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Assessment of peritoneal dialysis adequacy among continuous ambulatory peritoneal dialysis (CAPD) ppatients in Johannesburg Hospital

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CHAPTER 1

INTRODUCTION AND LITERATURE REVIEW

1.0 INTRODUCTION

End stage renal disease (ESRD) is now a global public health burden with more than one million patients on renal replacement therapy in 2004, projected to reach 2 million by the year 2010 at an annual growth rate of 7%.[1] Renal replacement therapy (RRT) for ESRD is offered in the form of dialysis consisting of haemodialysis (HD) and peritoneal dialysis (PD) or renal transplantation. The availability of RRT is quite variable with the worst scenario in sub-Saharan Africa where only small numbers of patients are on treatment, due largely to socio-economic factors.[2] Both HD and PD offer ESRD patients a means of partially replacing their kidney function. Initial selection of RRT modality may be influenced by several factors including patient's preferences, availability of and distance from an in-centre dialysis facility, physician knowledge and experience, pre-ESRD education, time of referral to nephrologists, co-morbidities, patient characteristics and other non medical reasons.[3]

Haemodialysis has remained the most common modality of treatment, comprising of 89% of the world dialysis population in 2004.[1] However, this global average is not reflected in all countries because of the world wide variations in the practice of PD. For example, PD is the predominant mode of RRT offered to 95% and 80% of ESRD patients in Mexico and Hong Kong respectively, while only 8-12% of ESRD patients are on PD in USA and Germany.[4,5] Psychosocial and economic factors, physician bias and inadequate pre-ESRD education to the patients are among several factors proposed to explain the minimal utilization of PD, for

example in the USA.[6] However in the Republic of South Africa (RSA), low socioeconomic status has been reported to place a further constraint on the type of RRT offered, as many of the patients are on PD as a first choice by default due to lack of HD slots and many of them cannot afford transportation to HD units three times a week.[7] This explains why more than 50% of ESRD patients in the Johannesburg hospital are on PD.

The concept of integrated care approach to ESRD advocates that HD, PD and transplantation should all be offered to the patient in an unbiased way, and all 3 modalities may be part of treatment during the patient's lifetime.[8]

Peritoneal dialysis has been an effective form of RRT since the introduction of continuous ambulatory peritoneal dialysis (CAPD) in the nineteen seventies. The provision of optimal dialysis is important in determining the overall prognosis of the patient. Studies have shown that the amount of delivered dose of PD is associated with patient outcomes. Solute clearance is the most objective means of quantifying the delivered dose of PD. There has been an evolution of guidelines by various national and international organisations on the target dose of PD to ensure the provision of optimal PD.[9,10] The National Kidney Foundation (NKF) has suggested that due to variations in population characteristics, individual dialysis units should establish their own target level, ensuring that the minimal recommended dose is delivered to the patient and that solute clearance should be assessed during the first month of initiating PD and at least every four months subsequently. [9] Clinical assessments of the patient, small solute clearance, fluid and blood pressure control, anaemia and nutritional status are also considered in the evaluation of PD adequacy.

Knowledge about peritoneal membrane transport characteristics is important for the formulation of an appropriate dialysis prescription. The amount of delivered dose of PD, the nutritional status and the membrane transport characteristics of PD patients in Johannesburg hospital were not studied in the past. This study therefore provides baseline data on PD adequacy, membrane transport characteristics and nutritional status in our patients.

1.1 Peritoneal Dialysis as a Form of Renal Replacement Therapy

1.1.1 **History and Evolution of Peritoneal Dialysis**

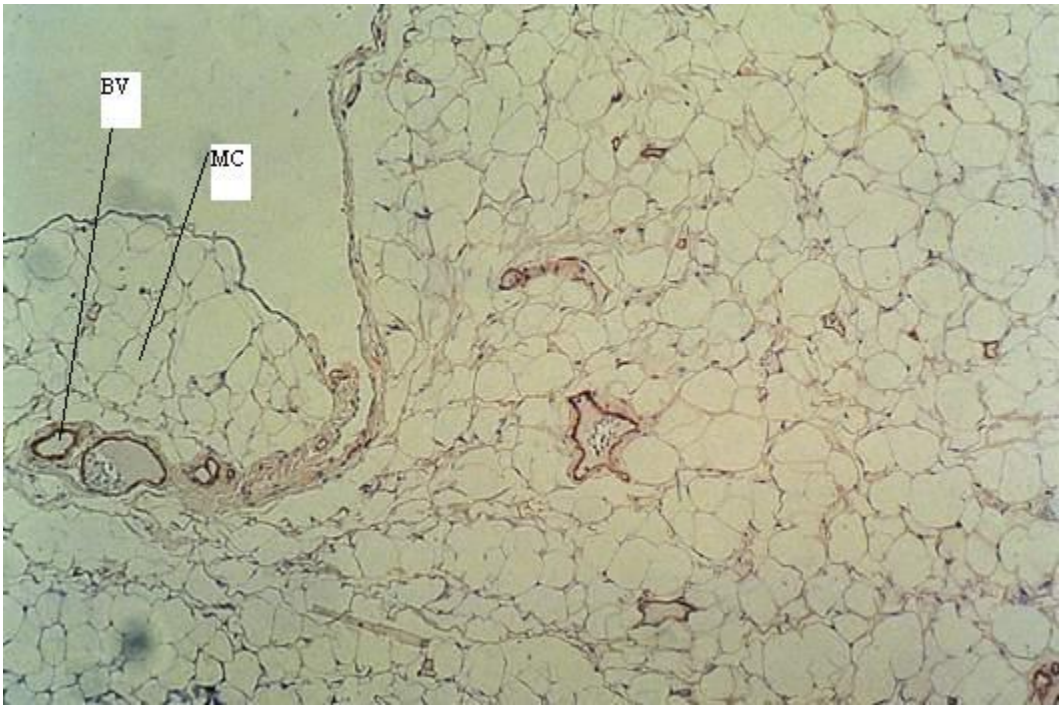
The concept of PD evolved from the presentation by Christopher Warwick in the early 1740's when he described the treatment of a 50 year old woman with severe ascites in whom he instilled Bristol water and claret wine into the peritoneum through a leather pipe.[11] Wegner and Starling described the absorptive and fluid removal characteristics of the peritoneum in 1877 and 1894 respectively.[12,13] Putnam in 1922 gave further insight into the physiological role of the peritoneum when he established that solutes and water could be added to or removed from the body by placing solutions of appropriate composition into the peritoneal cavity.[14] The first clinical application of PD was reported by Ganter in 1923 when he described the use of the peritoneal membrane to remove uraemic toxins in a kidney failure patient. [15] He also described most of the principles of PD which are still relevant at the present time. Problems of peritoneal access device, limited availability of acceptable dialysis solutions as well as morbidity and mortality from peritonitis hindered much progress in subsequent years. Rosenak and Sewon developed a metal catheter for continuous peritoneal lavage.[16] Paul Doolan and his group developed a unique catheter made of polyethylene which was flexible and contained a number of grooved segments which prevented blockage of drain holes and maximised drainage.[17] Further

development of the access device followed when Palmer R and Quinton W developed a catheter that sealed the exit site and prevented bacterial migration.[18] This was later improved upon by Tenckhoff through the introduction of silicon rubber, shortening the length and the addition of two Dacron cuffs which sealed the opening into the peritoneum. [19] The use of commercially available sterile solution in glass bottles was described by Maxwell in 1959 and this gave rise to more widespread use of PD in clinical practice.[20] The description of automated PD was made by Boen in 1964, when he described a closed system using large glass containers of dialysate and a simple device that cycled the solution into and out of the patient.[21] Norman Lasker [22] further improved on the work of Boen, Tenckhoff and Palmer to develop the PD cycler which uses gravity to pump the PD fluid into the peritoneum. Popovich et al[23] described the concept of the 'portable/ wearable equilibration PD' in 1976 which later developed into the currently practiced CAPD. Further developments occurred with the use of plastic bags as containers for the dialysate and the description of the 'Y' set with the flush after connect feature, both of which reduced the incidence of peritonitis.

1.1.2 Physiology of Peritoneal Dialysis

Peritoneal dialysis is a technique whereby infusion of dialysis solution into the peritoneal cavity is followed by a variable dwell time and subsequent drainage. Solutes and fluids are exchanged between the capillary blood and the intraperitoneal fluid across the peritoneum which has a surface area of approximately 1-2m^2. The peritoneum consists of 3 layers, the mesothelium, interstitium and the capillary wall.

Figure 1.1. Histological picture of normal peritoneum



Source: Krediet R Pathophysiology of peritoneal transport at **www.hdcn.com** with some modifications. (BV=blood vessel, MC mesothelial cell)

The mesothelium is made of a continuous monolayer of flat cells called the mesothelial cells (MCs). They are active in modulating host defense, and play an important role in regulating the inflammatory response in the peritoneal cavity by producing proinflammatory cytokines and chemokines such as transforming growth factor β and basic fibroblast growth factor. Other biological roles of the MCs include induction of angiogenesis via vascular endothelial growth factor, control of transcellular water transport via Aquaporins (AQP) and the expression of advanced glycosylation end-product receptors.[24] They also produce cancer antigen 125 (CA125)

and its appearance rate in the dialysate effluent may be used to estimate mesothelial cell mass and overall peritoneal membrane health.

The interstitium contains the blood and lymphatic vessels, glycosaminoglycans, and fibroblasts. It is basically a supporting structure and consists of aqueous and lipophilic phases. The aqueous phase mediates transport of water, electrolytes, protein, nutrients, and hormones.

The capillary wall consists of endothelial cells supported by a basement membrane. The parietal peritoneum covers the inner surface of the abdominal and pelvic walls including the diaphragm while the visceral peritoneum covers the visceral organs.

Blood supply to the peritoneum is from the mesenteric arteries and portal vein for the visceral peritoneum and arteries of the abdominal wall supply the parietal peritoneum. Peritoneal blood flow is about 60-70ml per minute.

Lymph drainage of the peritoneum is mainly through specialised lymph stomata located in the sub-diaphragmatic region; these passages open and close with respiratory movements of the diaphragm. Almost 80% of the lymph drains to the venous circulation is via the right lymph duct and this returns excess intraperitoneal fluid and protein from the peritoneal cavity to the systematic circulation. It also provides pathways for absorption of intra peritoneal biologically inert particles, colloids and cells.

During PD, it is the functional or effective surface area which is determined by the extent of the peritoneum in contact with dialysate fluid and by the magnitude of the microcirculation through the peritoneum and not the anatomical surface area of the peritoneum that is important for solute

and water movement. Factors such as loculation of fluid, adhesions and changes in the number of capillaries may influence effective surface area.

Solutes moving from the capillaries into the peritoneal cavity encounter anatomical and physiological resistances which were explained by Nolph et al[25] in their barrier model. These include a stagnant layer of fluid within the peritoneal capillary, the capillary endothelium, the capillary basement membrane, the interstitium, the mesothelium and a stagnant layer of fluid within the peritoneal cavity. Three different types of pores facilitate solute movement across the peritoneal barrier and these were explained by the three pore model. The small pores of radius 40-50Å correspond to the clefts or gaps between the endothelial cells which account for the diffusion of small solutes. The large pores of radius 250Å which correspond to the inter endothelial gaps are involved in the transport of macromolecules. The ultra small pores are located in the endothelial cells and are water specific.[26] The 'distributed model' suggests that peritoneal capillaries are uniformly distributed in the tissue space of the peritoneum but are separated by variable distances from the dialysate.[27] It is based on a two dimensional simulation that integrates the microvasculature with the surrounding cells and interstitium within the peritoneal membrane. Solute movement occurs as a result of diffusion and convective transport. The diffusive clearance of any solute depends on factors such as the "effective" peritoneal membrane surface area, the intrinsic permeability of the membrane, dialysate flow, concentration gradients, and the dwell time.[28]

Ultrafiltration occurs as a consequence of the osmotic gradient between blood and dialysate created by the addition of an appropriate osmotic agent, usually glucose, to the PD solution. Other membrane characteristics such as the effective surface area and its hydraulic permeability

also affect the ultrafiltration. There is evidence to suggest that AQP1 are the ultrasmall pores responsible for transcellular water permeability and may account for about 50% of the ultrafiltration during PD. [29] Peritoneal transport studies using AQP1 knockout mice have demonstrated that the osmotic water flux across the peritoneal membrane is mediated by AQP1.[30] This suggests that manipulation of AQP1 expression may be used to increase water permeability across the peritoneal membrane.

1.1.3. Peritoneal Dialysis Solutions

The first commercially available PD fluid was produced in 1959 [20]and since then there have been improvements on the composition of the fluid. While earlier investigators in PD like Ganter used saline, [15] it was Heusser who first described the addition of dextrose to improve UF and Rhodes later added lactate to correct acidosis.[31] The properties of an ideal PD solution include, a sustained and predictable solute clearance with minimal absorption of the osmotic agents and is able to provide electrolytes and nutrients if required. Furthermore it should aid in the correction of acid base problems without interacting with other solutes in the PD fluid, be free of and inhibit the growth of pyrogens and microorganisms, be free of toxic metals and inert to the peritoneum.[32]

1.1.3.1 Composition of Peritoneal Dialysis Solutions

The constituents of contemporary PD solutions are divided into 3 categories and they include osmotic agents, buffers and electrolytes. Osmotic agents are used to create a pressure gradient that allows the removal of water by UF. These agents are of either low or high molecular weight (MW). The former have MW of between 90 and 200 DA and include dextrose, amino acids and

glycerol, while the later have MW from 20,000 to 35,000 DA and they include glucose polymers such as icodextrin, polypeptides, and dextran.

Buffers in PD solutions are used mainly to correct acidosis and they include acetate, lactate and bicarbonate. Most commercially available fluids use acetate and lactate which are associated with inflow pain and metabolic complications. Newer agents use bicarbonate which is more physiological, though can be associated with problems such as precipitation of calcium (Ca) and magnesium (Mg) carbonate, as well as caramelisation of glucose during sterilization. To overcome these problems, a 2 chamber bag was introduced, separating the two solutions and mixed only when they are about to be infused.

