF, and to determine the effects of food ingestion on blood glucose levels in patients with and without food ingestion.

Urea is only a marker solute and measures of dialysis adequacy such as spKt/V and URR are only surrogates for the clearance of other small molecular weight solutes (National kidney foundation, 2009). Adequate dialysis means enough treatment to help patients live long and well. Hojjat (2009) demonstrated that progressive CKD and under-dialysis may result in exacerbation of heart disease, mineral and bone disease, amyloidosis, nerve damage, pericarditis, hyperkalemia, and hyperphosphatemia. Enhancing the quality of dialysis is the main factor for reducing these complications and mortality rate in patients with ESRD (Hojjat, 2009). High-adequacy dialysis may ameliorate uraemic side effects and increase quality of life in CKD patients (Shahdadi *et al*. 2015).

There are many factors that may influence adequacy of dialysis, e.g., the duration of a dialysis session, blood flow rate during the treatment, recirculation, adequacy of vascular access, and BUN sampling procedure (San Juan Miguelsanz, 2008; Singri, 2004; Teixeira Nunes, 2004). The KDOQI guidelines recommend that the minimum delivered dialysis dose per session should be Kt/V of 1.2 or a URR of 65% for HD patients dialyzed three times weekly (National kidney foundation, 2009).

Food ingestion during HD treatment has remained controversial. The effects of food ingestion on dialysis adequacy in patients undergoing HD have been studied but the effects on patients undergoing OL-HDF have not been studied. The present study examined the effect of intradialytic food ingestion in 52 adult patients undergoing OL-HDF. The sample comprised of two groups, the AV-Fistula group (73.1%) and the Permanent catheter group (26.9%).There were more females than males that participated in the study and the ratio of males to females was, approximately, 3:2 for the AV-Fistula group and 1: 6 for the Catheter group.

The Participants were allowed food ingestion in the second hour of their treatment. The results of the present study demonstrated that the spKt/V and URR values achieved from the OL-HDF sessions with and without intradialytic food ingestion were in optimal range as recommended by the KDOQI guidelines (mean URR with food ingestion 70.92% ($p = 0.918$) and without food ingestion 70.94%($p = 0.508$). The mean spKt/V with food ingestion was 1.26 ($p = 0.599$) and without food ingestion 1.26 ($p = 0.788$).This means that the intradialytic food ingestion did not negatively affect the spKt/V or URR achieved. This is evident in both patients with Permanent catheters and AV-Fistulas. The spKt/V and URR values for both groups were above the recommended target and there was no significant difference in these parameters in the sessions with and without food ingestion.

Four studies have examined the influence of eating before or during HD on treatment efficiency i.e., Kara and Acikel (2009), San Juan Miguelsanz *et al*. (2001), Muller-Deile *et al.* (2014) and Singri *et al.* (2004). The study conducted by Kara and Acikel (2009) in Turkey demonstrated the effects of intradialytic food ingestion on spKt/V and URR in 25 patients undergoing conventional HD. They found that food intake during HD session decreased the mean URR and spKt/V values. The mean URR of 67.8 % and spKt/V of 1.4 ($P < 0.001$) was obtained during sessions withfood ingestion and mean URR 72.1% and spKt/V of 1.6 ($P < 0.001$) during sessions without food ingestion. The spKt/V and URR results obtained in the present studyare within the recommended range according to the KDOQI guidelines but appearto be lower than that achieved by Kara and Acikel (2009).

In another study by Singri *et al.* (2004) which compared the efficiency of a single dialysis treatment after a 3 hour fast, to that of a meal 2 hours before the start of dialysis in 42 dialysis patients. They found that URR and spKt/V was not reduced as a result of eating a meal before the start of the treatment. These findings may be expected given that eating before the start of HD is unlikely to lead to the circulatory changes or early termination hypothesized to contribute to a reduction in treatment efficiency.

San Juan Miguelsanz *et al*. (2001) assessed 14 patients during standard dialysis in which they were allowed to eat, followed by restricting intradialytic food intake the following week. The results of this study demonstrated that efficiency was reduced in the treatment in which patients ate (URR 71.56% vs. 73.6%, and spKt/V 1.54 vs. 1.65). The present study differs from this, in that, 52 patients underwent OL-HDF treatment in which they were allowed to eat during the second hour of their treatment followed by restricting intradialytic food ingestion the following week, the results demonstrated no effect on dialysis adequacy.