Electrolytes used in PD solutions include sodium (Na), Mg, Ca and chloride (Cl). The concentration of Na has varied between 120 and 140 mmol/l, though the majority contain 132 mmol/l. Low Na solutions have been shown to have an advantage of net Na loss with better volume and BP control.[33] Varying concentrations of Ca are also used. However most solutions now contain a physiologic concentration of 2.5 mmol/l to avoid problems of hypercalcaemia and metastatic calcification, though with the risk of net Ca loss leading to hyperparathyroidism.[33] A low concentration of Mg of 0.5 mmol/l is now used as the problem of increased Mg levels may cause bone disease. Various modifications were made to allow for an individualised PD prescription based on the electrolyte and metabolic requirements of the patient.

Several other additives are often added in certain clinical situations, such as antibiotics in peritonitis, insulin in diabetic patients and heparin to prevent formation of fibrin which may cause PD catheter obstruction.

1.1.3.2 Dextrose Based Solutions

Dextrose based solutions are supplied in varying formulations with different dextrose concentrations and volumes. These include dextrose concentrations of 1.5%, 2.5%, and 4.25% with osmolality of 346, 396 and 485mOsmol/l respectively. The composition of a standard solution is shown in table1.

The main advantages of dextrose solutions are that they are cheap, safe, easily available and have been in use for a long time. However dextrose is easily absorbed, leading to short lived UF. Its absorption causes metabolic complications such as hyperinsulinaemia, hyperglycaemia, hyperlipidaemia and weight gain. During heat sterilization, glucose is degraded leading to generation of glucose degradation products (GDPs) which have been shown to cause inhibition of cell proliferation, necrosis of fibroblasts, macrophages and mesothelial cells. [33] Glucose degradation products also enhance the production of advanced glycation end products (AGEs) by the reaction of the aldehyde form of glucose, in the presence of amines or proteins, to produce Amadori glycosylation products.[32] Accumulation of AGEs has been implicated in the development of structural damage to the peritoneum and vasculature.[34]

Table 1.1 Composition of Standard Glucose Based PD Solutions

Constituent	Concentration
Sodium (mmol/l)	132-134
Potassium (mmol/l)	0-2
Calcium (mmol/l)	0.75-1.25
Magnesium (mmol/l)	0.25-0.75
Chloride (mmol/l)	95-106
Lactate (mmol/l)	35-40
Glucose (g/dl)	1.5, 2.5 and 4.25
pH	5.5-7.2

1.1.3.3 Amino acid based solutions

Amino acid based solutions are being used to replace losses of amino acids and proteins during PD, with the aim of improving nitrogen balance especially in patients with malnutrition. [35] Clinical studies have shown that amino-acid solution is more biocompatible as compared with conventional glucose solution and could improve nitrogen balance, increase the concentration of plasma proteins, improve anthropometric measurements, as well as improve the plasma amino acid profile.[35,36] However, the use of amino acid solution results in an increased generation of urea and acid, owing to the absorption and metabolism of delivered amino acids. As a consequence, serum urea levels increase and serum bicarbonate levels decrease. To prevent this high level of urea and acidosis, only one daily exchange or a maximum of two exchanges per day of 1.1% amino-acid solution is recommended.[34]

1.1.3.4 Icodextrin Based Solutions

Icodextrin is a polymer of glucose which offers a better UF for a longer period of time, because it is less well absorbed. A 7.5% solution with an osmolality of 284 mOsm/kg and pH of 5.2 – 5.6 is now available in several countries including the RSA. It offers better biocompatibility with the peritoneal membrane and produces a better UF compared with conventional glucose solution. Continuous use of Icodextrin solution in PD patients has been shown to improve fluid balance, reduce blood pressure (BP) and the use of antihypertensive medications, improve lipid profiles, and to extend technique survival.[37, 38] Icodextrin solution is especially effective during peritonitis and in high transporters in whom ultrafiltration is significantly reduced with glucose solution owing to increased absorption of glucose from the peritoneal cavity. [39, 40] The use of Icodextrin is associated with an increase in the plasma level of icodextrin metabolites such as maltose and other disaccharides, hence only one exchange in 24 hours is currently recommended.[34]

1.1.3.5 The newer generation solutions- pros and cons

The newer generations of PD solutions have sought to utilise more physiological intra peritoneal pH, reduce GDP production and enhance biocompatibility. This is achieved through the use of glucose alternatives as osmotic agents and improved manufacturing and product presentation, such as the multibag system which allows glucose to be stored at a lower pH and also minimises precipitation of Ca and Mg in the solution. These improvements have both local peritoneal and systemic effects. Local effects include improved viability and proliferation of mesothelial cells, as evidenced by increased levels of Ca-125 and fibronectin in peritoneal effluents and improved mesothelial-based healing.[41] Other local effects include improved preservation of peritoneal function, reduced intraperitoneal inflammation, better maintenance of macrophage function and

reduced infusion pain.[41,42] The systemic effects include adequate control of total body water and sodium through sustained UF, resulting in good BP control and better left ventricular (LV) function.[41] Metabolic effects such as improved blood glucose levels in diabetic patients and reduction in hyperinsulinaemia, abnormalities of lipid metabolism, and increased insulin resistance have also been reported.[43,45]

The main concern with these newer solutions is the cost implication, which is important especially in developing countries. Other issues include the associated side effects such as accumulation of metabolites like maltose in icodextrin based solution for which there is growing concern that long-term use of these agents may lead to unspecified storage or deposition diseases. [36]

1.1.4 Schedules of Peritoneal Dialysis

Several techniques are available for performing PD and these can be done manually or with automated devices (cyclers); it can be continuous (fluid in the abdominal cavity 24 hours a day) or intermittent (abdominal cavity dry for a part of the day). The various schedules for PD include CAPD, continuous cycler-assisted peritoneal dialysis (CCPD), nocturnal intermittent peritoneal dialysis (NIPD), and Tidal PD. Figure 2 depicts the various PD schedules. During CAPD only the connecting tubes and bags of solutions (2 to 3 L) are required and gravity is utilised to fill and empty the peritoneal cavity. The most commonly used schedule employs four exchanges per day, but in some patients, especially those who are anuric and have a high body mass index (BMI), five exchanges may be necessary while a small number of patients (low BMI, excellent residual renal function) may require only three exchanges per day. The night dwell for CAPD is

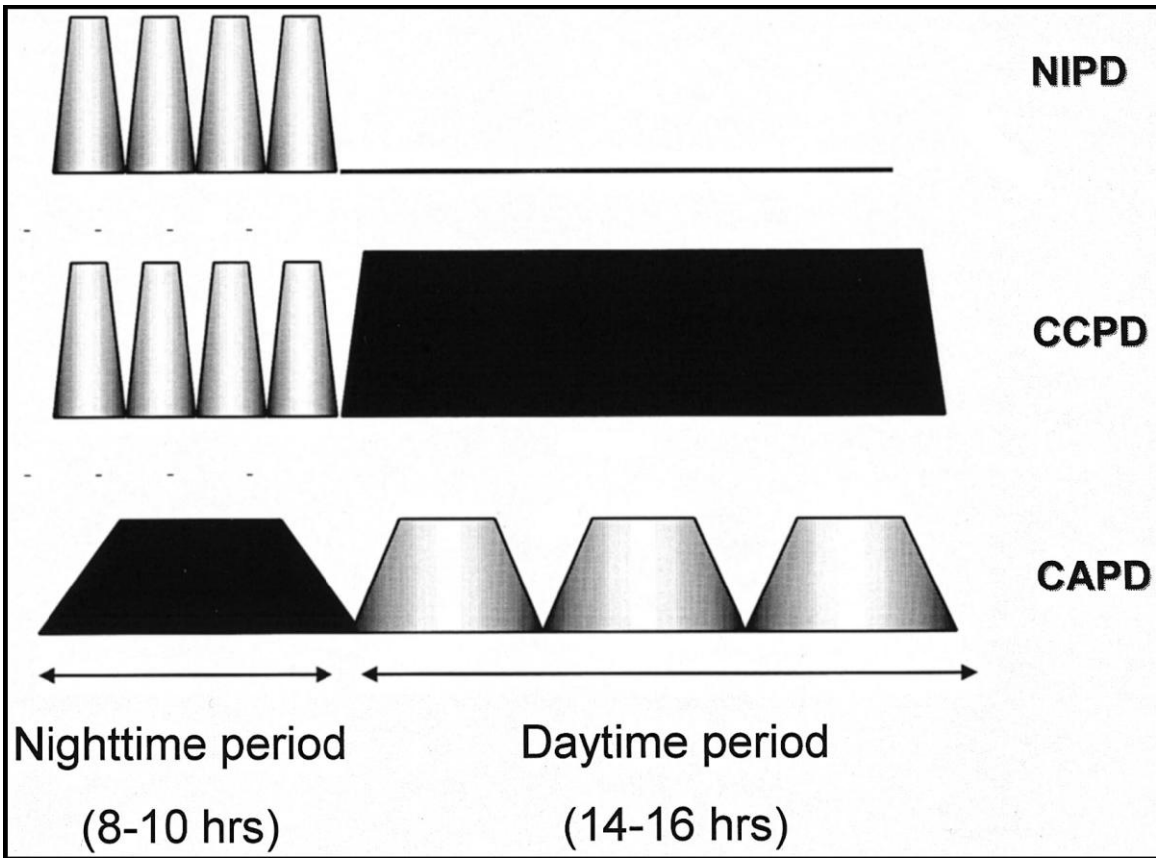
long (8-10 hours). Sometimes, enhancement of solute removal with CAPD can be accomplished by performing additional one or two nocturnal exchanges using a night-time automated device.

In CCPD, there is a long daytime dwell and several cycles overnight. The patient loads the bags of solutions onto a cycler and connects the catheter to the cycler at bedtime. The cycler is programmed to do three to five (or more) exchanges during the night. In the morning, 2 to 2.5 L of fluid is left in the abdomen for the long daytime dwell (14-16 hours). During the daytime period, usually there is no exchange and the procedure is repeated at night. Occasionally, an additional exchange is done during the day to improve clearance or UF. Another cycler-assisted nightly procedure is NIPD in which treatment periods alternate with times during which the peritoneal cavity has been drained of dialysate. It is usually offered to patients with excellent residual renal functions.

Tidal PD consists of exchanges in which the peritoneal cavity always contains at least some dialysate (usually one-half full), a feature that improves comfort and facilitates drainage in some patients.

Similar clinical outcomes in terms of hospitalisation rates, risk of peritonitis, fluid leaks, and effect upon residual renal function, have been reported among the different CAPD or APD modalities in a systematic review of three randomised controlled trials that consisted of 139 patients undergoing either APD or CAPD.[45]

Figure 1.2. Peritoneal dialysis schedules



CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycler assisted peritoneal dialysis; NIPD, nocturnal intermittent peritoneal dialysis. Source: Saxena R *Am J Med Sci* 2005; **330**: 36-47.

1.1.5. Advantages of Peritoneal Dialysis

Peritoneal dialysis is associated with a slower rate of decline in residual renal function (RRF) than HD and this has a direct influence on dialysis adequacy and superior patient survival. [45] Several factors have been proposed to explain this, for example PD offers more haemodynamic stability with less abrupt volume and osmotic shifts as well as better fluid and BP control.[46] This also makes PD more tolerable in patients with compromised cardiovascular status. The clearance

of larger molecular weight solutes, the so-called "middle molecules," is time-dependent and particularly enhanced by the long-dwell associated with PD. The needle-less nature of PD alleviates the anxiety of needle sticks and helps preserve the vasculature for future HD access, as well as preventing the transmission of blood borne infections.

The flexible schedule of PD gives the patient an opportunity to work and participate in day time activities, which may contribute to greater patient satisfaction with treatment compared to HD. Analysis of cohorts in the CHOICE study, showed that PD patients were 1.5 times more likely than HD patients to rate their care as excellent and their therapy had less impact on their lives.[47] Studies have shown that given an informed choice, approximately half of ESRD patients will choose PD.[48,49]

Some studies have reported survival advantage of PD over HD, though others do not. Fenton et al[50] and later Heaf et al[51] have reported a survival advantage for PD during the first 2 years of dialysis in Canadian and Danish populations respectively. This survival advantage may be real due to preservation of RRF or it may be due to differences in patient selection as both were epidemiological studies. However, a randomised controlled trial confirmed this 2 year survival advantage.[52] On the other hand, Jarr et al[53] have reported an increased mortality risk for PD in a cohort among the CHOICE study patients, although this has been criticised for recruitment bias, in that enrollment did not occur at the initiation of dialysis and that PD patients were over-recruited; such an approach favors HD survival because mortality is much higher during the first 90 days on HD compared to PD .[53] Maiorca et al[54] have reported a similar mortality risk between HD and PD patients.

Peritoneal dialysis is reported to be less expensive in many countries, in the USA for example Medicare savings with PD have steadily increased from $ 9,600 per patient per year in 1998 to $15,000 in 2002.[55] However, this has not been seen in the RSA where PD is reported to be an expensive modality due largely to cost of fluids.[2]

1.1.6. Drawbacks of Peritoneal Dialysis

Burn out of patients and families may occur due to the continuous nature of PD. Technique failure rates of 7-11% per year have been reported.[56] Infectious complications are among the major causes of treatment failure in PD. However in Johannesburg hospital, non compliance and psychosocial issues were among the major reasons.[7]

Advances in PD technology such as "Y-set" catheter connections, the use of the "flush before fill" technique as well as antibiotic prophylaxis have reduced the number of infectious complications. Aslam et al[57] examined infection rates among HD and PD patients in a single centre and found that overall, infection rates were the same but differed in type. Bacteremia and fungemia occurred only in HD patients; peritonitis occurred only in PD patients.

Mechanical complications such as increased intra-abdominal pressure with associated abdominal hernia, dialysate leak leading to hydrocoele and genital oedema can occur. Pleuroperitoneal communications causing hydrothorax are some of the drawbacks to PD therapy. Complications related to the access such as catheter malfunction, catheter migration and kinks do occur. [28]

Another important drawback to PD is the progressive loss of ultrafiltration due to structural and functional changes in the peritoneal membrane that occur over time. It is thought to be the

consequence of the toxicity of glucose through the formation of GDPs and AGEs which are generated during the sterilisation process. However the use of newer PD solutions has been shown to improve membrane preservation during long term PD.

1.2 Assessment of Peritoneal Membrane Transport Characteristics

The functional and morphological integrity of the peritoneal membrane are crucial to the success of PD treatment. The peritoneal transport status has been shown to affect the morbidity and mortality in PD patients.[58] Davies et al[59] have shown that peritoneal function is associated with clinical outcomes independent of urea clearance (kt/v) and residual renal function, age, plasma albumin, body size and sex.

There are various methods for assessing the peritoneal transport characteristics. These include among others: Peritoneal Equilibration Test (PET) described by Twardowski et al in 1987.[60] Peritoneal Function Test (PFT) described by Gotch et al, [61] which also measures the peritoneal mass transfer area coefficient (MTAC). It also give information on nutrition as well as water balance, however it is time consuming and requires a computerised kinetic modeling programme to determine the MTAC. The Peritoneal Dialysis Capacity (PDC) which was described by Rippe et al[26] is based on the three pore model. The Dialysis Adequacy and Transport Test (DATT) was first described by Rocco et al[62] and involves collection of 24 hour dialysate sample and has been validated on CAPD patients. Standard Peritoneal Permeability Analysis (SPA) is more comprehensive and involves the intra-peritoneal administration of dextran 70 to assess fluid kinetics during a 4 hour dwell.[63] Accelerated Peritoneal Examination (APEX) is similar to but shorter than PET.[64]

1.2.1 Peritoneal Equilibration Test

This is the most widely used test to evaluate peritoneal membrane characteristics in PD patients since it was described by Twardowski et al in 1987.[60] It is simple to perform without the need for expensive infrastructure or sophisticated equipment. This is relevant in developing countries where such equipments are not readily available. PET is highly reproducible and this has been demonstrated both in experimental animals and in humans especially when it is standardised for such factors as length of preceding exchange, time of inflow and drainage, methods of obtaining samples and laboratory assays. [65, 66]

Solute transport rates are assessed by rates of their equilibration between the peritoneal capillary blood and the dialysate. The ratio of solute concentration in the dialysate and plasma (D/P) at specific times during the dwell signifies the extent of solute transport. Creatinine, Urea and Sodium are the most widely tested solutes. The fraction of glucose absorbed from the dialysate at specific time is determined by the ratio of dialysate glucose concentration at specified time to the initial level in the dialysate solution (D/D0). However in practice, the D/P creatinine at the end of a 4 hour dwell and D/D0 glucose are used to categorise patients into different transport status. Patients are classified into one of four categories. These are High, High average, Low average and Low transporters. High transporter status is defined as having a D/P creatinine at 4 hours greater than +1 SD from the mean, or a glucose D/D0 of less than -1 SD from the mean. Low transporter is defined as a creatinine D/P of less than -1 SD from the mean or a glucose D/D0 of greater than +1 SD from the mean. The average transporter is defined as a creatinine D/P and a glucose D/D0 of between +1 SD and -1 SD around the mean.[67]

PET is used in the characterisation of membrane function which has been shown to have an impact on clinical outcome of PD patients in terms of technique failure and occurrence of comorbidities.[58] PET is also important for the prescription of adequate PD dose and regimen on an individual basis. High transporters tend to do best on PD regimens with frequent short duration dwells, while low transporters will do best on regimens with long duration and high volumes. Average transporters can do well on any regimen. Other clinical applications of PET include the diagnosis of UF failure and its causes, and assessment of the influence of systemic disease on peritoneal membrane function.[67]

There is wide inter-patient variability and differences in the reference values for D/P ratios and D/DO values in populations other than the North American population in which PET was originally based. [68, 69] Among the drawbacks of PET is that it is time consuming, requiring at least 5 hours to complete. The method for measurement of creatinine by Jaffe method is affected by dialysate glucose as it is known to markedly overestimate the results; hence a correction factor is needed. The terminology of high and low in the categorisation of membrane function is criticised as being misleading as they refer to amount of transport molecules, whereas what they really represent is speed of transport over the membrane. It only gives information on small solute transport and does not give separate information on convection, diffusion or ultrafiltration capacity.

1.3 Assessment of Peritoneal Dialysis Adequacy

Adequate dialysis is defined as the dose of dialysis associated with acceptable morbidity and mortality, while optimum dialysis is defined as the level beyond which the added clinical benefit is not worth the additional patient effort or cost. [70]

In the early days of dialysis, assessing adequacy was usually based on the clinical acumen of the physician to pick up on signs and symptoms of under-dialysis such as nausea and vomiting together with biochemical parameters such as blood urea, creatinine and haematocrit (Hct) level. However, while the symptoms and signs are still relevant, they have their own limitations; their quantitative assessment is difficult, other causes need to be ruled out and their appearance is a late feature and therefore the opportunity of detecting early under-dialysis is usually missed. Arkouche et al [71] have shown that this qualitative approach is not sufficient to predict the deleterious effects of under-dialysis. There is therefore the need for objective, quantifiable parameters to assess adequacy and early detection of under dialysis before the appearance of symptoms and signs. This will allow comparison with other patients or populations and correlation between the dialysis dose and clinical outcome. Small solute clearance indices of urea and creatinine are widely used as markers of PD adequacy. However several other factors are also known to affect optimal dialysis outcome. These include ultrafiltration, nutritional status, mineral metabolism, control of lipids and cardiovascular risks and acid base homeostasis. Recent reviews have focused attention on the effect of ultrafiltration as a marker of PD adequacy and studies have shown that fluid removal is an independent factor affecting survival in PD patients.[72] This may be related to the consequences of fluid accumulation as a result of low UF such as congestive cardiac failure, increased left ventricular mass, and poor blood pressure control.

1.3.1 Urea Kinetic Model in Assessment of Peritoneal Dialysis Adequacy

Results of the National Cooperative Dialysis Study (NCDS) and its re-analysis by Gotch and Sargent provided objective parameters for measuring adequacy of dialysis in HD patients. [73,74] They showed that indices derived from Urea Kinetic Modeling (UKM) were predictive of clinical outcome. Similarly, the Mayo clinic study by Dyck et al attests to the significance of UKM in HD patients.[75] This UKM is a dimensionless measure of fractional clearance of body water for urea. It integrated efficiency of solute clearance (k), treatment time (t) and patient size (v) expressed as kt/v. It has been validated and accepted as an index of adequacy for HD for many years. Attempts were made to extrapolate these same concepts to predict outcome in PD patients. Teehan et al [76]were the first to show that measurement of blood urea nitrogen (BUN), normalized protein nitrogen appearance (nPNA) and kt/v provide a reasonable basis for uniform prescription of PD and allow comparison of treatment centres as well as optimisation of dialysis and nutrition therapy. Rodby et al[77] later reported on the reproducibility of the UKM in PD patients. Keshaviah et al[78] described the peak urea concentration hypothesis which indicates that a weekly kt/v of 1.67 in CAPD was equivalent to a three times per week kt/v of 0.86 for HD and for a three times per week HD kt/v of 1.3, the corresponding equivalent weekly kt/v is 2.0 for CAPD. However in applying UKM to PD, several assumptions were made; the rate of solute removal changes during dialysis in HD patients because the concentration of urea decreases during dialysis while in CAPD, clearance and solute removal stay about the same and are related in a linear fashion because the blood urea concentration is relatively constant. Urea achieves ultra equilibration between dialysate and plasma at the end of the exchange in most CAPD patients, thus drain volume is analogous to urea removal (kt). Measurement of kt/v in CAPD patients involves the measurement of both the renal and peritoneal urea clearances through the

determination of the serum urea as well as the 24 h dialysate and urine urea. The urea distribution volume (V) is usually estimated either using a fixed percentage of body weight or using anthropometric formulae such as the Watson's formula.[79] The estimation of V has a great impact on the kt/v equation and it can be inaccurate in individual patients.[10] Overestimates of V are present in obese patients, and underestimates in those who are underweight. These inaccuracies must be taken into consideration when kt/v targets are interpreted. To overcome these inaccuracies, most investigators now consider the calculation of V based on the Watson formula as the method of choice rather than estimation as a fixed fraction of body weight.

1.3.2 Creatinine Clearance in the Assessment of Peritoneal Dialysis Adequacy

Creatinine clearance (CrCl) is used less often than UKM as an estimate of PD adequacy. This may be related to the familiar use of kt/v in the HD literature. However CrCl is also known to have certain limitations. Glucose interferes with many of the biochemical methods for the estimation of creatinine in the dialysate solution. There is controversy regarding the correct method for estimating residual glomerular filtration rate (GFR), though it is now recommended that the average of urea and creatinine clearances should be used. Estimates of CrCl are usually normalised by body surface area (BSA). Creatinine clearance is expressed per 1.73m^2 body surface area and it has been suggested that the systematic error reported for V derived from anthropometric formulae would also apply to BSA derived in a similar manner.[80]

National guidelines from the United States, Canada, and Europe no longer recommend the use of creatinine clearance as the surrogate solute for dialysis adequacy.[9,10] However, it is

acknowledged that one could continue to monitor 24 hour dialysate and urine creatinine removal because it is an estimation of muscle mass and CrCl is a reflection of phosphate clearance in PD.

1.3.3 Solute Clearance and Patient Outcomes in Peritoneal Dialysis

Several prospective cohort studies have been published on the effects of small solute clearance and other factors on mortality, morbidity and quality of life of PD patients. Blake et al[81] reported a small increase in the probability of death for those with a weekly kt/v <1.5 among 76 CAPD patients in Canada. Teehan et al[82] reported an increased survival in those with a weekly kt/v value >1.89. De Alvaro[83] followed 102 CAPD patients for 12 months in a multicentre study in Spain; survivors had an average kt/v of 2.0 compared to 1.7 for those who died. Lameire et al[84] reported a mean kt/v of 1.89 in 16 patients who had survived 5 years on CAPD. Brandes et al[85] found that good clinical outcomes were associated with a mean weekly kt/v value of 2.3 compared to 1.5 for poor clinical outcomes. Lo et al[86] in a study of 150 anuric PD patients, showed that kt/v less than 1.7 was associated with greater mortality. In another prospective observational study on anuric patients in the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD), peritoneal kt/v below 1.5 and creatinine clearance below 40 L/week/1.73 m^2 were associated with increased mortality. [87]

There are also some prospective controlled studies that used multivariate analysis to assess the relationship between solute clearance and other variables on patient outcomes. Maiorca et al[88] in an Italian study of 68 prevalent PD patients reported that kt/v less than 1.7, old age, peripheral vascular disease, dyslipidaemia, arrhythmia and initial low albumin are associated with poor

outcome. Genestier et al[89] in their study of 201 patients found that lower kt/v, cardiovascular disease, older age and diabetes were associated with worse survival.

The CANUSA study[90] was a large multicenter prospective study, performed among 680 incident CAPD patients in Canada and the USA with a mean follow up of 1.2 years per patient. The result showed a 6% reduction in the relative mortality risk for every 0.1 increase in kt/v urea per week and 7% reduction for every 5 l/week/1.73m2 increase in creatinine clearance; also, a kt/v urea of 2.1 and a weekly creatinine clearance of 70 L/1.73 m^2 body surface area were both associated with a 78% expected two year survival rate.[90] However in a re-analysis of the CANUSA Study, it was found that residual kidney function had confounded the prior results; residual kidney function and not dialysate clearance was associated with improved survival.[91]

Randomised controlled studies however found that greater clearances did not lead to improved patient survival. In the Adequacy of PD in Mexico (ADEMEX) study involving 965 patients, randomly assigned to continue their usual prescription (4 exchanges of 2L) versus a more aggressive dialysis prescription to reach a CrCl greater than 60 L/wk/1.73 m^2, survival was found to be the same in both groups. [92] A subsequent randomised controlled trial from Hong Kong showed no difference in survival among three groups of CAPD patients with total kt/v of 1.5 to 1.7, 1.7 to 2.0, and greater than 2.0 with minimal residual kidney function. However, patients with a kt/v <1.7/week had more clinical problems, and higher erythropoietin requirements.[93]

1.3.4 Solute Clearance Targets

The last decade has witnessed the evolution of guidelines by various national and international organisations on the target dose of PD based on solute clearance parameters. The National Kidney Foundation (NKF) through the Kidney Disease Outcome Quality Initiative (KDOQI) issued the first guideline on the target dose of PD in 1997 which was revised in 2000, recommending a kt/v greater than 2.0 and creatinine clearance (CrCl) greater than 60 L/wk/1.73 m2 based largely on the data derived from the CANUSA study as well as the Italian study. [88] The guidelines were later revised in 2006 after the release of data from the ADEMEX and Hong Kong studies, [92,93] the findings of which supported the recommendation of lower weekly solute clearances. The current recommendations of the K/DOQI is a minimum kt/v of 1.7 in anuric patients and eliminated CrCl as a target.[9] This is similar to those recommended by the European Best Practice Guidelines (EBPG) even though the EBPG added a minimum peritoneal target for net ultrafiltration in anuric patients to be 1.0 liter/day.[10] The International Society for Peritoneal Dialysis (ISPD) has also recommended that the total (renal + peritoneal) kt/v urea should not be less than 1.7 at any time.[94]

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1.3.5 Creatinine Clearance or kt/v

There are no data to suggest that one index is better than the other. For most patients, total weekly kt/v and CrCl are highly correlated. However, up to 20% of patients will reach target with one adequacy measure, but not the other.[95] The reasons for these discrepancies are multifactorial, and include the amount of residual renal function present and its relative contribution to total kt/v or CrCl. The latter is much more dependent on residual renal function. Another factor is the difference in peritoneal transport characteristics and the influence of patient size on normalization for v and also the BSA.[95]

1.4 Assessment of Nutritional Status in Peritoneal Dialysis Patients

The prevalence of malnutrition is high among PD patients and is reported to reach up to 40 to 66 percent among PD patients in the United States.[96] Despite a reported paucity of data on nutritional parameters and adequacy of dialysis in Africa, Naicker[97] has recently reviewed a few available studies from this part of the world and confirmed the high prevalence of malnutrition among ESRD patients. Several small and large scale cohort studies have revealed that protein energy malnutrition is associated with increased morbidity, mortality and impaired quality of life among dialysis patients. [98]

Malnutrition in PD patients may result from many factors, including inadequate nutrient intake as a result of inadequate dialysis, dietary restrictions and reduced appetite, which may be caused by increased intra peritoneal pressure, hyperglycaemia from dialysate glucose absorption as well as medications. Others include loss of protein and amino acids from the peritoneum which may reach up to an average of 5- 15g per day, and increased catabolism due to factors such as coexisting systemic diseases, infections such as peritonitis, chronic inflammation and inadequate dialysis.[99] Attention is being focused on the association between malnutrition, inflammation and atherosclerosis in chronic kidney disease, the so called MIA syndrome.