Using different methodology Muller-Deile *et al*. (2014) further examined the effect of eating during HD on treatment efficiency. They continually monitored treatment efficiency by both UV absorbance and dialysate collection. Efficiency as measured by UV absorbance, but not dialysate clearance, was transiently influenced by eating. Potential explanations for the transient reduction in efficiency with UV absorbance include increasing solute appearance because of rapid absorption or release from other compartments. The combination of results from these studies suggest that observed reductions in measurements of efficiency may be the result of increased appearance rather than reduced clearance, and the clinical significance of these reductions may be limited (Kistler *et al*. 2014).

There are two proposed mechanisms that explain why intradialytic food ingestion may reduce dialysis adequacy. The first is that the treatment is prematurely discontinued due to severe symptoms of hypotension. The shortened HD time would eventually lead to poor solute removal hence poor dialysis adequacy and quality of life, although this has not been documented in literature (Kara and Acikel, 2009). During the present

study there were no reported cases of shortened treatment time or premature termination of treatment during the sessions with and without intradialytic food ingestion. Although 38.5% of the participants experienced hypotensive episodes during food ingestion and 13.5% without food ingestion, there were no drastic interventions required such as premature termination of treatment.

All of the participants completed their treatment as prescribed. The second is that food ingestion may lead to sequestration of blood in the digestive tract which minimizes the blood available to be dialysed. Thereby reducing the concentration gradient between blood and dialysate and this may lead to symptoms of post- prandial hypotension (San Juan Miguelsanz *et al*. 2001). A healthy individual is predicted to have a 20% decrease in systemic vascular resistance, 35% increase in the splanchnicblood flow and 69% increase in the hepatic blood flow following a meal (Sherman et al. 1988). Furthermore digestion of food decreases the amount of blood filtered duringa certain period, which could influence urea removal (Eggers, 2000).

Decreasing blood flow and UF rate in hypotensive patient's further decrease HD adequacy. The patient receives less than the prescribed HD dose and cannot reach the UF target. Hypotension episodes during the present study were primarily treated with trendelenburg position. The patients UF goal and blood flow rates remained unchanged; this would have played a vital role in the patients achieving their target spKt/V and URR. Prolonged hypotension during the HD session is also associated with an increases urea rebound (National kidney foundation, 2009).

Several studies have also examined the relationship between food intake and hypotension during HD. Zoccali *et al*. (1989) evaluated the blood pressure changes after food intake and during HD. They studied the impact of an identical meal (400 kcal) on 13 patients with uraemia undergoing HD. Mean blood pressure was significantly reduced two hours after the meal in the group compared to the control group. In another study Sherman *et al.* (1988) investigated the effect of food intake on blood pressure during HD on 9 non-diabetic patients with CKD. The results showed that after about an hour of eating both systolic blood pressure and diastolic blood pressure significantly dropped than those who were kept fasting during HD at the

same time. Kistler *et al*. (2014) found that people who consumed food during HD suffered from hypotension. The results of Sivalingam *et al*. (2008) study showed a significant decrease in blood pressure 30 minutes after food intake. In the study by Kara and Akil (2009) both sessions showed a trend for a gradual decrease in the MAP value and an increase in the heart rate. The MAP value for the participants was lower in the session with food intake than the other session. Muller *et al*. (2014) study can be noted as another conflicting study. This study was conducted on 40 patients to evaluate the impact of food intake on haemodynamic status and treatment effectiveness. The results did not show any reduction in the systolic and diastolic blood pressure and also MAP after the food intake. Therefore, the researchers suggested that food intake during HD, especially in stable patients can be tolerated better.

The present study differs from previous studies in that all the patients studied underwent OL-HDF treatment, whereas, in the studies conducted by San Juan Miguelsanz *et al.* (2001), Muller-Deile *et al.* (2014), and Kara and Acikel (2009) patients underwent conventional HD. The benefits of haemodynamic stability during OL-HDF treatment is likely to have played a vital role in the results obtained. As proven in a study conducted by Tiranathanagul *et al.* (2009) where a decrease in the incidence of intradialytic undesired events, including hypotension was noted in patients undergoing OL-HDF treatment. An apparent increase in appetite and improvement in overall wellbeing were recorded by most patients after switching to OL- HDF.