Causes of inflammation in PD patients include peritonitis and exit site infection, bio-incompatible PD solutions and exposure to endotoxins and other cytokines inducing substances in a contaminated PD solution. Inflammation is associated with endothelial dysfunction, insulin resistance and increased oxidative stress, all of which may accelerate atherosclerosis. Nutritional

and inflammatory markers are reported to be closely linked to cardiovascular (CV) disease and mortality in PD patients.[99]

Monitoring of the nutritional status in PD patients is important, as early identification of malnutrition and its management through optimal use of diet, appropriate dialysis dose, and perhaps protein and amino acid supplements will lead to an improvement in nutritional status and patient outcome.[99] It is recommended that in the absence of malnutrition, nutritional status should be monitored every 6 months in patients of greater than 50 years of age while patients of less than 50 years of age and those on maintenance dialysis for more than 5 years, should be monitored every 3 months. [98]

There is no single parameter that provides complete and unambiguous assessment of the nutritional status of PD patients. The ideal nutritional marker should be able to predict outcome, is inexpensive, reproducible and an easily performed test that is not affected by such factors as inflammation, gender, age and systemic diseases. Such an ideal nutritional marker is not available at present; hence various national and international organisations have recommended that nutritional status should be assessed by a number of assessment tools. The EBPG for example recommended the use of dietary assessment, body mass index, subjective global assessment (SGA), anthropometry, nPNA, serum albumin, serum prealbumin, serum cholesterol and technical investigations such as bioimpedance, dual X-ray absorptiometry, and near infrared reactance. [98]

1.4.1 Dietary Assessment

Dietary assessment can be obtained through dietary records and/or food questionnaires, which involves a record of food intake of individual patients ranging from 24 hour-recall to 3 and 7 days diet diaries.The expertise of a qualified dietitian is essential to complete and calculate these accurately. The K/DOQI Recommendations for Nutritional Management suggest a 3-day diary which includes a dialysis day, a weekend day and a non-dialysis day. [100] Dietary assessment may be limited by the fact that recalling food intake even during the previous 24 h may be difficult for the elderly suffering from memory impairment while longer recall periods may provide inaccurate information as patients become less motivated.

1.4.2 Anthropometry

Anthropometry provides a semi-quantitative estimate of the components of body mass, particularly of bone, muscle, and fat to give information concerning nutritional status. Anthropometric monitoring of the same patient longitudinally may provide valuable information concerning changes in nutritional status for that individual. The anthropometric parameters that are generally assessed include body weight, height, skeletal frame size, skin fold thickness (an indicator of body fat), mid-arm muscle circumference (an indicator of muscle mass), and BMI. Anthropometry has the advantages of being easy to use, is widely available and cost effective; however it requires precise techniques of measurement and the use of proper equipment to give accurate, reproducible data. Otherwise, the measurements may give variable results. Another limitation is that the optimal anthropometric measures for indigenous African CAPD patients have not been defined.

1.4.2 Biochemical Assays

Measurement of serum albumin levels is inexpensive, easy to perform and widely available even in developing countries. Studies have demonstrated an association between serum albumin concentrations and patient outcome.[100] However serum albumin, and prealbumin levels may be insensitive to changes in nutritional status and do not necessarily correlate with changes in other nutritional parameters. It is also known to be influenced by non-nutritional factors, such as infection or inflammation, hydration status, peritoneal or urinary albumin losses. Therefore hypoalbuminaemia in PD patients does not necessarily indicate protein-energy malnutrition (PEM).

Serum cholesterol concentration may be a useful screening tool for detecting chronically inadequate protein-energy intakes. It is too insensitive and nonspecific to be used for purposes other than for nutritional screening, and it is recommended that dialysis patients with serum cholesterol concentrations less than approximately 150 to 180 mg/dL (3.9-4.68mmol/l) should be evaluated for malnutrition as well as for other co morbid conditions. It was more extensively studied in HD patients where the relationship between serum cholesterol and outcome has been described as either 'J-shaped' or 'U-shaped'; with increasing risk for mortality as serum cholesterol falls below approximately 2 g/l (5.2 mmol/l) or rises above 3 g/l (7.8mmol/l).[98] However the relationship between low serum cholesterol and increased mortality is not observed in the CAPD population,[100] possibly because sample sizes in studies of individuals undergoing CAPD are smaller and possibly are confounded by hyperglycaemia due to increased glucose absorption and/or hypertriglyceridemia. However, in one study, higher serum cholesterol

concentrations [250 mg/dL (6.5mmol/l)] were associated with increased mortality in CAPD patients.[100]

1.4.3 Protein Equivalent of Total Nitrogen Appearance

The protein equivalent of total nitrogen appearance (PNA) provides an independent assessment of dietary protein intake and it is based on the rationale that in a steady state condition, the difference between nitrogen intake and losses, is zero or slightly positive. The PNA is usually normalised to some function of body weight (nPNA) because body mass strongly influences both net protein breakdown and dietary protein requirement. It is recommended that PNA should not be used alone to evaluate nutritional status, but rather as one of several independent measures when evaluating nutritional status. There are several important limitations to the use of PNA in the assessment of nutritional status. It approximates protein intake only when the patient is in a steady state condition i.e. neither in anabolic nor in catabolic state. This is because in the catabolic patient, PNA will exceed protein intake to the extent that there is net degradation and metabolism of endogenous protein pools to form urea. Conversely, when the patient is anabolic, dietary protein is utilised for accrual of new body protein pools, and PNA will underestimate actual protein intake. Variations in protein intake cause rapid changes in the PNA, hence it fluctuates from day to day as a function of protein intake, and a single PNA measurement may not reflect usual protein intakes. Normalising PNA to body weight can be misleading in obese, malnourished, and oedematous patients.

1.4.4 Subjective Global Assessment

Subjective global assessment (SGA) was initially developed to determine the nutritional status of patients undergoing gastrointestinal surgery and subsequently was applied to other populations. It has been validated in PD patients and its correlation with other measures of nutritional status is well described.[99]

The initial 3 point scale was modified to a 7 point scale which was shown to provide greater sensitivity and more predictive power in PD patients than the original 3-point scale and this was used in the CANUSA study.[90] It is recommended by the major practice guidelines for the assessment of nutritional status of PD patients. It has the advantage of being simple and is easy to perform with minimum training. It is reproducible and is based on subjective and objective aspects of the medical history and physical examination. Disadvantages of the SGA include the fact that visceral protein levels are not included in the assessment and that it is focused on nutrient intake and body composition. It is subjective and its sensitivity, precision, and reproducibility over time have not been extensively studied.

1.5 ECHOCARDIOGRAPHY ASSESSMENT IN PERITONEAL DIALYSIS PATIENTS

Cardiovascular diseases are frequent in ESRD patients and are the main causes of morbidity and death in them.[101] This high prevalence of cardiovascular diseases, is not only due to the presence of traditional cardiovascular risk factors, but also the non traditional risk factors such as inflammation and oxidative stress as well as the fact that CKD in itself been shown to be a cardiovascular risk factor.[102] Those CKD related factors such as anaemia, mineral metabolism and poorly controlled hypertension as a result of fluid overload may be influenced by the dialysis dose and adequacy. Although some argued that the modality of RRT itself may contribute to the

cardiovascular damage and a very important question is, between HD and PD, which is more harmful and this has been debatable. In a recent review, arguments in support of PD were cited though it has been concluded that the way each of the RRT modality is performed is more important.[101] Echocardiography is a useful tool in the assessment of cardiovascular function and structural parameters with the advantages of being simple, non invasive and widely available. It is important for the diagnosis of clinical and subclinical cardiac dysfunction, prediction of cardiac risk as well as the follow up of treatment.[103] The identification of cardiac abnormalities such as the left ventricular hypertrophy is known to have diagnostic and prognostic significance.[101]

1.6 HYPOTHESIS

CAPD patients in Johannesburg Hospital are receiving adequate dialysis in accordance with international standards and guidelines.

1.7 AIMS AND OBJECTIVES

1. To measure the solute clearance in CAPD patients for assessing the adequacy of peritoneal dialysis.

2. To asses the correlation between the amounts of dialysis dose received in terms of solute clearance and presence of co morbidities as measured by cardiac function, level of haemoglobin, blood pressure control and nutritional status of the patients.

3. To perform PET for the establishment of the peritoneal membrane characteristics of CAPD patients.

4. To assess the nutritional status in these patients and its relationship to PD adequacy.

CHAPTER 2

MATERIALS AND METHOD

The study was conducted in the Division of Nephrology of the Johannesburg Hospital between April and November 2008. The protocol for the study was approved by the Human Ethics Committee of the University of Witwatersrand; ethics clearance certificate protocol number M080452.

2.1 Study population

The study population consisted of all 80 adult CAPD patients (which is the maximum number of patients permitted on the PD program of the Johannesburg Hospital at any one time) receiving treatment at the PD unit of the Johannesburg hospital, who satisfied the inclusion criteria and consented to participate in the study. Almost all the patients studied were on 4 exchanges of 2 liters 2.5% dextrose solution.

2.1.2 Inclusion Criteria

1. ESRD patients aged 18 years and above who are on CAPD
2. Patients who are on CAPD for at least one month

2.1.3 Exclusion Criteria

1. Patients who had peritonitis episodes in the last 1 month.
2. Patients with catheter malfunction, or dialysate leaks
3. Patients who did not give consent.

2.2 METHOD

This work was a cross sectional study. Using a semi-structured interview form, information on age, race, gender, aetiology of CKD, duration on PD, type of PD solution, number of exchanges per day and erythropoietin dose was obtained.

Blood pressure (BP) was recorded non-invasively in the arm with an Acusson Mercury Sphygmomanometer in the sitting position after resting for at least 5 minutes. The average of three readings, taken 5 minutes apart was recorded as the blood pressure.

2.2.1 Solute clearance measurement

Patients were given adequate information on the procedure and also on the accurate method for collection of both the 24 hour urine and the 24 hour dialysate samples by the researcher and the head nurse of the PD unit. Bottles were supplied for the urine collection which started a day prior to the next clinic visit and ended in the morning at the clinic when specimens were collected. Patients came to the CAPD Clinic with the previous day's drainage fluid and the overnight dwell was drained in the morning at the clinic. Those without residual renal function (defined as having less than 100mls of urine over 24 hours period) [9] were not given bottles for the 24 hour urine collection, but arrived the morning with the previous day's drained dialysate. The 24 hour dialysate samples were measured and the volume recorded. After thorough mixing, a 10ml sample was collected in a lithium heparin tube and sent to the laboratory for the determination of fluid urea and creatinine. Another 5 ml sample was taken in a fluoride oxalate tube for the estimation of fluid glucose. The 24 hour urine volume was also measured and the volume recorded; aliquots were sent for the estimation of the urine urea and creatinine. Both the urine

and the dialysate urea and creatinine were used for the calculation of the solute clearance. Blood samples were also taken in a lithium heparin tubes for the serum urea and creatinine estimations. Solute clearance measurement included the kt/v and the creatinine clearance. For those with residual renal function it included both the residual renal and peritoneal components.

Thus, Total kt = peritoneal kt + renal kt

Peritoneal kt was calculated as the value of urea in the 24 hour dialysate sample divided by the serum urea, while the renal kt was the 24 hour urine urea divided by the serum urea. The total kt was divided by v which was calculated by using the Watson formula which is based on the age, sex, height and weight of the patient.[79] The value obtained was multiplied by 7 to give the weekly kt/v.

Total creatinine clearance = peritoneal creatinine clearance + renal creatinine clearance,

Peritoneal clearance was obtained by dividing creatinine level in the 24hour dialysate (after being corrected for the interference of glucose in the measurement) by serum creatinine level. The renal component was calculated as the average of urea clearance and creatinine clearance in the urine. The value of the total clearance was corrected for 1.73m^2 body surface area (BSA) and then multiplied by 7 to get the weekly creatinine clearance. The BSA was obtained using the formula of Du Bios.[104]

2.2.2 Peritoneal Equilibration Test

The PET test was done following a standard protocol as described by Twardowsky et al.[60] Patients came to the clinic with an overnight 8-10 hour dwell, which was drained in the clinic over 20 minutes with the patient in the upright position. Two liters of 2.5% glucose dialysis solution were infused over 10 minutes with the patient in the supine position after the bag was

weighed. The patient rolled from side to side after every 400 ml infusion. At the completion of infusion (0 time) and at 2 hours dwell time, 200 ml of dialysate was drained and a 10 ml sample was taken while the remaining 190 ml was infused back into the peritoneal cavity. At 2 hours time a 5ml blood sample was also collected into two sample bottles, one lithium heparin for the estimation of creatinine and another 5ml in fluoride oxalate tube for determination of glucose. During the 4 hour dwell time, the patient remained upright and was allowed to freely ambulate. The dialysate was drained in the upright position over 20 minutes at the end of the 4 hour dwell. The drained dialysate was measured and a 10 ml sample was taken from the drain together with another blood sample in both lithium heparin and fluoride oxalate tubes. All the samples were sent for the laboratory measurement of creatinine, urea and glucose. The ratio of the dialysate to plasma values (D/P) for creatinine and urea were calculated. The ratio of the dialysate glucose at 2 and 4 hours to that at time 0 were also calculated. The researcher and a nurse from the PD unit conducted all the PET tests on the study patients.

2.2.3 Measurement of Dialysate and Serum Creatinine

Serum and dialysate creatinine were measured at the National Health Service Laboratories (NHLS) at the hospital by a dedicate staff using the modified Jaffe method.[105] This is based on the principle that creatinine in alkaline solution forms a yellow-orange complex with picrate. The colour intensity is directly proportional to the creatinine concentration and was measured spectrophotometrically at 510nm.

Creatinine + picric acid → creatinine-picric acid complex

2.2.4 Measurement of Dialysate Glucose

The dialysate glucose was measured using the glucose hexokinase procedure. Glucose is phosphorylated with adenosine triphosphate (ATP) in the reaction catalysed by the hexokinase (HK). The glucose-6-phosphate (G6P) product formed is then oxidised with the concomitant reduction of nicotinamide adenine dinucleotide (NAD) to NADH in the reaction catalysed by Glucose-6-phosphate-dehydrogenase (G6PDH). The formation of NADH causes increase in absorbance which is directly proportional to the glucose concentration and was measured at 340nm.

2.2.5 Measurement of the correction factor for the glucose interference with the creatinine measurement in the dialysate

The glucose and creatinine in an aliquot of a fresh bag of 2.5% dextrose dialysis solution were measured. The glucose value obtained was divided by the measured creatinine value to give the correction factor. There was a linear relationship between dialysate glucose level and the extent of the false elevation in creatinine. Thus the dialysate creatinine was corrected as follows: Corrected creatinine = apparent creatinine – correction factor x glucose.

2.2.6 Other Biochemistry Tests

All the biochemistry tests were done in the National Health Laboratory (NHLS) at the Johannesburg Hospital. All samples were analyzed using the Roche/Hitachi Modular ISE 900 automated analyzer (Roche Diagnostics Corporation, Mannheim Germany). The tests were measured with commercially available kits and carried out according to manufacturers'

instructions. Serum calcium, phosphate, and parathyroid hormone as well as haemoglobin measurements were done as part of the routine monthly tests in the peritoneal dialysis patients.

2.2.6.1 Serum albumin

Albumin binds with bromocresol green (anionic dye*)* at a pH value of 4.1 to form a blue-green complex. The colour intensity of the blue-green complex is directly proportional to the albumin concentration and was determined spectrophotometrically at 510nm. Laboratory normal range is 34– 48g/L.

2.2.6.2 Serum cholesterol

Serum total cholesterol was determined using cholesterol esterase and cholesterol oxidase enzymatic colorometric test.

$$\text{Cholesterol esters} + H_2O \xrightarrow[\text{esterase}]{\text{cholesterol}} \text{cholesterol} + \text{RCOOH}$$

Cholesterol esters are cleaved by the action of cholesterol esterase to yield free cholesterol and fatty acids.

$$\text{Cholesterol} + O_2 \xrightarrow[\text{Oxidase}]{\text{Cholesterol}} \text{cholest-4-en-3-one} + H_2O_2$$

Cholesterol is converted by oxygen with the aid of cholesterol oxidase to cholest-4-en-3-one and hydrogen peroxide. Hydrogen peroxide created forms a red dyestuff by reacting with 4-aminophenazone and phenol under the catalytic action of peroxidase. The color intensity is directly proportional to the concentration of cholesterol and can be determined spectrophotometrically.

2.2.6.3 Serum calcium

Serum calcium was determined using the complexometric methods in addition to atomic absorption spectrometry. This method is based on the reaction of calcium with o-cresol-phthalein complexone in alkaline solution to form calcium-o-cresolphthalein complex. Magnesium is masked with 8-hydroxyquinoline. The colour intensity of the purple complex formed is directly proportional to the calcium concentration and was measured spectrophotometrically. Laboratory normal range is 2.15 – 2.55mmol/L.

2.2.6.4 Serum phosphate

Serum phosphate was measured based on the reaction of phosphate with ammonium molybdate to form ammonium phosphomolybdate. Inorganic phosphate forms an ammonium phosphomolybdate complex with ammonium molybdate in the presence of sulphuric acid. The complex was determined spectrophotometrically in the ultraviolet region (340nm). Laboratory normal range is 0.87 – 1.45mmol/L.

2.2.6.5 Serum Intact Parathyroid Hormone

The measurement of intact PTH using two-site immunoassays provides a more accurate assessment of parathyroid secretory status especially with renal impairment. Intact PTH was measured using the ADVIA Centaur Intact PTH assay (Bayer Diagnostics, United Kingdom). The ADVIA Centaur Intact PTH assay is a two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amounts of two anti-human PTH antibodies. The first is a polyclonal goat anti-human PTH antibody labeled with acridinium ester directed at the N-terminal (N-terminal 1-34). The second antibody is a biotinylated polyclonal

goat anti-human PTH (39-84 regions) antibody. Streptavidin in the Solid Phase is covalently coupled to the paramagnetic latex particles. The system performs a series of steps. The amount of PTH in the patient's sample is equivalent to the amount of relative light units (RLU) detected by the system. Laboratory normal range is 7– 53ng/L

2.2.7 Nutritional Parameters

The nutritional status of the patients was assessed using measurements of serum albumin, cholesterol, anthropometric parameters, dietary recall and the subjective global assessment instrument.

2.2.7.1. Anthropometric Parameters

2.2.7.1.1 Weight and Height

Weight and height were measured using the Secca scale weight/height meter by the dietetian. The patient's Body Mass Index (BMI) was calculated as weight in kilogram/ height in metres square. Normal/Healthy BMI = 18.5 – 25kg/m^2
Overweight = 25 – 30kg/m^2
Obese = ≥30 kg/m^2

2.2.7.1.2 Mid Upper Arm Circumference (MUAC)

This was measured from the midpoint between the lateral projection of the acromion process of the scapula and the inferior margin of the olecranon process of the ulna of the dominant arm which is marked with a non -permanent marker by a trained dietitian. This was measured three times to the nearest 0.1cm using a metric tape measure. A MUAC ≥ 24.3cm is considered normal, and an MUAC < 24.3cm is considered indicative of the presence of PEM.

2.2.7.1.3 Triceps Skin Fold Thickness (TSF)

Triceps Skin Fold Thickness (TSF) was measured to the nearest 0.2mm on the posterior aspect of the dominant arm, over the triceps muscle, at the midpoint line determined for the MUAC (refer to 2.2.7.2) using a Harpenden Calliper (model HSK-BI). The measurement was repeated three times for precision and the average of these readings were recorded.

2.2.7.1.4 Arm Muscle Area

The Arm Muscle Area (AMA) is used to reflect Lean Body Mass (LBM) and was determined from the upper arm anthropometric measurements; the MUAC and the TSF using the formula by Frisancho.[106]

Patients were classified according to the percentile values. Those with percentage AMA below the 5th percentile are classified as being wasted, while those above the 95th percentile are considered as having high muscle mass, while those between the 25th and 75th percentile are considered as having average LBM.

2.2.7.2 Dietary Recall

This was conducted with the help of an experienced Dietician. The patient was asked during a 15 – 20minute interview to recall in detail all the food and beverages consumed over a typical 24-hour day. The dietician helped the patient remember all that was consumed during the period in question and assisted in estimating the portion sizes thereof with the use of food aids/photos manual developed by the Medical Research Council (MRC). The findings were recorded under four measurements, namely ‘time’, ‘what’, ‘size thereof’, and ‘description’ of what the patient reported to have consumed within a typical 24-hour day. Time included the time of the day when

the food/beverages were consumed by the patient. The food/beverages indicated by the patient to be consumed were listed under the 'what' column, for example brown bread. The portion size was noted under the 'size thereof' column, and finally the preparation method used was indicated under the 'description' column. These were later assessed using the FoodFinder which is a computerised diet analysis program. The FoodFinder used in the study was developed by the MRC using common South African based foods, preparation methods, and portion sizes thereof.

2.2.7.3 Subjective Global Assessment

The SGA instrument used in the study is attached as appendix 1 and was administered on the patient with the help of an experienced dietitian who is a co researcher in this work. The first part of the SGA comprised of the patients' history which included weight change, dietary intake relative to normal over the past 2 weeks, gastrointestinal symptoms lasting greater than two weeks, and the patients' functional capacity.

The second part of the SGA consisted of the physical examination where loss of subcutaneous fat in four different areas (shoulders, triceps, chest and hands), presence of muscle wasting, and the presence of oedema in various areas (hands, sacrum and or pedal) were assessed. These variables were individually scored, and the sum of the scores was classified with the help of an experienced dietician as Normal, Mild, Moderate or Severe.

The final section of the SGA consisted of the overall rating of the patient's nutritional assessment, well nourished was classified as a patient who has experienced an improvement in historical features, such as the appetite or weight gain. A patient was classified as being mild/moderately undernourished when there was at least 5% weight loss without stabilization or weight gain, had a definite history of reduced dietary intake, and exhibited mild loss (1+) of

subcutaneous tissue as per the SGA assessment tool scoring system (appendix1). Patients presenting with any physical signs and ongoing weight loss of at least 10% were classified as severely undernourished.

2.2.8 Echocardiography in the assessment of cardiac structure and function

Echocardiography is a non invasive test that is used for the assessment of heart dimensions and geometry as well as wall motion abnormalities. Echocardiography was done in the Cardiology Unit using the Acuson Sequoia C256 machine (Acuson Corporation California USA) equipped with 2 to 4-MHz probes allowing M-mode, two dimensional, and pulsed doppler measurements. Echocardiography was performed by one Cardiologist under the supervision of a senior cardiologist, according to the standard guidelines.[107] All scans were performed with the head of the table inclined at an angle of 15 degrees and the patient rotated 30–45 degrees in the left lateral decubitus position at end-expiration. Left ventricular internal dimension measurements in end-diastole (LVEDD), and end-systole (LVESD) were made at the level of the mitral valve leaflet tips in the parasternal long-axis view. The normal range for LVEDD is 3.5- 5.6cm while that of LVESD is 2.0-4.0cm.[107] The interventricular wall thickness during diastole ($IVST_d$) and posterior wall thickness during diastole (PWT_d) were measured by M-mode. The cutoff points for LV hypertrophy using the LVM/BSA ratio were 136 g/m^2 for males and 100 g/m^2 for females.[107]

Relative wall thickness (RWT) was used to characterize LVH into eccentric and concentric LVH. RWT greater than 0.45 in the presence of LVH is indicative of concentric hypertrophy and eccentric hypertrophy if less than 0.45 in the presence of LVH.

RWT = (2 x PWTd)/ LVEDD

Diastolic function was assessed using M-mode. The anterior mitral valve leaflet (AMVL) during diastole has a characteristic M- shaped (E-A) pattern assuming the individual is in sinus rhythm and does not have mitral stenosis. The E-wave is the result of passive early diastolic left ventricular filling. The A-wave represents active late diastolic LV filling due to atrial contraction. The acceleration time (AT) and deceleration time (DT) of the E-wave can be measured. The former is the time from the onset of diastolic flow to the peak of the E-wave while the latter is the time from the E-wave peak to the point where the deceleration slope hits the baseline. The E-wave is often greater than the A-wave. If the left ventricle is stiffer than usual, there may be diminished anterior mitral valve leaflet (AMVL) excursion (E-wave) and an increase in A-wave size (as the atrial contraction contributes to a greater extent to ventricular filling of the left ventricle); the E: A ratio is thus reduced. The E-wave, E: A ratio and E-wave deceleration times tend to fall with increasing age. The normal ranges are E:A ratio of 1.04 ± 0.38 for men and 1.03 ± 0.34 for women.

Systolic function was assessed by measuring the left ventricular ejection fraction and fractional shortening. Systolic dysfunction was defined as a shortening fraction less than 28% or ejection fraction less than 50%.

2.3 Statistical analysis

Data were reported as mean ± SD. Tables and figures were used to present the findings as appropriate. Linear regression analysis was used to determine factors associated with solute clearance while analysis of variance was used to test the differences in three groups based on weekly kt/v results in terms of blood pressure, haemoglobin and biochemical parameters. Student

t-test was used to test differences in D/P creatinine as well as D/D0 glucose result between the study population and those reported for the USA, Mexico and Chinese populations respectively. Pearson's correlation coefficient was used to measure the relationship between the SGA and the anthropometric parameters in the assessment of the nutrition status of the study patients. Linear regression analysis was used to assess the relationship between the systolic function as assessed by ejection fraction and shortening fraction as well as diastolic function as assessed by the EA ratio on the solute clearance as measured by the weekly kt/ v, haemoglobin, blood pressure and serum albumin levels. All analyses were done using computer based software, the statistical package for social sciences (SPSS version 13.0).

CHAPTER THREE

RESULTS

3.1 Demographic Data

In this cross sectional study, 80 consecutive patients on CAPD were studied. One patient withdrew his consent before the end of the investigation while another one had incomplete data, therefore 78 patients were analysed giving a response rate of 97.5%. There were 67 (86%) blacks and 11 (14%) non-black patients in the study. Thirty three (42%) were females while 45 (58%) were males. The mean age of the study population was 38.10 ±12.43 years with a range between 18 and 65 years.