In the present study, MAP was recorded for the assessment of post-prandial hypotension. During the sessions with no intradialytic food ingestion, 13.5% ofpatients experienced hypotensive episodes while 86.5% of patients did not experience hypotensive episodes. During food ingestion 38.5 % of patients experienced a decrease in MAP by 20 mmHg or asymptomatic hypotensive episodesand 61.5% did not. Although more hypotensive episodes occurred during the sessions with food ingestion as compared to no food ingestion (38.5% vs 13.5%) for each timeperiod, there was no significant difference between the two groups with and without intradialytic food ingestion (all $p > 0.05$).

A Wilcoxon test between consecutive time periods showed no significant difference in the average value, except for the time difference 4.0 hr - 3.5 hr without intradialytic food ingestion for the Fistula group ($p = 0.030$) were there appears to be an increase in MAP. All episodes of hypotension were mild, asymptomatic and were treated with trendelenburg position and fluid adjustments. There was no implementation of a decrease in blood flow rate or UF rate during hypotensive episodes as patients remained stable and responded well to the trendelenburg position as treatment for hypotensive episode, there was no compromise to adequacy of OL-HDF treatment.

This method of corrective action for hypotensive episodes differs from other studies in that there was no premature termination of treatment or decrease in blood flow rate which has a substantial impact on adequacy of dialysis.

During the present study blood glucose levels were also investigated with and without food ingestion during OL-HDF as majority of the participants suffered from type II diabetes and were accustomed to eating often in order to stabilise their blood glucose levels. Diabetic nephropathy is one of the leading causes of ESRD (Coresh *et al*. 2007). Hyperglycaemia is reported to be strongly associated with sudden cardiac death in HD patients with type II diabetes, which accounted for increased cardiovascular events and mortality (Drechsler *et al*. 2009). On the other hand, hypoglycaemia is also fatal, especially in the presence of cardiovascular diseases (The Diabetes Control and Complications Trial Research Group, 1993). Although there is no evidence based guideline for the glycaemic targets for haemodialysed patients with type II diabetes, adequate glycaemic control in this population seems to be a predictor of survival (Morioka *et al.* 2001).

In the present study we studied glucose stability during food ingestion compared to sessions without food ingestion in the two groups. It can be concluded that in the AV-Fistula group there was a significant difference between the Pre-Hgt verses Post-Hgt for No intradialytic food ingestion (No IFI) ($p < 0.001$), but not for intradialytic food ingestion (IFI) ($p = 0.482$).The pre-Hgt versus post-Hgt without food ingestion was significantly lower than the pre verses post with food ingestion. The lack of food ingestion caused a decrease in blood glucose levels compared to when food was

ingested ($p < 0.001$ verses $p = 0.482$). The present study also compared pre-Hgt values for No IFI and IFI and post-Hgt values for No IFI and IFI. The results demonstrated that there was a significant difference between the No IFI post-value and the IFI post-value. The Hgt values obtained post dialysis without intradialytic food ingestion was significantly lower.

With the permanent catheter group, it was observed that there was a significant difference between the Pre- verses Post- No IFI ($p = 0.002$), but none for the other comparisons ($p > 0.05$). The Permanent catheter group had no change in pre- and post-Hgt outcomes with food ingestion; however without food ingestion more participants experienced normal post-Hgt levels (85.7%) as compared to with food ingestion (78.6%).

There were no patients with hypoglycaemia as all of the minimum values were greater than 4.0mmol/L. There were significantly more patients with normal readings. There is limited literature on eating during dialysis and blood glucose variability in patients undergoing HD. Although, in a study conducted by Sara *et al.* (2009) glucose values were significantly lower on dialysis days than on non-dialysis days despite similar energy intake. The risk of asymptomatic hypoglycaemia was highest within 24h of dialysis. In another study by Jung *et al*. (2010) nine medically stable patients with type 2 diabetes under maintenance HD were studied for hypoglycaemia associated with HD in diabetes and they found that glucose variability was not affected by HD. However, in spite of glucose-containing dialysate, HD seemed to increase the risk of hypoglycaemia.