Table3.1. Distribution of the different age groups and the sex of the study patients

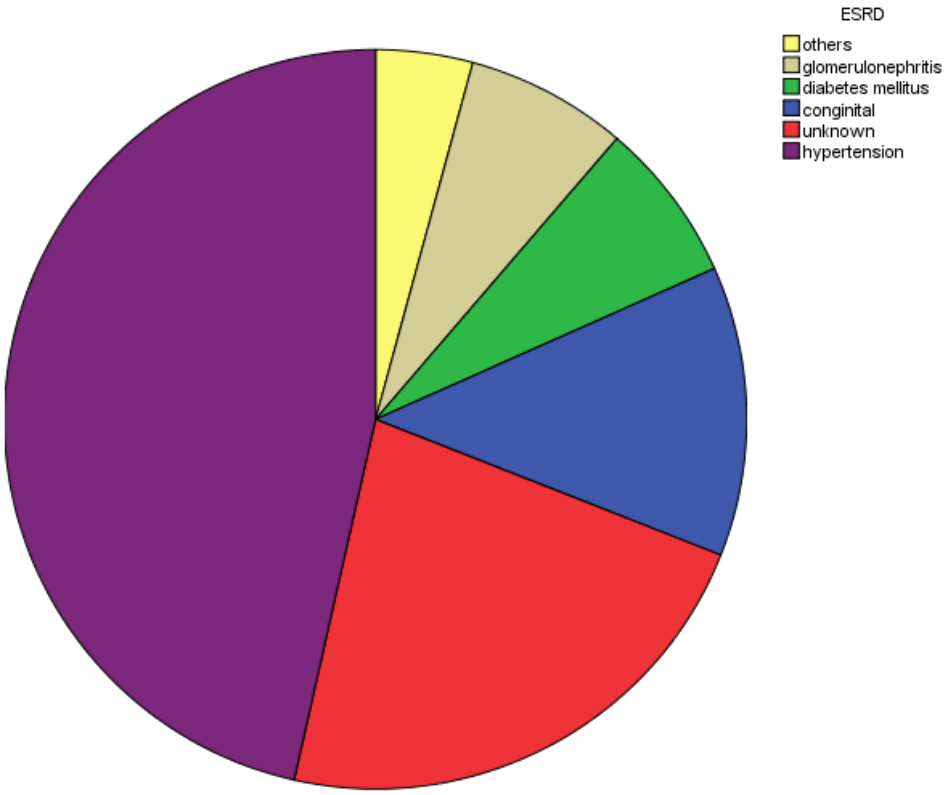
Age group (years)	Females	Males	All
18 – 20	3 (3.84%)	4 (5.1%)	7 (8.8%)
21 – 30	7 (8.8%)	8 (10.2%)	15 (19.2%)
31 – 40	9 (11.5)	13 (16.7%)	22 (28.2%)
41 – 50	8 (10.2%)	12 (15.4%)	20 (25.6%)
51 – 60	6 (7.7%)	7 (8.8%)	13 (16.7%)
Above 60	0 (0%)	1 (1.3%)	1 (1.3%)
All	33 42%	45 58%	78 100%

The mean duration on CAPD was 19.48 ± 20.67 months with a range between 2 and 147 months. Mean diastolic blood pressure was 92.24 ± 17 mmHg with a range between 53 and 145 mmHg, while the mean systolic blood pressure was 144.96 ± 27.88 with a range between 95 and 231

mmHg. 42.3% of the patients had a systolic blood pressure of 140 or less while 45.07% had a diastolic blood pressure of 90 or less. Forty two (53.8%) patients were on recombinant human erythropoietin injection with a weekly dose ranging between 4000 and 18000 iu. The mean Hb was 10.99 ± 2.14 g/dl with a range between 7.2g/dl and 17.9 g/dl. A target Hb of 11-12 g/dl was achieved in 55.8% of the study patients.

The various causes of ESRD in the study population and their relative frequencies are shown in figure 2. Hypertension was the major cause of ESRD in the study population (46.5%). The congenital anomalies of the kidneys varied from autosomal dominant polycystic kidney disease to dysplastic kidneys. Though four of the patients were positive for HIV, none was a histologically confirmed case of HIVAN. Other miscellaneous causes included chronic interstitial nephritis. Three of the patients had a previous renal transplant.

Figure 2. Causes of ESRD in the study population



3.2 Solute Clearance Results

Eight patients had significant residual renal function with a mean renal kt of 3.12 ± 1.70. The BSA of the patients ranged from 1.35 to 2.27 with a mean of 1.72± 0.19. The mean volume of distribution (v) was 36.03 with a range between 25.15 and 53.35. Table 3.2 shows the values for the solute clearance results. The correction factor used for the interference of glucose in the measurement of creatinine in the dialysate was 0.000325. Thus corrected creatinine was determined as measured dialysate creatinine – dialysate glucose x 0.000325.

Table 3.2 solute clearance parameters

Parameter	Mean	SD	Minimum	Maximum
24 hour dialysate volume (L)	9.62	1.27	5.10	12.50
24 hour dialysate urea	20.00	6.69	6.60	34.60
24 hour dialysate creatinine	732.91	247.29	251	1405
Plasma urea (mmol/l)	22.81	7.30	7.20	38.00
Plasma creatinine (µmol/l)	1068	363.33	356	1899
24 hour D/P urea	0.87	0.11	0.41	1.30
24 hour D/P creatinine	0.70	0.13	0.33	1.01
Weekly kt/v	1.72	0.32	1.11	2.67
Weekly creatinine clearance	49.72	9.83	32.79	82.38

D/P = dialysate to plasma ratio.

Linear regression analysis was used to assess the relationship of certain factors to the solute clearance in terms of the weekly kt/v. The mean kt/v was within the recommended value of 1.7 in the major international guidelines; however 29 (37%) of the patients had a weekly kt/v of less than 1.7. Factors like SBP, Hb level, serum cholesterol and serum albumin were not significantly associated with the weekly kt/v results in the study population (table 3.3).

Table 3.3. Linear regression analysis for weekly kt/v and other parameters

Weekly kt/v	**Coefficient β**	**t value**	**p value**
Systolic Blood Pressure	-0.102	-0.78	0.44
Haemoglobin level	0.08	0.58	0.56
Serum cholesterol	0.09	0.67	0.50
Serum Albumin	-0.23	-1.64	0.11

The study patients were grouped into three based on the weekly kt/v results. Those with weekly kt/v values below 1.7 (n=29) were classified as group 1, while those with values between 1.7 and 2.0 formed group 2 (n=34) and those with values above 2.0 formed group 3(n=15). Analysis of variance (ANOVA) was performed to test for any significant difference between the three groups in terms of clinical and laboratory parameters like the duration on PD, diastolic and systolic blood pressures, serum urea, serum creatinine, serum albumin, serum cholesterol and haemoglobin. The results were as shown in table 3.4. There was no statistically significant difference in all the parameters tested.

Table 3.4. Analysis of variance between the different groups based on the weekly kt/v

Parameter	Mean± SD values in each group			F value	P value
	Group 1 N=29	Group 2 N=34	Group 3 N=15		
kt/v	1.44±0.16	1.82±0.09	2.20±0.16	159.31	0.000
Haemoglobin(g/dl)	10.67±2.28	11.77±2.04	10.61± 1.83	2.07	0.135
Albumin(g/dl)	39.45±4.63	36.23±6.70	35.50±7.76	2.88	0.063
Cholesterol(mmol/l)	4.76±1.98	5.79±1.85	5.22±1.36	1.90	0.158
Urea(mmol/l)	23.14±6.82	21.70±7.35	23.99±8.49	0.48	0.620
Creatinine(mmol/l)	1145.0±418.2	976.8±296.6	1052.5±313.0	1.51	0.229
Duration on CAPD (mths)	16.84±12.86	22.33±30.11	21.64±15.79	0.55	0.579
BMI	23.79±3.45	26.05±5.51	23.97±2.88	2.18	0.12
Systolic BP(mmHg)	148.66±28.9	143.67±24.7	137.71±31.60	0.76	0.470
Diastolic BP (mmHg)	92.16±18.01	93.17±15.24	90.36±19.22	0.12	0.89

3.3 Echocardiograhic Assessment

Echocardiographic assessment could not be done on all the patients due to logistic problems encountered during the study period; as a result only 44 (56.4%) patients had complete echocardiographic assessment and these are patients who were able to present themselves for the study on a non-clinic day including weekends. The results of the measurements are shown in table 3.5. Left ventricular hypertrophy was present in 30 (68%) of the patients, 13 (29%) had various forms of valvular abnormalities, including mitral regurgitation, aortic regurgitation and various other combinations of mitral and tricuspid regurgitation. Nine patients had pericardial

effusions of sizes between 0.46 cm and 1.46cm posteriorly. None of the patients had wall motion abnormalities. Linear regression analysis was used to study the association between systolic function as assessed by ejection fraction and shortening fraction as well as diastolic function as assessed by the EA ration on the solute clearance as measured by the weekly kt/ v, haemoglobin level, serum albumin as well as the diastolic and systolic blood pressures. A significant relationship was noted (p=0.02) between the diastolic function and the haemoglobin level while no significant relationship noted between the other parameters and cardiac function both systolic and diastolic. The results are shown in table 3.6 below.

Table 3.5. Echocardiography Parameters

Parameter	**Mean**	**SD**	**Minimum**	**Maximum**
IVSd (cm)	1.43	0.35	1.02	2.27
IVSs (cm)	1.57	0.34	1.13	2.44
LVIDd (cm)	4.79	0.85	3.12	6.58
LVIDs (cm)	3.30	0.67	2.10	4.71
LVPWd (cm)	1.18	0.26	0.68	1.70
LVPDWs (cm)	0.72	0.80	0.00	2.01
EA Ratio	1.16	0.52	0.40	2.53
Ejection Fraction (%)	58.13	8.10	36.07	75.94
Shortening Fraction (%)	31.07	5.63	19.00	43.94

Table 3.6 Linear Regression Analysis of certain parameters and Left Ventricular Systolic and Diastolic Function

Parameter	**Left ventricular function**	**Coefficient β**	**T value**	**P value**
Haemoglobin	E/A ratio	-1.80	-2.48	0.02
	Ejection fraction	-0.21	-0.72	0.48
	Shortening fraction	0.24	0.58	0.57
Systolic BP	E/A ratio	0.92	0.12	0.91
	Ejection fraction	-3.5	-1.16	0.25
	Shortening fraction	4.23	0.98	0.34
Diastolic BP	E/A ratio	0.28	0.06	0.95
	Ejection fraction	-0.56	-0.3	0.76
	Shortening fraction	0.35	0.13	0.90
Weekly kt/v	E/A ratio	-0.26	-1.46	0.16
	Ejection fraction	-0.54	-0.05	0.96
	Shortening fraction	0.21	0.19	0.99
Albumin	E/A ratio	-0.70	-0.32	0.75
	Ejection fraction	-0.85	-0.93	0.36
	Shortening fraction	1.17	-0.73	0.34

3.4 Peritoneal Equilibration Test Results

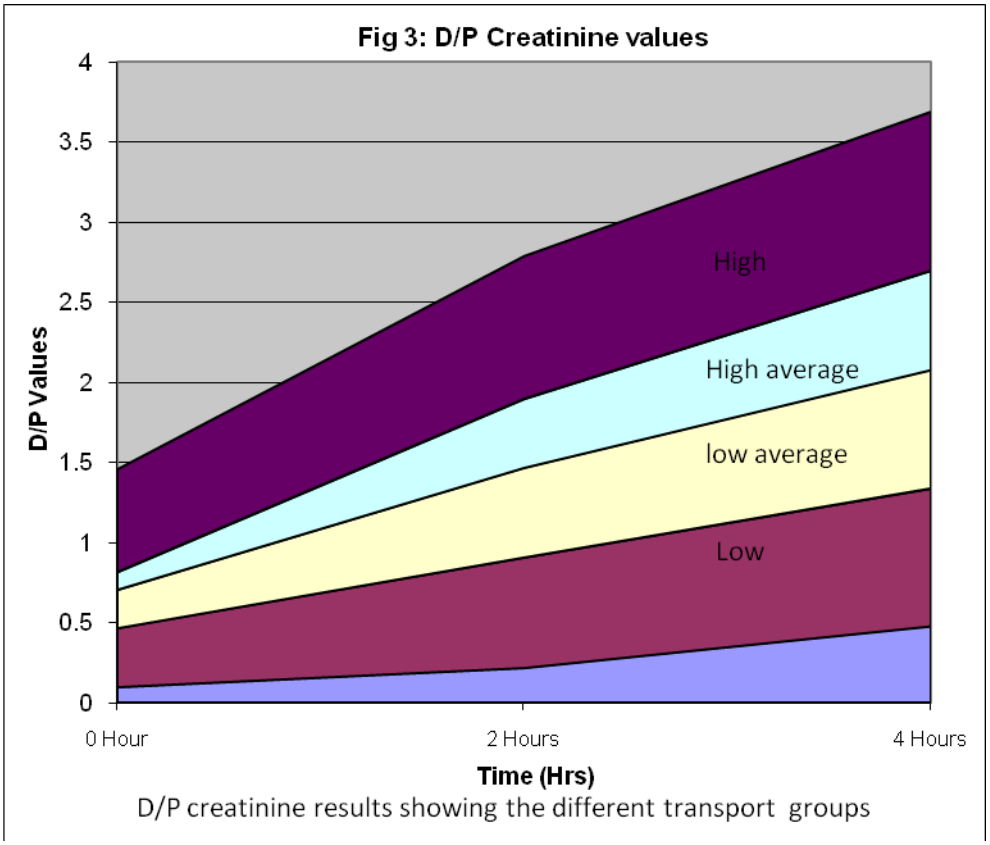
The results of the D/P creatinine is shown in table 3.7, while Figure 3 shows the graphic representation of the D/P creatinine results. The reference ranges used for the classification of the patients into the various transport groups is shown in table 3.8. Based on these 4 hour D/P creatinine reference values, 14 (18%) of the studied patients were high transporters, 26 (33.8%) high average, 29(36.9%) low average and 9(12%) low transporters. A comparison of the D/P creatinine results at 0.2 and 4 hours with those from the North American[60], Mexican [108] and Chinese [69] populations was made. The results are shown in table 3.9. Table 3.10 shows the t-test results comparing the D/P creatinine results. A linear regression analysis was done to assess the effect of duration on PD, weekly kt/v, serum albumin and age on the D/P creatinine at 4 hours, and the results are shown in table 3.11. The results of the D/D0 glucose at 2 and 4 hours are shown in table 3.12 and table 3.13 show the student t-test results comparing the D/D0 glucose result with those from other population. Table3.14 shows the D/P urea results.

Table 3.7. D/P Creatinine Results

D/P creatinine/ Time	0 Hour	2 Hours	4 Hours
Minimum	0.1	0.22	0.48
Mean + 1 SD	0.37	0.69	0.86
Mean	0.24	0.56	0.74
Mean – 1 SD	0.11	0.43	0.62
Maximum	0.64	0.89	0.99
SD	0.13	0.13	0.12

Table 3.8 Proposed Reference Range for Classification of Patients

High Transporters	D/P creatinine at 4 hrs above 0.86
High Average Transporters	D/P creatinine at 4 hrs 0.86- 0.739
Low Average Transporters	D/P creatinine at 4 hrs 0.74- 0.61
Low Transporters	D/P creatinine at 4 hrs Less than 0.61



D/P creatinine results showing the different transport groups

Table 3.9. D/P creatinine results in various populations

Population	D/P creatinine 0 hr	D/P creatinine 2hr	D/P creatinine 4hr
USA (n=101)	0.07±0.05	0.48±0.14	0.56±0.10
Mexican (n=86)	0.12±0.06	0.48±0.10	0.68±0.12
Chinese (n=100)	0.00±0.07	0.52±0.15	0.71±0.15
This study	0.28±0.13	0.56±0.13	0.74±0.12

Table3.10. Comparison of the means of D/P creatinine in different populations study

D/P creat/ time	Population	T value	df	P value
D/P creatinine at 4 hours	Chinese	1.45	178	0.147
	Mexican	3.22	164	0.001
	USA	11.01	179	0.000
D/P creatinine at 2 hours	Chinese	1.88	178	0.06
	Mexican	4.46	164	0.00
	USA	3.94	179	0.00
D/P creatinine at 0 hour	Chinese	18.4	178	0.00
	Mexican	10.3	164	0.00
	USA	14.9	179	0.00

Table3.11. Linear Regression analysis for D/P Creatinine at 4 Hours and other Parameters

D/P creatinine at 4hours	Coefficient β	t value	p value
Duration on PD	0.00	0.61	0.54
Weekly kt/v	-0.02	-0.36	0.72
Age	0.00	0.77	0.45
Serum Albumin	-0.01	-3.51	0.001

Table 3.12 D/D0 Glucose Results in the Study Population

Time/ D/D0 Glucose	Minimum	Mean ± 1SD	Mean	Mean ±1SD	Maximum	SD
D/D0 glucose 2 hrs	0.38	0.52	0.62	0.73	0.99	0.10
D/D0 glucose 4 hrs	0.18	0.27	0.43	0.59	0.99	0.16

Table3.13 Student t- test result comparing the D/D0 glucose result with other populations

D/D0 glucose/time	Population	T value	df	P value
D/D0 glucose at 2 hours	Chinese			
	Mexican	2.10	164	0.034
	USA	4.42	179	0.000
D/D0 glucose at 4 hours	Chinese	2.87	17	0.004
	Mexican	2.0	164	0.046
	USA	2.35	163	0.019

Table3.14. D/P Urea Results

Time/ D/P urea	Mean	SD	Minimum	Maximum
0 hours	0.39	0.39	0.09	0.98
2 hours	0.79	0.10	0.43	1.00
4 hours	0.93	0.08	0.72	1.2

3.5 Biochemistry results

The biochemistry results of the study population are as shown in table 3.15.

Table3.15. Biochemistry Results

Parameter	Mean ± SD	Minimum	maximum
Serum Urea (mmol/l)	22.81 ± 7.30	7.20	38.00
Serum Creatinine(µmol/l)	1068 ± 363.33	356.00	1899.00
Serum Albumin (g/l)	37.49 ± 6.26	16.00	49.00
Serum Cholesterol (mmol/l)	5.20 ± 1.83	2.70	14.00
Corrected calcium (mmol/l)	2.26 ± 0.33	0.87	3.23
Serum phosphate (mmol/l)	1.68 ± 0.62	0.53	3.89
Parathyroid hormone (ng/L)	83.23 ± 58.64	10.8	201

3.6 Nutritional Status Assessment Results

Various nutritional parameters including anthropometric measurements and biochemical methods were used in the nutritional assessment of the study population.

3.6.1 Anthropometric Parameters

Anthropometry provides a semiquantitative estimate of the components of body mass.
The anthropometric parameters assessed in this study include body weight, height and BMI, skin fold thickness and mid-upper arm muscle circumference (MUAC). Table 3.16 shows the descriptive statistics of the various anthropometric parameters in the study population. Further analysis of the BMI results showed that 54% of the patients had a BMI <25kg/m^2 while only 1 patient had a BMI less than 18.5kg/m^2. Among those found to be overweight, 69% of them had oedema, indicating that it may have been due to an increase in hydration status and not LBM. There was no significant correlation between the oedema status and the serum albumin level (r= -0.25, p= 0.09). Majority (63%) of the patients had average to high LBM assessed using AMA, only 23% were below average and 14% were wasted. The TSF result showed that 17% had values <50th percentile and 29% had values >100th percentile, and the mean TSF was above average.

Table3.16. Anthropometric Parameters

Parameter	Mean	SD	Minimum	Maximum
Weight(Kilograms)	66.1	12.12	48.20	100.8
Height (meters)	1.64	0.10	1.37	1.87
BMI	24.76	3.58	18.60	35.00
TSF (mm)	85.60	41.48	35.00	255.00
MUAC (cm)	28.53	3.89	21.50	39.00

3.6.2 Dietary Recall

Analysis of the dietary history showed that 49% of the patients had suboptimal intake in terms of both protein and energy, 6% had mild suboptimal dietary intake, and 43% had moderate suboptimal dietary intake. For energy intake, 14% of the patients had a positive energy balance ie they consumed >100% of total energy requirements, while in terms of the protein intake, 74% of the patients consumed <75% of the recommended protein (8% of whom consumed <25% protein requirements) and 27% of this was <50% high biological value (HBV).

3.6.3 Subjective Global Assessment

Analysis of the history aspect of the SGA showed that less than half of the patients (46%) experienced weight loss within the last 6 months. A continuous weight loss was noted in 23% of the patients. Among those that had experienced a weight gain, 35% of them had oedema.

Gastrointestinal symptoms were present in 26% of the patients. Fatigue and the resultant suboptimal ability to work were experienced by 34% of the patients while none of them was bedridden.

Physical examination revealed that oedema was noted in 37% of the patients. Forty three percent had subcutaneous fat loss (of whom 20% had more than 1 sign of subcutaneous fat loss), and 34% had muscle wasting (of which 25% had more than 1 sign of muscle wasting present).

The overall SGA scores in this study showed that 42% were well nourished, 50% were moderately under nourished and 8% were severely under nourished

Significant correlation was noted between SGA score and anthropometric parameters like the BMI($r = -0.93$, $p = 0.000$) and the MUAC($r = -0.96$, $p= 0.000$) while there was no correlation with the biochemical parameters like the serum albumin level($r= -0.128$, $p= 0.38$) and the serum cholesterol($r= 0.16$, $p=0.26$).

There was no significant correlation between weekly kt/v results and the nutritional status assessment parameters; table 3.17 shows the results of the correlation coefficient between these parameters.

Table 3.17. Correlation between weekly kt/v and nutritional status parameters

Parameter	**R**	**P value**
BMI	-0.26	0.86
MUAC	0.37	0.84
TSF	0.102	0.49
Cholesterol	-0.33	0.82
Albumin	-0.21	0.09

Chapter Four

Discussion

More than 50% of ESRD patients are receiving CAPD as a form of RRT at the Johannesburg Hospital, as there are 55 patients on HD compared to 80 patients on CAPD at any given time. The assessment of the PD adequacy in these patients has not been reported in the past, neither has the assessment of the peritoneal membrane characteristics been carried out. Despite the continued debate on the interpretation and precise prognostic value of small solute clearance in PD patients, dialysis recommendations based on kt/v have gained acceptance in clinical practice with the issuance of practice guidelines by national and international organisations on the target dose of PD based on the kt/v value achieved. Peritoneal membrane characteristic of patients is important for the prescription of adequate PD dose. The monitoring of nutritional status is recommended for early detection and treatment of malnutrition, which is known to affect patient outcome. This cross sectional study was carried out to assess the PD adequacy in 80 consecutive CAPD patients, and to study peritoneal membrane characteristics, as well as the nutritional status.

4.1 Demographic data

The studied patients were predominantly blacks, a reflection of the general population demographics, as the predominant population in RSA are blacks. However, it may also be a selection bias as most of the patients in public hospitals are likely to be those without medical aid coverage. Many of the non black population may therefore be found in the private sector, as their medical aids will provide cover for their treatment. The patients studied were young, with a mean age of 38.10 ±12.43 years, a reflection of the selection criteria for RRT in RSA; this is

similar to the findings by others.[109] It has been reported that ESRD patients in sub-Saharan Africa are usually young and in their economically productive life.[110] However, the relatively young age of the patients may also be due to the fact that in RSA patients who are older than 60 years, patients with advanced cardiovascular disease, and diabetic patients with cardiovascular disease are not accepted onto the public sector chronic dialysis programmes because of limited resources.[111]There was a slight male preponderance. This gender distribution differs with that reported in a similar study in Durban[109] in which two third of the patients were males. The mean duration on CAPD was similar to those reported in a similar study in the RSA.[109]

4.2 Solute Clearance Results

The correction factor for the glucose interference in the measurement of fluid creatinine by Jaffe method has been shown to vary between laboratories.[112] Our correction factor varied slightly from that reported in other populations.[60,69,108] Although omitting this correction factor resulted in only a modest error in the D/P creatinine, it is however recommended for comparison with other results as well as in the determination of solute clearance with short dwell exchanges.[112]

Residual renal function is known to influence patient survival as well as dialysis adequacy.[45] However, only 8 of the patients studied had significant residual renal function. This may be due to late presentation or as a result of long duration of disease, as CKD is known to be a progressive disease.

The majority (62.8%) of the patients studied had a kt/v of more than 1.7 as recommended by the major international practice guidelines.[9,10] This is similar to the findings in CAPD patients in Durban where 76% of the patients studied had a kt/v above 1.7.[108] This finding is very important

because majority of the patients studied were of low socio economic background as most patients in public sector facilities are those with no medical aid cover and are mostly unemployed. Studies in the USA and Europe did not find a significant difference in the urea kinetic parameters among the different ethnic groups. [68,113] The mean creatinine clearance of the study patients was 49.72± 9.83 L/week/1.73 m^2 which is within the earlier recommended targets in major practice guidelines. We noted a significant correlation between the weekly kt/v and weekly creatinine clearance (r=0.547, p= 0.000) and this is similar to reports by others.[109] However, recent national and international guidelines from the United States, Canada, and Europe no longer recommend the use of creatinine clearance as the surrogate solute for dialysis adequacy.[9,10]

Linear regression analysis was used to quantify the relationship between the solute clearance results in term of weekly kt/v values as dependant variable and other factors such as the blood pressure, Hb level, serum cholesterol and serum albumin level. There was no significant relationship observed between these parameters and the weekly kt/v. Latiff et al[109] in a similar study using Spearman's correlation coefficient did not find a significant correlation between weekly kt/v, blood pressure, Hb level and other parameters although in their study they used a computer based kinetic modeling programme to determine the kt/v.

The studied patients were grouped into three: those with weekly kt/v below 1.7, those with values between 1.7 and 2 and those with values above 2.0. Analysis of variance (ANOVA) was done to study the differences between these groups in terms of other parameters like the haemoglobin, blood pressure control, and biochemical indices of nutrition and mineral metabolism. There was no significant difference between the three groups in the various

parameters. In a prospective study amongst Hong Kong CAPD patients, Lo et al[86] did not find differences between similar groupings in terms of mortality. Latiff et al[109] grouped their patients into 2, those with kt/v below 1.7 and those with kt/v above 1.7 and found no significant difference between the 2 groups in terms of BP control, Hb, serum urea, creatinine and other parameters.

Amongst the limitations of this study is its cross sectional nature and was therefore not designed to study the long term effect of small solute clearance on patient outcomes in terms of morbidity, technique survival and mortality. Small solute clearance as a sole marker of PD adequacy has been challenged following the release of large randomized controlled trials such as the ADEMEX and the Hong Kong studies.[92,93] However, studies have shown that small solute clearance become important determinants of both patient and technique survival in anuric PD patients.[110] Several other studies have been published showing the effects of small solute clearance on survival in anuric PD patients.[86,114,115] Considering the fact that the majority of our CAPD patients are anuric, it is important to monitor the small solute clearance regularly as recommended by major international guidelines.[9,10]

4.3 Peritoneal Equilibration Test

The peritoneal membrane characteristic of a patient is an important variable in the prescription of adequate dialysis and is a critical factor in fluid removal as well.[116] It is also an important determinant of patient and technique survival as a number of prospective studies have demonstrated that high transport status is associated with technique failure and reduced patient survival.[117,59] The most widely used peritoneal function test is PET. This is because of its

simplicity and less need for sophisticated machine or infrastructure. It has been extensively studied and its reproducibility has been demonstrated in various populations as well as in animal models.[65,66]

This study validated the PET in CAPD patients in our centre for the first time, and the distribution of the peritoneal transport types was given using our own reference values as shown in table 3.8. The D/P creatinine ratios at 0, 2 and 4 hours were compared with those reported in the literature obtained from other populations. The D/P creatinine at 4 hours was significantly higher than those reported for the USA and Mexican populations, but was not significantly different from those reported for the Chinese population.[60,69,108] Wong et al[69] also reported that the mean D/P creatinine at 4 hours in their patients was higher than those for the USA population as reported by Twardowsky et al[60] and they suggested that the creatinine transfer rate was higher in the Chinese population. We also noted a significant difference in the mean D/P creatinine values at 0 hour between our results and those reported for other populations. This difference may be as a result of incomplete emptying or may be a reflection of higher serum creatinine levels as the serum creatinine level in our patients was significantly higher compared to those reported in other studies. Patients with catheter malfunctioning were excluded from the study. Latiff et al[109] in their paper did not report on the detailed D/P creatinine ratios in their study. The majority of the patients studied were average transporters and this is similar to those reported by others.[108,109] The percentage distribution of the transporter types was similar to those reported for the RSA population studied in Durban as well as in other studies.[108,109,69]

Solute transfer is proportional to the surface area of the peritoneal membrane and its intrinsic permeability to the solute. The peritoneal membrane surface area is supposed to be proportional

to the body size. However we found no significant correlation between the D/P creatinine at 4 hours and either BMI (p= 0.06) or BSA (p= 0.16) though there was a tendency toward significance in the former. With chronic CAPD treatment, there may be alterations in the permeability of the peritoneal membrane, as it is known to undergo morphological changes that may manifest as loss of solute clearance and downward shift of the D/P ratio. We found no significant correlation between D/P creatinine at 4 hours and the duration on PD. This may be because of the design of the study, as long term follow up of the patients was not studied. Others have reported longitudinal changes in peritoneal membrane characteristics in CAPD patients over time.[116,118]

Regular follow up of the functional status of the peritoneal membrane is important to detect alterations in transporter status of the patients and to assess the required dialysis dose. The current practice in our unit is that of a uniform prescription of dialysis irrespective of the transporter type. This study and others as well as have reported non-uniformity in the transport characteristic of PD patients.[60, 69,108]

4.4 Aetiology of End Stage Renal Disease

There was a high prevalence of hypertension as the presumed cause of ESRD in the study population. Hypertension and glomerulonephritis were reported to be the major causes of ESRD in sub-Saharan Africa.[110] However the policy of exclusion of diabetics with significant comordid disease from the chronic dialysis programme in our centre may also contribute to the high incidence of hypertension as the cause of ESRD in the study population.