There were few limitations to the study, because of the nature of the study group. Firstly, it was difficult to recruit non-diabetic patients only, and therefore patients with hypertension and diabetes were recruited. Secondly, the number of patients who dialysed via AV-Fistula were also limited and we then had to utilise patients with AV-Fistulas and Permanent catheters in consideration of the inclusion criteria as this study was only based on 2 small dialysis centres. Thirdly, observations at home for the participants during the study period were limited in terms of their diet restrictions and whether or not food ingestion occurred prior to treatment.

There were very few interruptions that occurred during the sessions with and without food ingestion such as occasional lower arterial alarms due to movement, none of which resulted in a significant change in the patient's treatment plan. It was however noted that a number of patients even though their blood glucose levels were stable did verbally express that they felt severe hunger post-dialysis in the sessions without food ingestion. Pre- and post-Hgt levels were affected depending whether or not food ingestion occurred, even though patients did not experience hypoglycaemia they did experience a decrease in the hgt levels during sessions without food ingestion.

Overall the results of the study demonstrated that even though it has been noted that during sessions of food ingestion a decrease in MAP can be noted (post-prandial hypotension), none of which was significant enough to result in premature termination of treatment and adjustments which affect dialysis adequacy. The patients tolerated food ingestion during OL-HDF treatment well with no negative effect on spKt/V or URR.

CHAPTER SIX

CONCLUSION

The prospective study on the effect of intradialytic food ingestion in chronic renal failure patients undergoing online HDF treatment was successful in that the aim was achieved.

Clinical outcomes associated with intradialytic food ingestion in patients undergoing OL-HDF demonstrated that food ingestion during OL-HDF treatment did not influence adequacy of dialysis in terms of the spKt/V and URR achieved by the participants.

Although it is common for CKD patients to experience post-prandial hypotension, the frequency of the episodes in the present study were greater in the sessions with food ingestion as compared to without food ingestion. There were no drastic interventions required such as termination of treatment which effects dialysis adequacy. Minor interventions such as trendelenburg position and fluid adjustments should be implemented as the first line of treatment to improve the hypotensive episode before considering more advanced interventions.

This is important because HD is a highly catabolic process and nutrition influences mortality and morbidity. CKD patients have an inadequate protein-energy intake and malnutrition is prevalent in these patients. OL-HDF has been proven to promote better blood pressure stability in CKD patients and this may have also positively contributed to the results of the present study. Eating during dialysis may be of greater help than harm for patients undergoing OL-HDF. Patients with type II diabetes did not experience episodes of hypoglycaemia in the sessions without food ingestion indicating that the glucose containing dialysate maintained blood glucose levels adequately.

From findings of the present study intradialytic food ingestion is recommended for patients undergoing OL-HDF treatment. It is recommended that CKD patients may still be observed for personal characteristics which may contribute to intradilaytic

hypotension and instability during food ingestion. Patients that suffer severe malnutrition and low albumin levels should be considered to be treated with OL-HDF treatment and intradialytic feeding should introduced. This may contribute to an increase in quality of life in patients with CKD.

As a recommendation to minimize malnutrition in CKD patients it would be interesting to study protein energy wasting in patients undergoing OL-HDF versus patients undergoing HD, as well as normalized protein catabolic rate (nPCR) with and without intradialytic food ingestion in patients undergoing OL-HDF.

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Appendix 1(a)

LETTER OF INFORMATION

Title of the Research Study: ***Clinical outcomes associated with intradialytic food ingestion in patients undergoing high-volume online HDF.***

Principle investigator: Archal Nundlal – B-Tech Clin Tech. Nephro

Patients diagnosed with chronic renal failure undergo haemodialysis therapy to increase quality of life and reduce mortality. During haemodialysis we measure Kt/V and Urea reduction ratio as markers to determine if you are being effectively dialyzed. Kt/V can be calculated by online clearance monitoring of the Fresenius 5008 Cordiax machine and URR by pre-dialysis and post-dialysis urea blood sampling. As a dialysis patient you are offered a light meal while receiving your treatment, the aim of this study is to determine whether eating during dialysis may interrupt the your Kt/V and URR level achieved.

Outline of the Procedures:

Patients that fall within the inclusion criteria and consent to enrol will be allowed to participate in the study. The study will be done as you go about receiving your prescribed treatment. Variables that will be measured will include: The patient's blood pressure, pulse rate, mean arterial pressure. The patients Kt/V and URR to determine the effectiveness of the treatment. The study will require you to receive one mid-week treatment with and without food ingestion where blood sampling pre and post dialysis will be performed for the calculation of Urea reduction ratio. Kt/V values will be obtained post-dialysis as calculated by the online clearance monitoring system of the Fresenius 5008s Cordiax machine.

Risks or Discomforts to the Participant:

The study will not cause any risk to you as the participant, it will not interfere with the

adequacy of your treatment nor put you the patient in any physical or emotional trauma.

Benefits:

We hope that the information obtained from this study may improve your quality of treatment and therefore your quality of life.

Reason/s why the Participant May Be Withdrawn from the Study:

Your participation in this study is voluntary. It is up to you to decide whether or not to take part in this study. If you do decide to take part in this study, you will be asked to sign a consent form. If you decide to take part in this study, you are still free to withdraw at any time and without giving a reason. You are free to not answer any question or questions if you choose. This will not affect the relationship you have with the researcher.

Remuneration:

There is no monetary compensation to you for your participation in this study.

Costs of the Study:

There are no costs to you for your participation in this study

Confidentiality:

Every effort will be made by the researcher to preserve your confidentiality including the following:

Assigning code names/numbers for participants that will be used on all researcher notes and documents.

Notes, interview transcriptions, and transcribed notes and any other identifying participant information will be kept in a locked file cabinet in the personal possession of the researcher. When no longer necessary for research, all materials will be destroyed,

The researcher and the members of the researcher's committee will review the researcher's collected data. Information from this research will be used solely for the purpose of this study and any publications that may result from this study. Any final publication will not contain the names of the public figures that have consented to participate in this study (all participant will remain anonymity).

Participant data will be kept confidential except in cases where the researcher is legally obligated to report specific incidents. These incidents include, but may not be limited to, incidents of abuse and suicide risk.

Persons to Contact in the Event of Any Problems or queries

Should you have any questions about the research or any related matters, please contact;

Researcher: *archalnundlalnundlal@gmail.com*, *Tel: 032 5516796*

Supervisor: *Mr ME Memela- memelame@dut.ac.za*

Co-supervisor: Prof Adam- adamjk@dut.ac.za

Appendix 1(b)

CONSENT

Statement of Agreement to Participate in the Research Study:

- I hereby confirm that I have been informed by the researcher, Archal Nundlal, about the nature, conduct, benefits and risks of this study-Research Ethics Clearance Number: _____
- I have also received, read and understood the above written information (Participant Letter of Information) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerized system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which May relate to my participation and will be made available to me.

_____	_____	_____	_____
Full Name of Participant	**Date**	**Time**	**Signature / Right Thumbprint**

I,_____(name of Researcher) here with confirm that the above participant has been fully

Informed about the nature, conduct and risks of the above study.

_____	_____	_____
Full Name of Researcher	**Date**	**Signature**
_____	_____	_____
Full Name of Witness (If applicable)	**Date**	**Signature**
_____	_____	_____
Full Name of Legal Guardian (If applicable)	**Date**	**Signature**

Appendix 2(a)

INCWADI
YESAZISO

Isihloko socwaningo: ukuhlola imphumela ehlangene nokudla okudliwa iziguli eziphetwe izinso abenza i-high volume online HDF.

Umphenyikazi: Archal Nundlal – B-Tech Clin Tech. Nephro

Iziguli ezixilongelwa isifo sezinso ezivamise ukwenza i-hemodialysis ukuthuthukisa izinga lempilo nokwehlisa inani labafayo. Ekwenziweni kwe-hemodialysis sihlola ukucipha kwesilinganiso se Kt/V ne Urea njegophawu lokuqinsekisa ukusebenza kwe-dialysis. I-Kt/V ibaleka ngomshini we online clearance ye Fresenius 5008 Cordiax, i URR yona ihlolwa ngaphambi nasemva kokwenziwa-dialysis, kusetshenziswa isihlolo segazi se-urea. Izigulu ezenza i-dialysis ziyezithole ukudlana zibezithola ucwaningo, inhloso yokwenza lesisicwaningo ukuhlola ukuba ukudla ube uwenza i-dialysis kungaphazamisa ukuhlolwe kwakho kwe Kt/V ne URR.

Uhlaka lwenqubeko:
Iziguli ezi faneleke, nangemvume yabo abazokwazi ukuba bebe ingxenye yalesi scwaningo,mhla bethola imtholampilo yabo ebekiwe. Izinto (eziguqukayo) ezobezibukwa; I-blood pressure, isilinganiso lokushaya kwenhliziyo kanye nokusho kwengcindezi yemithambo. I Kt/V ne URR yeziguli ihlola ukusebenza kahle kwetholampilo enikezwayo. Lesicwaningo sidinga ukuthi uthole imtholampilo kanye maphakathi nesento, kwesinye isikhati ufike udlile nagesenye ufike ungadlile, lapho kuthatwa isihlolo segazi se-urea sibala ukwehla kwesilinganiso sayo, elizothatwa ngaphambi nasemva kwe dialysis. Izibalo ze Kt/V zizothatwa ekuqedeni kwe-dialysis ezobe ibalwe ngomshini we-online clearance ye Fresenius 5008s cordiax.

Ubungozi noma ubuzulube kwababambiqhaza
Lesicwaningo asizokubeka ebungozini futhi angeke sishintse izinga lomtholampilo yakho Kanye futhi angeke ikubeke ebunzimeni ngokomzimba kanye nemizwa.

Izinzuzo

Sithemba izasizo salesicwaningo sithuthukise izinga lomtholampilo yakho ngakho-ke kuthuthuke nezinga lempilo yakho.

I(z)sizathu sokube ababamba iqhaza bekhiswhe kulomcwanango ukuba:

Ukubamba iqhaza kulomcwaningo ukwenza ngokuzithandela. Kukwena uma ufuna ukuba ingxenye. Uma ucabanga ukuba ingxenye kuyo kufanele ugcwalise uphawu lakho kwi dokhumenti. Uma ucabangile ukuba ingxenye yalesicwaningo, ungakwazi ukuzikhipha noma inini ngaphandle kwesizathu. Ukhululekile ukungaphenduli imibuzo uma uthanda. Lokho angeke kulimaze ubudlelwane bakho nomcwaningi.

Ukukhokhelwa:

Ukukho ukukhokhelwa kwe kwamali kulabo ababambe iqhaza kololucwaningo.

Izindleko zalolucwaningo

Azikho izendleko kulabo abayingxenye yalomcwaningo.

Ukufihleka kweniningwana

Umcwaningi uzokwenza ngayo yonke indlela ukufihla imininigwane yakho ngalendlela:

Uzonika ababambiqhaza ikhodi iliyigama okanye inombolo ezosetsenziswa kuwowonke amadokhumendi azobe esetsenziswa.

Amanothi, izingxoxo ezilotshiwe noyowonke amanothi abhaliwe akhipha imininigwane yakho izobe ikhiyelwe ekhabetheni ezandleni zomcwaningi. Uma sesidlule isikhati somcwaningo yonke imininingwane izobhubhiswa.

Umcwaningi kanye nalaba abasebenzisana naye bazoyibheka idatha ethathiwe. Izaziso ezizotholakala kulolocingwane sizo setsenziswa kululucwaningo kuphela futhi nokushicilelwa kwemiphumela yocwaningo. Okuzobe kushicilelwa ekugcineni angeke kuvesi imininigwane yalabo aba yinxenye yocwaningo, akhekho ozovezwa ukhuthi ungubani.

Imininigwana yababambiqhaza izofihlwa ngaphandle uma kuvela isimo la umcwaningi ngokomthetho kufanele acaze isimo, izimo ezifana nokuhlukumeza noma ukuzibulala.

Ukulimala kwakho ekwenzeni kwalolucwaningo

Kungaba nengozi esigayilindelanga kodwa siyokwenzwa ngayo yonke indlela ukunciphisa izingozi.

Abantu abangatholakala uma kukhona izinkinga ezenzekayo

Uma unemibuzo eqondene nolomcwaningo, ungashayela lezinombolo ezingenhla

Umcwaningi: *archalnundlalnundlal@gmail.com*, *Tel: 032 5516796*

Umphathi: *Mr ME Memela- memelame@dut.ac.za*

Isekela likamphathi : Prof Adam- adamjk@dut.ac.za

Appendix 2(b)

Imvume

Isitatimende simvumelwane soku bambaiqhaza kulomcwaningo :

Ngiyavuma ukuthi mcwaningi u Archal Nundlal ungasisile ngequbeko, indlela yokwenza, ukuzuza kanye nobungozi balobubucwaningo I-numbolo ye ethics clearance ithi ____
Ngitholile, ngifundile futhi nga qonda yonke into abhalwe ngemininigwane eqondene nocwaningo.
Ngiyazi ukhuthi iphumela wocwaningo, ehambisane nemininigwane yami ehlangane nebolili, iminyaka, usukulokuzalwa, iziqalo kanye nesifo sami angeke saziswe emphumelweni wocwaningo.
Ngokocwaningo ngiyavuma ukuthi idatha ethathiwe kulolocwaningo izofakwa kuhlelo lekhomphutha ngumcwaningi.
Nginalo ithuba elanele ukubuza imibuzo (ngenhloso yami) futhi ngizimemezele ukuthi ngi lindela ukuba ingxenye wocwaningo.
Ngiyaqonda ukuthi imphumela wocwaningo entsha ephathekayo ebalulekile ekwenzeni lolucwaningo elihlangene nokubamba iqhaza kwami bazongazisa.

_____	_____	_____	_____
Igama eligcwele sesendla sokudla	**usuku**	**Isikathi**	**uphwu/isithupha**

Mina,_____(igama lomcwaningi) la ngiqiniseka ukuthi laba abay yinxenye bacazeliwe yonke into kanye nezingozi kulomcwaningo.

_____	_____	_____
Igama eligcwele likamcwaningi	**usukhu**	**uphawu**
_____	_____	_____
Igama eligcwele lomfakazi (uma ekhona).	**usuku**	**uphawu**
_____	_____	_____
igama eligcwele lomzali (uma ekhona)	**usuku**	**uphawu**

Institutional Research Ethics Committee
Research and Postgraduate Support Directorate
2nd Floor, Berwyn Court
Gate I, Steve Biko Campus
Durban University of Technology

P O Box 1334, Durban, South Africa, 400 I

Tel: 031 373 2375
Email: lavishad@dut.ac.za
http://www.dut.ac.za/research/institutional_research_ethics

www.dut.ac.za

Appendix 3

21 July 2017

IREC Reference Number: REC 24/ I 7

Ms A Nundlal
PO Box 2119
Stanger
4450

Dear Ms Nundlal

Clinical outcomes associated with intradialytic food ingestion in patients undergoing high volume online hemodiafiltration

The Institutional Research Ethics Committee acknowledges receipt of your gatekeeper permission letter.

Please note that Full Approval is granted to your research proposal. You may proceed with data collection.

Yours Sincerely,

Professor M N Sibiya
Deputy Chairperson: IREC

Appendix 4

Faculty of Heath Sciences
Department of Biomedical and Clinical Technology

01 July 2016
Fresenius Medical Care South Africa (PTY) Ltd.

To whom it may concern: Fresenius Medical Care South Africa (PTY) Ltd.

I am currently pursuing my Master of Health Sciences in Clinical Technology - Nephrology at the Durban University of technology. I would like your permission in the use of the patients that are being dialyzed at the Stanger, Victoria, Mount Edgecombe kidney and dialysis centers to be part of my research project assessing ***Clinical outcomes associated with intradialytric food ingestion in patients undergoing High-volume online HDF***.

I have provided a copy of my research proposal in which explains my aims and objectives of my study.

I would like to emphasize that I will be performing a quantitative prospective observational study. The study will not cause any risk to the participant, it will not interfere with the adequacy of their treatment nor put the patient in any physical or emotional trauma.
Every effort will be made by the researcher to preserve the confidentiality of the participants. The researcher and the members of the researcher's committee will review the researcher's collected data. Information from this research will be used solely for the purpose of this study and any publications that may result from this study. Any final publication will not contain the names of the public figures that have consented to participate in this study (all participant will remain anonymity).

Participant data will be kept confidential except in cases where the researcher is legally obligated to report specific incidents.

Patient's participation is based on a voluntary basis and no Patient will be obligated to participate.

There may be risks that are not anticipated. However every effort will be made to minimize any risks.

The study will not incur any costs to the company nor for the participant.

I would like for my study to provide value to the company in terms of quality and efficiency of treatment as well growth and development in the renal health care sector.

Your signing of this letter will also confirm that you { Fresenius Medical Care, South Africa } grants Archal Nundlal B-Tech Clin Tech -Nephrology, the permission to perform the research under the above mentioned regulations and obligations.

If these arrangements meet with your approval, please sign this letter where Indicated below.

Thank you

Sincerely,

Archal Nundlal	Mr M.E Memela	Prof J.K Adam
B-Tech Clin Tech	M-Tech Clin Tech	D-Tech Clin Tech
074 427 0865	memelame@dut.ac.za	adamjk@dut.ac.za

_____ _____ _____

PERMISSION GRANTED FOR THE
USE REQUESTED ABOVE:

_____(Name)

_____(Signature)

FRESENIUS MEDICAL CARE

Fresenius Medical Care South Africa (Pty) Limited

Appendix 5

Fresenius Medical Care South Africa (Pty) Ltd

31A Lake Road
Longmeadow Business Estate
Edenvale, 1609

Private Bag X10039
Edenvale, 1610

T +27 (0)11 457 9300
F +27 (0)11 457 9552/3

TO WHOM IT MAY CONCERN

20 June 2017

Student Name: Archal Nundlal
I.D Number: 920410 0529 089
Student No: 21001360
University: Durban University of Technology

TOPIC: CLINICAL OUTCOMES ASSOCIATED WITH INTRADIALYTIC FOOD INGESTION IN PATIENTS UNDERGOING HIGH VOLUME ONLINE HEMODIAFILTRATION

Dear Sir/Madam

This is a letter of confirmation that the above-mentioned student will be conducting his/her research in the following Fresenius Medical Care South Africa (Pty) Ltd Kidney & Dialysis Centers:

- Stanger Kidney & Dialysis Centre
- Victoria Kidney & Dialysis Centre
- Mount Edgecombe Kidney & Dialysis Centre

Fresenius Medical Care South Africa (Pty) Ltd is permitting this student to make use of the relevant information without disclosing the identification of the staff members.

Yours sincerely

Hanti e
Member of the Executive Committee
Nephrocare Operations Manager

Appendix 6

Record sheet 1 – Intradialytic food ingestion. Date: _____

Patient ID No.	
Name/ Code	
Age	
Gender	
Race	
Access	
Frequency /duration	
Dry weight	
Ultrafiltration Goal	

Pre Urea	Post Urea	URR	Pre hgt	Post hgt	Kt/V

Treatment commenced (Time) _____

Observation

Time	Systolic	Diastolic	Pulse	MAP	Qb	Qd

Intradialytic complications. (Please tick appropriate)

Event	Time	Intervention
Hypotension		
Hypertension		
Hypoglycaemia		
Hyperglycaemia		
Disequilibrium		
Nausea		
Vomiting		
Diarrhoea		
Cramping		
Other, Specify		

Treatment completed (Time) _____

Notes: _____

Appendix 7

Record sheet 2 – Non -Intradialytic food ingestion. Date: _____

Patient ID No.	
Name / code	
Age	
Gender	
Race	
Access	
Frequency /duration	
Dry weight	
Ultrafiltration Goal	

Pre Urea	Post Urea	URR	Pre hgt	Post hgt	Kt/V

Treatment commenced (Time) _____

Observation

Time	Systolic	Diastolic	Pulse	MAP	Qb	Qd

Intradialytic complications. (Please tick appropriate)

Event	Time	Intervention
Hypotension		
Hypertension		
Hypoglycaemia		
Hyperglycaemia		
Disequilibrium		
Nausea		
Vomiting		
Diarrhoea		
Cramping		
Other, specify		

Treatment completed (Time) _____

Notes: _____