4.5 Haemoglobin levels

The mean Hb level of the studied patients was within the recommended target level of 11-12g/dl, even though only about 50% of the patients were receiving erythropoietin. This low requirement for erythropoietin in our patients has been reported earlier and is one of the economic advantages of CAPD treatment. [7]

4.6 Biochemistry Results

The current trend is that provision of adequate PD requires much more than achieving a certain level of small solute clearance. Several other parameters including mineral metabolism, ultrafiltration and nutritional status need to be considered as well. The mean serum phosphate and calcium level in the study patient were within the reference ranges for our laboratory. The serum intact PTH level was however higher than the reference values. It has been reported that optimal levels of intact PTH necessary for abnormal bone histology and function range between 2-3 times the upper limit for normal subjects.[119] Studies have shown the importance of mineral metabolism in the mortality and morbidity of PD patients. Noorddzj et al[120] reported from the NECOSAD data that serum phosphate above the KDOQI recommended levels and increased calcium phosphate product (Ca X P) were associated with an increased cardiovascular mortality. The possible mechanism by which abnormal calcium/phosphate product increases cardiovascular risk may be via PTH. PTH is a growth factor for smooth muscle cells and may contribute to sclerosis of the major peripheral vessels, causing increased after-load and subsequent LV dysfunction.

4.7 Nutritional Status

Malnutrition is common among CAPD patients and studies have shown that nutritional status is an independent predictor of survival in these patients.[98] It is recommended that periodic assessment of nutritional status should be part of the routine care of dialysis patients to permit early recognition of malnutrition and the institution of appropriate therapy.[97] There is no single parameter that provides a complete assessment of the nutritional status of CAPD patients, hence various national and international organisations have recommended that nutritional status should be assessed by a number of assessment tools.[97] In this study nutritional status was assessed using biochemical methods, anthropometry, dietary recall as well as the subjective global assessment tool.

4.7.1 Biochemical methods for nutritional assessment

The mean serum albumin level in the study patients was within the reference range for our laboratory. However we noted that 25% of the patients had a serum albumin level below the lower limit of the normal range for our laboratory. Severe hypoalbuminaemia was reported in 14% of PD patients in Durban.[96] We compared the serum albumin level in three groups of the study patients based on the weekly kt/v above 2, between 1.7 and 2 and those below 1.7. There was no significant difference between the three groups ($F= 2.88$, $p=0.063$; ANOVA). This is similar to that reported among CAPD patients in Durban, where there was no difference in the serum albumin level between 2 groups of PD patients with kt/v below 2.1 and those with kt/v above 2.1.[96] Harty et al[121] in a review of dialysis adequacy and nutrition in CAPD patients reported that a positive correlation between dialysis dose kt/v and serum albumin has only been

found in a few studies whereas the majority of cross sectional studies report no correlation or an inverse one.

Serum albumin alone is not sufficient as a clinical marker for malnutrition in CAPD patients, as it is known to be affected by many factors, including the hydration status of the patient, underlying inflammatory process due in part to the use of bioincompatible PD solutions, underlying access infections, or other occult infections.

The mean serum cholesterol in the study patients was within normal limits. Serum cholesterol is mostly recommended for use as a screening tool for malnutrition in chronic kidney disease. The relationship between low serum cholesterol and increased mortality was not observed in the CAPD population.[98]

Serum urea and creatinine levels may also be helpful in monitoring protein intake and nutritional status of dialysis patients. Serum creatinine production has been used to assess lean body mass in stable patients on maintenance dialysis. The studied patients have a high mean serum urea and creatinine levels.

4.7.2 Dietary Recall

Half of the patients studied had suboptimal intake of both energy and protein, and this is below the recommendations of the major international guidelines.[97] However, in those with higher mean protein intake we noted that more than 60% was of high biologic value, which is within the recommendation of K/DOQI guidelines of more than 50% of protein intake to be of HBV. Higher protein intake is usually recommended for CAPD patients compared to HD patients to

account for protein losses in the dialysate. Higher energy intake is required in patients who are young, those who are engaged in strenuous activity, those below their desired weight and hospitalised patients. It has been suggested that up to 30% of caloric intake of CAPD patients may be derived from glucose absorption from the PD fluid.[121] Although dietary recall has the advantage of being easy and quick, with high patient compliance, however among its limitations is the use of a single day's intake which may not represent the patient's usual intake, its dependence on patient's memory and the estimation of portion sizes may not always be correctly interpreted.

4.7.3 Anthropometric Parameters

The use of anthropometrics is an indirect and rather insensitive method of nutritional assessment, although it has the advantage of being simple and provides different measures, for instance the TSF provides an estimate of body fat while the MUAC gives an estimate of muscle mass. The mean BMI of the studied patients was similar to that reported in other South African CAPD patients.[109] Among the problems with anthropometrics is insensitivity and errors including sensitivity to hydration status. In this study we demonstrated the problem of using the actual weight of the patient in calculating the BMI as the majority of the patients classified as being overweight also had oedema, when we were assessing them for the physical examination aspect of the SGA. Another disadvantage of using Anthropometrics is the lack of standard reference values for indigenous African patients. The values obtained are mostly compared with the standard values given for other populations. Despite these challenges, the estimation of lean body mass and fat mass using the Anthropometrics was reported to agree reasonably well with

results from DEXA, and anthropometrics were among the various tools recommended for assessment of nutrition in CAPD in the major practice guidelines.[97]

4.7.4 Subjective Global Assessment

Subjective Global Assessment has been validated in CAPD patients previously and its usefulness and reproducibility has also been reported. [103] It is one of the recommended tools for the assessment of nutritional status in CAPD patients by most of the major international practice guidelines in CAPD.[97]

The overall SGA scores in this study showed that 42% were well nourished, 50% were moderately under nourished and 8% were severely under nourished. We also noted significant correlation between the SGA score and the Anthropometric parameters. Our percentage of malnutrition was lower than that reported in a study from Durban where 76.2% of the CAPD patients studied were malnourished, with 46.8% having mild and 23.8% having moderate malnutrition although a different assessment tool was used.[96] However our finding is similar to findings by Tapiawala et al[122] in India. Using SGA as their assessment tool, they reported that 50% of their patients were malnourished. They also noted significant correlation between the SGA and Anthropometric parameters.

4.8 Echocardiographic Assessment

Cardiovascular disease is frequent in patients with ESRD as many of them rarely reach RRT with normal cardiac function and structure. [123] Maher et al[124] have estimated that 80% of patients referred for CAPD have some form of heart disease. In this study 30 (68%) of the patients who

had echocardiography had LVH. In a study of 55 normotensive patients receiving CAPD Huting et al [125] reported that LVH was present in 84% of the patients.

Several factors are known to contribute to cardiac abnormalities in ESRD, including long standing hypertension, volume overload and chronic elevated cardiac output due to anaemia.[123] In this study, hypertension was the major cause of ESRD, and although the mean Hb was within the recommended target value we noted significant relationship by linear regression analysis between the haemoglobin level and the diastolic function as assessed by E/A ratio. This is not a surprise as anaemia is known to cause elevated cardiac output and this has been implicated in the cardiac abnormalities seen in CAPD patients.[123]

The LV internal diameters in systole and diastole in this study were all within normal values. The mean SF and EF (used to assess systolic function) were all with in the normal ranges. In the study by Huting et al[126], LV internal dimension in diastole and LV systolic function were normal or high-normal in all the patients they studied.

The mean E/A ratio was slightly higher than the normal range suggesting the presence of diastolic dysfunction in our patients. Others have also shown that LV diastolic function is abnormal in CAPD patients both with LVH and those without LVH but is more consistently abnormal in those with LVH; this was demonstrated in a study of 48 CAPD patients in which 25 had LVH.[126]

Pericardial effusion was present in 9 of the patients studied and this may be as a result of uraemic pericarditis. Two forms of pericarditis have been described in ESRD patients. Uraemic and dialysis associated. Uraemic pericarditis occurs before or within 8weeks of initiation of maintenance dialysis and is observed in 6-10% of patients with advanced renal failure. Dialysis associated pericarditis evolves after 8 weeks of initiation of maintenance dialysis and occurs in about 13% of patients on maintenance haemodialysis and may also be seen in peritoneal dialysis patients.[127]

None of the patients in our study had abnormal wall motion to suggest the presence of myocardial ischaemia. It has been hypothesised although not proven that myocardial oxygen demand (hence fewer episodes of myocardial infarction) may be lower in CAPD patients, as a result of relatively normal LV volume and systolic function and the lack of variation in heart rate, BP and intravascular volume in comparison to HD. [123]

2.4 Limitations of the Study

1. Cross sectional nature of the study does not allow for the study of long term effects of solute clearance and other indices of PD adequacy on patient outcome measures.
2. The use of 2.5% dextrose solution for the PET study does not allow for proper evaluation of ultrafiltration in the patients. Cross sectional nature of the study does not allow the study patients to be studied in their best fluid status as not all the patients studied could be said to be in their dry weight state.
3. Inability to perform cardiac function assessment on all the study patients.

4. The relatively small sample size calls for more studies to verify the findings, especially our proposed criteria for classification of patients into the various membrane transporter types

Chapter Five

Conclusions and Recommendations

5.1 Conclusions

The findings from this study, demonstrate that:

1. The dose of PD received by CAPD patients in terms of the small solute clearance measure of kt/v is within the recommended values set by major international practice guidelines.
2. The bone mineral metabolism of our patients based on the serum calcium, phosphate and intact parathyroid hormone are within the reference values of our laboratory which is also with in the recommendation of KDOQI guidelines.
3. Peritoneal membrane characteristics of our patients has been assessed using our own reference values for the first time, and the percentage distribution of the different membrane transporter types is similar to those reported in the RSA and the international literature.
4. Malnutrition is common in CAPD patients in this centre.
5. Subjective global assessment is a useful tool for the assessment of malnutrition in CAPD patients in this centre.
6. Cardiac dysfunction especially left ventricular hypertrophy and diastolic dysfunction are common in CAPD patients from this center.

5.2 Recommendations for Clinical Practice

1. Regular monitoring of small solute clearance to ensure that patients are receiving an adequate dialysis dose as recommended by major international practice guidelines.
2. Assessment and regular follow up of the peritoneal membrane transport characteristic to detect alterations in the membrane function, as well as prescriptions of required dose on an individual patient basis.
3. Periodic assessment of nutritional status should form part of routine care of patients for early detection and management of malnutrition.
4. Echocardiography should be included in the initial evaluation of all patients starting CAPD and it should be repeated in those presenting with cardiac symptoms.

5.3 Recommendations for Research

1. The cross sectional nature of this study constitutes a limitation. There is the need for a longitudinal study to evaluate the relationship between the solute clearance, membrane characteristics and nutritional status on patient outcomes.

2. More studies on the membrane characteristics are required, so as to validate our proposed reference values for the classification of patients into the different membrane transporter types.

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APPENDIX 1 Subjective Global Instrument.

HISTORY

1. Weight Change
   Maximum body weight _____
   Weight 6 months ago _____
   Current Weight _____
   Overall weight loss in past 6 months _____
   Percent weight loss in past 6 months _____
   Change in past 2 weeks: _____ Gained _____ Stabilized _____ Cont Loss

2. Dietary Intake (relative to usual)
   No change _____
   Change _____ Duration: _____ Weeks _____ Months
   Uninentional: _____ Intentional: _____
   Type: _____ Increased Intake
   _____ Suboptimal intake (24hr recal***)
   _____ Full liquid diet
   _____ IV or Hypocaloric liquids
   _____ Starvation/NPO

   ******Normal/A = 100-75%; Mild/B = 75-50%; Moderate/C = 50-25%; & Severe/D = 25-0%***

3. Gastrointestinal Symptoms (?2weeks)
   None _____
   Diarrhoea _____ Vomiting _____ Nausea _____ Anorexia _____
   Dysphagia _____

4. Functional Capacity (daily activities done according to normal)
   No dysfunction _____
   Dysfuntion _____ Duration: _____ Weeks _____ Months
   Unintentional: _____ Intentional: _____
   Type: _____ Works suboptimally
   _____ Ambulatory (can walk by themselves)
   _____ Bedridden

PHYSICAL

(Normal = 0; Mild Loss = 1; Moderate Loss = 2; or Severe Loss = 3)

1. Subcutaneous Fat Loss
   Shoulders _____ Triceps _____ Chest _____ Hands/Palmar _____

2. Muscle Wasting
   Quadriceps _____ Deltoid _____ Temporal _____

3. Presence of Oedema
   Hands _____ Sacral _____ Pedal _____

Rating of Nutritional Assessment

A. Well Nourished: Recent improvement in appetite or any other historical features of the SGA Increase in weight (not fluid overloaded) even if their net weigt loss was between 5th & 10th percentage over the past 6 months. _____

B. Mild/Moderate Malnutrition: Reduced dietary intake, weight loss of at least 5%, and mild to moderate loss of subcutaneous fat and muscle wasting. _____

C. Severe Undernutrition: Continuous weight loss of greater than 10%, poor dietary intake, and severe loss of subcutaneous fat and muscle wasting. _____

Appendix 2 ethics clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Abdu

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M080452**
PROJECT	Assessment of peritoneal dialysis adequacy among CAPD patients in Johannesburg hosptial
INVESTIGATORS	Dr A Abdu
DEPARTMENT	Department of Medicine
DATE CONSIDERED	08.04.25
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 08.06.23 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr S Naidoo

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES