

**INTEGRATING BIOELECTRICAL IMPEDANCE ANALYSIS
(BIA) AND ESTIMATED GLOMERULAR FILTRATION RATE
(eGFR): A NOVEL APPROACH TO THE ASSESSMENT OF
NUTRITIONAL STATUS OF HAEMODIALYSIS PATIENTS
(CERCS B560)**

PRESENTED BY:

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INTERNAL MEDICINE, UNIVERSITY OF TARTU, IN
FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF
A MASTER'S DEGREE IN CLINICAL NUTRITION.**

**SUPERVISED BY PROFESSOR ALASTAIR FORBES AND DR.
KÜLLI KÕLVALD**

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**BIOELEKTRILISE IMPEDANTSI ANALÜÜSI (BIA) JA
HINNANGULISE GLOMERULAARFILTRATSIOONI KIIRUSE
(EGFR) INTEGREERIMINE: UUDNE LÄHENEMISVIIS
HEMODIALÜÜSIPATSIENTIDE TOITUMISSEISUNDI
HINDAMISEKS
(CERCS B560)**

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**TARTU ÜLIKOOLI SISEMEDITSIINILISTE OSAKONNASSE
ESITATUD MAGISTRITÖÖ KLIINILISE TOITUMISE
MAGISTRI ANDMISE NÕUETE TÄITMISEL.**

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JUUNI 2025

DECLARATION

I, Anum Basit, declare that this project titled "Integrating Bioelectrical Impedance Analysis (BIA) And Estimated Glomerular Filtration Rate (eGFR): A Novel Approach to The Assessment of Nutritional Status of Haemodialysis Patients" is the result of my original research efforts. I conceptualised the initial protocol design and implemented subsequent modifications, incorporating references from properly recognised sources and textbooks. This study was conducted under the guidance and supervision of Professor Alastair Forbes from the Institute of Clinical Medicine at the University of Tartu and Dr Külli Kõlvald, a nephrologist at the Tartu University Hospital.

DEDICATION

This project report is dedicated to my parents, family, friends, and colleagues, who have supported me on this challenging yet incredible journey.

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ABSTRACT

Rationale: Haemodialysis (HD) patients have a high prevalence of malnutrition, which worsens prognosis, but its identification from nutrition screening is confounded by fluid retention, and diagnosis is often late. Estimated Glomerular Filtration Rate (eGFR) indicates renal status, and it is proposed that its integration with Bioelectrical Impedance Analysis (BIA) parameters could better identify the patient's nutrition status and overall prognosis.

Methods: 25 adults undergoing HD for at least 6 months were recruited. BIA was conducted pre-dialysis, and contemporary eGFR was recorded. BIA parameters included the Fat-Free Mass Index (FFMI) and Body Fat Mass Index (BFMI), which were standardised using T-scores; the ratio of Extracellular Water (ECW) to Total Body Water (TBW) and phase angle (PhA) were considered markers of malnutrition.

Results: Pearson correlation analysis suggested an inverse relationship between eGFR and PhA ($r = -0.354$, $p = 0.082$). The mean eGFR was 6.80 (SD $\pm$ 2.14) and the mean PhA was 1.83 (SD $\pm$ 4.37). Based on a PhA threshold of $<4.5^\circ$, 80% of patients were at risk of malnutrition. A possible negative correlation was found between the ECW/TBW ratio and PhA ($r = -0.316$, $p = 0.124$). The BFMI and FFMI T-scores had non-significant relationships with eGFR. A possible positive correlation was found between PhA and FFMI T-Score ($r = 0.373$, $p = 0.066$).

Conclusion: Our results suggest clinically useful correlations, but conclusions are limited by the small sample size. Larger longitudinal studies, however, appear justified in order to validate the relationships between body composition and eGFR. The inverse association between phase angle and eGFR, and the relationships between eGFR/TBW and hydration ratios, suggest complex interactions between cellular health, fluid balance, and kidney function. BIA data indicate that a low PhA with a high ECW/TBW ratio is predictive of malnutrition in patients on HD and that higher fat-free mass is associated with better cellular health. These observations are likely to be of prognostic value.

CHAPTER ONE

INTRODUCTION

1.1 Background

Chronic kidney disease (CKD) marks the progressive loss of kidney function. Without adequate intervention to slow down progression and manage the symptoms, the result is renal failure. The National Kidney Foundation divides CKD into five stages based on the estimated glomerular filtration rate (eGFR), the rate at which kidneys filter waste. Anatomic issues, proteinuria and haematuria mark early stages, stages 1 and 2. This stage often goes unnoticed due to its asymptomatic nature, and even high-risk groups are missed due to a lack of screening for early detection. Stages 3 and 4 indicate the advanced stage, and stage 5 is called end-stage renal disease (ESRD). ESRD results in death unless timely dialysis begins, or the patient is transplanted.

CKD is diagnosed using two laboratory methods based on evidence-based guidelines. These include eGFR and urine albumin-creatinine ratio (uACR) in urine. Even then, a single eGFR measurement is not enough to make a diagnosis. The test must be repeated at least 3 times and should consistently give an eGFR below 60 ml/min/1.73m²

ESRD refers to the kidney's inability to excrete waste products, produce hormones and regulate fluid and electrolyte balance. The accumulation of waste products leads to uraemia, a condition causing symptoms such as malaise, weakness, nausea and vomiting, muscle cramps, itching and a metallic taste in the mouth. It can cause neurological impairment because of increased levels of nitrogenous waste in the body. ESRD can stem from many diseases, with 90% of patients having diabetes mellitus, glomerulonephritis or hypertension. Unfortunately, no laboratory parameter is associated with the beginning of symptoms. Still, blood urea nitrogen (BUN) more than 100 mg/dL and creatinine of 10 to 12 mg/dL are used as a rule of thumb.

Treatment options for ESRD include dialysis, transplantation or medical management of symptoms till death. The patient may choose peritoneal dialysis, which provides continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD). Another option for dialysis is haemodialysis (HD); the decision to choose either one lies with the patient and their

physician based on what is deemed best for the patient's condition. A combination of the two methods can also be used. For the administration of HD, permanent access to the bloodstream is required through a fistula. In the case of fragile blood vessels, a graft is implanted. Before the creation or maturation of a fistula, a central venous catheter (CVC) may be used, which is not preferred due to the risk of infection.

Dialysis is a lifesaving intervention that removes toxins and excess fluids. Although it cannot fully replace the functions of a kidney, it helps to sustain life when a transplant is due or not an option. Dialysis has both its advantages and disadvantages. Apart from the high cost, time consumption and risk of infections, the dietary and fluid requirements of the patient are significantly altered. Sodium, potassium, phosphorus and fluid intake must be carefully managed to prevent complications. The intake of protein needs to be adjusted accordingly to avoid malnutrition.

1.2 Scientific Problem

Malnutrition, fluid imbalance, and protein-energy wasting (PEW) are frequent in haemodialysis patients because of CKD and dialysis treatment. Dialysis acts as a drain on body protein. The prevalence of PEW is different in all patients; an estimated value gives a prevalence of 28% to 54%. HD patients may receive dialysis up to 3 times a week, and the exposure of blood to an artificial membrane causes chronic inflammation. As a result, during each session, the patients tend to lose almost 15g of protein. This increases the protein requirement to 1.2g/kg of body weight. PEW leads to sarcopenia, higher morbidity and mortality, and higher susceptibility to infections. A common cause of PEW is inadequate dietary protein. Patients ingest less protein as they complain of an unpleasant taste caused by uraemia. Another reason is due to the dietary restrictions placed upon patients. Limitations on sodium and phosphate can easily cause the patients to stray from food that would benefit them protein-wise.

Nutritional status is a critical factor influencing patient outcomes, yet it is often under-monitored. Haemodialysis patients often suffer from complex nutritional challenges due to the interplay between kidney function, protein-energy wasting, and fluid management. Current nutritional assessments in haemodialysis settings are limited, with most relying on clinical observations or basic biochemical tests. There is a need for a more comprehensive, non-invasive approach to assess

both nutritional status and fluid management. The study determines whether comparing BIA metrics with eGFR provides a better picture of the patient's nutritional and renal health, potentially improving patient outcomes and dialysis management.

eGFR is a standard measure of residual renal function, but it does not measure body composition or hydration status, both of which significantly influence patient outcomes. BIA fills this gap by providing non-invasive, objective measurements of fat-free mass, fat mass, phase angle, and fluid distribution ratios like ECW/TBW. These markers are essential for identifying protein-energy wasting, sarcopenia, and fluid overload conditions that are prevalent in dialysis patients but often missed by traditional biochemical assessments. Minimal residual renal function can have a significant impact on fluid clearance, toxin removal, and the body's ability to tolerate protein and electrolyte loads. While BIA can identify malnutrition and overhydration, it cannot explain the underlying cause, such as impaired filtration capacity. eGFR thus offers insight into whether fluid imbalance and nutritional decline may be driven by the loss of renal function. The combination helps to differentiate whether abnormalities in body composition are due to inadequate dialysis, poor intake, or progressive renal failure.

1.4 Aims

This study aims to bridge the gap between kidney function assessment and nutritional evaluation by exploring the combined use of BIA and eGFR. Integrating these measures can provide a more accurate understanding of patients' nutritional status, helping to optimise individualised nutritional interventions, reduce the risk of malnutrition and PEW, and improve clinical outcomes for haemodialysis patients. This approach can also serve as a foundation for further research and influence clinical practices in managing nutritional health in patients undergoing dialysis.

1.3 Objectives

The primary objective of the research is to assess the correlation between BIA-derived body composition parameters (e.g., fat mass, lean body mass, total body water, phase angle) and eGFR in haemodialysis patients.

The research explores how BIA and eGFR can be used together to monitor nutritional interventions more effectively in haemodialysis patients. Using BIA and eGFR data, the study will also evaluate the prevalence of malnutrition and protein-energy wasting (PEW) in the study population.

Integrating bioelectrical impedance analysis (BIA) and estimated glomerular filtration rate (eGFR) to assess nutritional status in haemodialysis patients is an active research area. Although several studies have investigated the use of BIA in determining body composition and nutritional health in a patient population, integrating BIA with eGFR is an emerging area in this case.

A comprehensive review highlighted the use of BIA in the nutritional management of patients with chronic kidney disease (CKD) receiving haemodialysis. It brought to light the role of BIA in measuring body composition parameters such as fat-free mass, fat mass, phase angle, and body water, which are crucial for assessing nutritional status and guiding interventions. [4] Another study examined changes in body composition during the transition to maintenance dialysis using BIA to assess nutritional status (phase angle) and hydration. Findings showed that starting dialysis was associated with changes in body composition, reflecting cellular integrity and volume control changes. [5] Another study examined the performance of BIA and anthropometric measurements in patients with stages 3–5 of CKD, including those on dialysis. The study found that BIA could assess body composition across different stages of CKD, with eGFR calculated using the CKD Epidemiology Collaboration equation. This highlighted the potential of combining BIA and eGFR estimates to monitor nutritional status and disease progression. [6] Further studies are needed to validate the combined assessment models and establish standardised protocols for their clinical practice.

Direct studies combining BIA and eGFR to assess nutritional status in haemodialysis patients are limited, but existing studies suggest that both measures are valuable. Their combined application promises to provide a more comprehensive assessment of patient health, which warrants further investigation.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Malnutrition and protein-energy wasting (PEW) is a prevalent problem in dialysis patients. A meta-analysis of 16,434 dialysis patients found a 28% to 54% PEW prevalence. Since dialysis patients often suffer from sarcopenic obesity, methods like BMI are unable to distinguish between muscle loss and fat accumulation. Bioelectrical Impedance Analysis (BIA) has therefore become an effective non-invasive tool for the assessment of body composition and nutritional status. [1] [8] With the evolution of single-frequency (SF-BIA) to multi-frequency (MF-BIA) and bioimpedance spectroscopy (BIS), it has garnered better accuracy in assessing dialysis patients, particularly by differentiating between extracellular water (ECW) and intracellular water (ICW). This makes it an apt tool for dialysis patients for whom this distinction is critical. [1] [2] [6] [8]

2.1.2. BIA vs Traditional Methods

Traditional methods for determining dry weight, like clinical evaluation, are imprecise, hence the use of BIA. One method for assessing volume overload through BIA is normovolemia/hypervolemia slope method. This estimates dry weight by comparing the slopes of normovolemia. The intersection of slopes shows dry weight. Other studies have shown that reducing dry weight by 0.5 to 2kg over a few weeks improves blood pressure and reduces use of antihypertensive medications by 86%.

Another method of hydration status assessment is the ECW/TBW ratio, but its significant standard deviation makes it less practical in some cases. The resistance-reactance (RXc) graph, which plots resistance (R) and reactance (Xc) normalised by height, is also used. The vector within the 75% ellipse indicates normal hydration. The body composition monitor (BCM) measures overhydration (OH) by calculating absolute fluid overload (AFO) and relative fluid overload (RFO), with normohydration defined as AFO within the 10th and 90th percentile range. The use of BCM can significantly reduce RFO and systolic blood pressure in dialysis patients. Another marker is the calf-BIS method, which monitors extracellular resistance in the calf during haemodialysis. It

determines dry weight by identifying the point where the resistance curve flattens, indicating the removal of excess fluid. [8]

Loss of lean tissue is linked strongly to increased mortality, with a lean tissue index (LTI) below the 10th percentile associated with a 60% higher chance of death. A study involving 37,345 haemodialysis (HD) patients found that 47% of the study population had an LTI below the 10th percentile despite having a mean BMI of 26 kg/m², proving that BMI alone is not an adequate assessment tool. [1]

Furthermore, another meta-analysis concluded that every 1° decrease in phase angle (PhA) increases the risk of hospitalisation by 21% and cardiovascular events by 30%. [1] [2] These findings encourage using BIA as a more precise tool for nutritional assessment and fluid management of dialysis patients.

2.1.3 Limitations of BIA

Despite its fair precision, the tool still faces several limitations. These limitations include its reliance on population-specific prediction equations, variability of hydration status and the effect of timing of dialysis. This necessitates a wait time of at least 60 minutes post-dialysis before conducting BIA. Research is therefore needed to establish optimal cut-off values for BIA parameters. Though limitations exist, it has shown a trend of muscle loss and fat gain in these patients, which puts stress on the need for early nutritional interventions. [1] [2]

2.2. Effect of Dialysis on Body Composition

The nutritional status of patients changes after starting haemodialysis treatment. Two studies have discussed this by examining chronic renal failure patients. Ninety-seven patients had their nutritional markers tracked at Harbor-UCLA Medical Centre over six months and had recently started haemodialysis. Mehrotra et al. found that the results showed significant increases in serum albumin. Iron, transferrin saturation, creatinine and normalised protein equivalent of total nitrogen appearance (nPNA). Body weight decreased initially for 4 months but then increased, probably due to improved protein intake and relief of uremic symptoms. At Vanderbilt University Medical Centre, 50 patients were tracked by Pupim et al. for 1 year. Biochemical markers and body composition were assessed using BIA and DEXA scans. Inflammation markers like C-reactive

protein (CRP) were also measured. Results showed that serum albumin, prealbumin, nPNA, BIA-derived reactance, phase angle and fat mass improved over time. However, the extent of improvement was dependent on baseline nutritional status. Patients who started dialysis with poor nutritional status saw a significant recovery in their nutritional markers. Both studies saw an initial weight loss due to fluid removal, followed by weight gain, which was attributed to increases in lean body mass in the UCLA study and fat mass in the Vanderbilt study. 34.1% of patients were malnourished at the start of dialysis, having worse outcomes in the long term. Findings suggested that dialysis be started early, before malnutrition develops, especially in elderly patients who respond less favourably to nutritional improvement. The studies align with the National Kidney Foundation (NKF-K/DOQI), which recommends early dialysis for malnourished patients with advanced CKD. These observational studies strongly indicate that earlier dialysis can solve the problem of malnutrition and improve survival. [5]

A case-control study examined the nutritional status, inflammation, and body composition in 84 elderly haemodialysis (HD) patients compared to 84 age- and sex-matched controls, with a mean age of 76–77 years and a predominantly female cohort (52.4%). Using the Geriatric Nutritional Risk Index (GNRI), the study found that HD patients had a significantly higher prevalence of malnutrition risk (32.1% vs. 6.0%, $p < 0.001$), along with lower serum albumin (3.73 vs 3.98 g/dL, $p = 0.03$) and elevated C-reactive protein levels (1.21 vs 0.64 mg/dL, $p < 0.001$), indicating chronic inflammation. [10]

Body composition analysis via bioelectrical impedance revealed reduced muscle mass (41.1% vs 38.3%, $p < 0.001$) and lower mid-arm muscle circumference (MAMC%: 95.2% vs 110.3%, $p < 0.001$) in HD patients, alongside a trend toward sarcopenic obesity (15.5% vs 14.3%). [10]

Additionally, HD patients exhibited fluid overload, with higher extracellular water (ECW%: 18.98 vs 14.68 L, $p < 0.001$) and elevated exchangeable Na/K ratios (1.32 vs 0.93, $p < 0.001$). Multivariate regression identified age < 75 years, BMI ≥ 23 kg/m², and serum albumin ≥ 3.8 g/dL as protective factors, while higher ECW% and CRP ≥ 1 mg/dL increased nutritional risk. The study emphasises the need for integrated assessments of nutrition, inflammation, and hydration in elderly HD patients, as traditional BMI measurements may overlook critical risk factors. Limitations include the cross-sectional design and lack of residual urine volume data, warranting further longitudinal research. [10]

2.2.1. Protein-Energy Wasting

Multiple clinical studies have found that lean tissue mass decreases throughout the progression of chronic kidney disease (CKD). With every 10ml/min/1.73m² drop in estimated glomerular, the whole-body muscle mass decreases by 0.59kg. 24% of pre-dialysis patients are suffering from sarcopenia, with 62.5% of patients being affected by sarcopenic obesity. [2]

BIA correlated lean mass index with grip strength, serum albumin, and mortality outcomes in haemodialysis patients. Meanwhile, visceral fat levels were associated with increased cardiovascular risk. [2]

The relationship between BIA and PEW has been explored to establish a reliable diagnostic model. Six hundred nine dialysis patients from Zhejiang University and 52 additional patients were recruited and analysed. PEW was diagnosed based on the International Society of Renal Nutrition and Metabolism (ISRNM), and BIA-derived parameters like water ratio, visceral fat area (VFA), body cell mass (BCM) and phase angle along with nutritional markers were examined. [3]

Findings showed that age, type of dialysis, subjective global assessment (SGA), and water ratio were independent risk factors for PEW. Triglycerides, urea nitrogen, calcium, ferritin, BCM VFA and phase angle were protective factors. A new diagnostic model combining BIA with cholesterol was developed, demonstrating strong predictive ability. An AUC of 0.841 in internal validation was achieved, which proved to be better than the previous PEW models. [3] BIA is a valuable assessment tool for PEW, but further validation in larger populations is needed to confirm its predictive power for clinical outcomes such as mortality and hospitalisation risks. [3] [4]

The ability of BIA and PA to predict PEW in maintenance haemodialysis (MHD) has been studied. 173 MHD patients and 173 healthy adults were included in the study. Results showed that 34.1% of MHD patients had PEW, and their mean PA was lower than that of healthy patients. PA was positively associated with serum albumin, prealbumin fat-free mass and mid-arm muscle circumference. On the other hand, it did not correlate significantly with fat mass or body fat percentage. Logistic regression analysis identified PA as a strong predictor of PEW with an odds ratio of 5.37, which makes it a better predictor than BMI. Receiver operating characteristic (ROC) curve analysis determined an optimal PA cut-off value of 4.6° for predicting PEW, with 86.4% sensitivity, 76.3% specificity, and an area under the curve (AUC) of 0.87. [4]

2.2.2 Obesity and eGFR

The impact of body weight on the accuracy of (GFR) estimators in individuals with type 2 diabetes was examined. The researchers assessed the performance of three commonly used GFR estimation formulas: the Modification of Diet in Renal Disease (MDRD) formula, the Cockcroft-Gault equation, and the Creatinine Clearance (CrCl) method in a cohort of 91 subjects with type 2 diabetes. The findings indicated that body weight significantly influenced the performance of these GFR estimators. In particular, the Cockcroft-Gault equation showed a better correlation with measured GFR ($r = 0.91$) in obese individuals compared to the MDRD formula, which was less reliable in overweight patients. [16]

2.2.3 Role of BIA in Assessing Malnutrition

In addition to fluid management, BIA is increasingly recognised as an essential tool for assessing the nutritional status of dialysis patients. Malnutrition and muscle wasting are significant concerns in ESRD, as they are associated with higher mortality rates. Low serum albumin levels (<40 g/L) have been linked to an increased risk of death, making early detection of nutritional deficiencies crucial. However, conventional nutritional assessments, such as body weight and anthropometric measurements, can be misleading due to fluid retention. BIA allows for the differentiation between lean body mass (LBM) and excess fluid, improving the ability to detect malnutrition in dialysis patients. In peritoneal dialysis, where patients may gain fat mass due to glucose absorption from the dialysate, BIA is particularly useful in tracking body composition changes over time. Nevertheless, hydration status must be carefully considered when interpreting BIA-derived LBM values, as overhydration can lead to overestimating muscle mass. [7]

2.2.4 Dry Mass Index

Body composition in CKD patients was evaluated using the dry mass index (DMI) and the ratio of total body water (TBW) to estimated volume, both based on bioelectrical impedance analysis (BIA). A study involving 49 CKD patients found that DMI was significantly correlated with nutritional status ($r = 0.73$) and could serve as a valuable marker for malnutrition. Additionally, the ratio of TBW to estimated volume was effective in predicting fluid overload in these patients, providing valuable insights into hydration status and nutritional health.

2.3. Phase Angle

Phase angle (PhA), derived from BIA, is a marker for muscle health and health-related quality of life (HRQoL) in patients with CKD. A study included 149 participants from a multicentre randomised trial (RECOVERY trial). It assessed PhA, skeletal muscle mass index (SMI), handgrip strength (HGS), 6-meter gait speed (GS), and HRQoL at baseline, 24 weeks, and 48 weeks. The results demonstrated that PhA was linearly correlated with SMI ($r = 0.616$), HGS ($r = 0.619$), and GS ($r = 0.290$), all with ($p < 0.001$), indicating a strong relationship between PhA and muscle health. PhA was also significantly associated with low muscle mass and low muscle strength (both ($p < 0.001$)) and predicted the presence of sarcopenia ($p = 0.001$).

2.3.1. Phase Angle and Sarcopenia

A study by Shin et al. found substantial agreement between PhA and the diagnosis of sarcopenia using the Asian Working Group for Sarcopenia 2019 algorithm (Cohen's kappa = 0.510, ($p < 0.001$)). Additionally, PhA was related to various aspects of HRQoL, including physical functioning, general health, mental health, and social support ($p < 0.05$). In the longitudinal analysis, participants were divided into three groups based on their PhA slope: decreasing PhA (slope $< -0.2^\circ$ per year), constant PhA (slope -0.2° to 0.2° per year), and increasing PhA (slope $\geq 0.2^\circ$ per year). The increasing PhA group showed an increase in SMI ($p = 0.054$), while the decreasing PhA group experienced a reduction in HGS ($p = 0.054$). The prevalence of sarcopenia increased in the decreasing PhA group and decreased in the increasing PhA group over time ($p = 0.058$) at 48 weeks). Furthermore, role limitations due to physical health problems worsened in the decreasing PhA group, highlighting the impact of PhA changes on HRQoL. The study concluded that PhA is a reliable marker for estimating muscle health and HRQoL in CKD patients, particularly for identifying sarcopenia and monitoring longitudinal changes in muscle mass and function. The optimal cut-off values for PhA to predict sarcopenia were 4.75° for men and 4.15° for women, with area under the curve (AUC) values of 0.875 and 0.916, respectively. These findings suggest that PhA can serve as a practical and non-invasive tool for assessing muscle health and HRQoL in CKD patients. However, further research with larger sample sizes and more extended follow-up periods is needed to validate these results. The study also highlighted the limitations of its secondary analysis design, potential confounding factors, and the relatively short duration of follow-up, which may affect the generalizability of the findings. [9]

2.3.2. Phase Angle and Diabetic Chronic Kidney Disease

The relationship between bioimpedance PhA and diabetic CKD stage 5 was explored in a study involving 120 haemodialysis patients. Phase angle measurements were taken using bioelectrical impedance analysis (BIA), and the results showed that patients with diabetic CKD stage 5 had significantly lower phase angle values (mean PhA = 3.6°) compared to healthy controls (mean PhA = 6.2° , $p < 0.001$). The decreased phase angle was associated with poor nutritional status, muscle wasting, and increased inflammation, all of which are common complications in advanced kidney disease. The study concluded that phase angle could be a valuable marker for assessing nutritional and inflammatory status in patients with diabetic CKD stage 5, potentially aiding clinical management. [19] In a separate study involving 232 haemodialysis patients, low phase angle was found to be significantly associated with more significant fluid overload ($p < 0.05$) and higher mortality rates (hazard ratio = 1.82, $p = 0.01$) over a follow-up period of 24 months. Patients with low phase angle values had poorer nutritional status, muscle mass depletion, and higher levels of inflammation, which contributed to adverse clinical outcomes. The authors concluded that phase angle could be a useful clinical marker for assessing fluid overload and predicting mortality risk in haemodialysis patients, potentially improving patient management. Both studies highlight the importance of phase angle as a clinical tool for evaluating nutritional status and fluid overload and predicting adverse outcomes in patients with advanced CKD and those on haemodialysis. [20]

2.4 Fluid Overload

Due to its ability to identify fluid overload, BIA has become of interest in haemodialysis patients. With multiple types of BIA technologies, the results must be interpreted carefully, considering their unique algorithms. The results should be evaluated alongside clinical assessment to avoid any misinterpretations. Proper procedures should be followed to get accurate results. Although single measurements are not sufficient, repeated measurements provide some valuable insights. Incorporating BIA into clinical decision-making to improve dialysis outcomes can be beneficial, but refined predictive models for CKD management are still required. [6]

2.4.1 Goals of Dialysis and BIA in Fluid Management

The goal of dialysis is to maintain an optimal fluid balance or "dry weight," as excess fluid removal can lead to hypotension, muscle cramps, and vomiting. In contrast, inadequate fluid removal can

result in hypertension, oedema, and pulmonary congestion. By directly measuring TBW and ECW, BIA provides a quantitative approach to monitoring fluid shifts and optimising ultrafiltration targets, helping clinicians achieve better fluid balance. [7]

Over a 4-hour session, haemodialysis removes 1-4 litres of water from the patients. Patients suffering end-stage renal disease (ESRD) go through frequent fluid shifts which alter TBW, ICW, and ECW. BIA is, therefore, an effective tool for measuring body composition and hydration status. BIA in dialysis management functions to assess volume status, monitor physiological changes, evaluate dialysis adequacy, and assess nutritional status. [7]

2.4.2. Role of BIA in Fluid Assessment

Beyond fluid assessment, BIA monitors physiological and hemodynamic changes during dialysis. It helps evaluate trans-compartmental fluid shifts and offers insights into how various interventions, such as sodium concentration adjustments, affect patient hydration and blood volume. One of the most common complications of haemodialysis is dialysis-induced hypotension, often caused by excessive ultrafiltration leading to a decline in blood volume. Measuring ECW-to-TBW ratios using BIA allows for better prediction of hypotension risk and helps adjust treatment strategies to minimise adverse effects. Combining BIA with optical reflection techniques for continuous blood volume monitoring has shown the potential to prevent hemodynamic instability during dialysis. [7]

BIA also plays a role in determining dialysis adequacy, particularly by improving TBW estimates, a critical component of urea kinetic modelling (Kt/V). Traditional methods assume that TBW is approximately 58% of body weight, but this estimation may not be accurate for all patients. BIA provides a more individualised measurement, improving dialysis prescriptions' precision. Studies comparing BIA-derived TBW with urea kinetic modelling estimates have shown correlations ranging from $r = 0.79$ to 0.97 , demonstrating its potential as a useful clinical tool. However, variations in body composition and hydration state must be considered, as these can influence the accuracy of TBW predictions. [7]

2.4.3 Total Body Water and Kidney Function

Further analysis in a larger cohort of 149 CKD patients, with a mean age of 66.6 ± 12.0 years, focused on the ratio of extracellular water (ECW), obtained via BIA, to estimated TBW, calculated using the Watson formula ($\%ECW_BIA/TBW_Watson$). This ratio was found to be significantly associated with older age, male sex, diabetes, resistant hypertension, lower eGFR, lower serum albumin, and greater proteinuria. Multivariate analysis confirmed proteinuria as an independent factor linked to an increased ECW/TBW ratio ($\beta = 0.19$, $P = 0.02$). The study found that patients with the highest tertile (T3) of the ECW/TBW ratio had a greater incidence of adverse renal events, including a $\geq 50\%$ decline in eGFR or progression to dialysis. Survival analysis showed that each 1% increase in the ECW_BIA/TBW_Watson ratio was associated with a 21% higher risk of renal deterioration (Hazard Ratio: 1.21; 95% Confidence Interval: 1.10–1.34; $P < 0.001$). Both studies concluded that BIA-derived body composition measures, including DMI and the ECW/TBW ratio, are valuable tools for assessing nutritional status, fluid overload, and predicting poor renal outcomes in CKD patients. [14] [17]

The relationship between whole-body water mass and kidney function was investigated using a Mendelian randomisation (MR) approach. The study included genetic data from over 500,000 individuals to assess whether whole-body water mass directly influences kidney function. The authors identified several genetic variants associated with whole-body water mass and analysed their causal impact on the estimated glomerular filtration rate (eGFR). The results suggested a significant causal relationship between higher whole-body water mass and improved kidney function, with a positive association between whole-body water and eGFR ($\beta = 0.18$, $p = 0.004$). The study concluded that increasing whole-body water mass may benefit kidney function, highlighting its potential as a modifiable factor for improving renal health. (18)

2.5 Limitations of BIA in Dialysis Patients

Despite its many advantages, BIA measurements in dialysis patients are subject to several physiological challenges. Changes in electrolyte concentrations, haematocrit levels, and fluid shifts can impact impedance readings, necessitating careful interpretation of results. Additionally, while whole-body BIA provides useful information, segmental BIA has been found to be more effective in detecting localised fluid changes, such as peripheral oedema or peritoneal fluid

accumulation. Studies indicate that ECW/TBW ratios are reliable indicators of overhydration, making them valuable in determining dry weight. Advanced real-time BIA monitoring, combined with hemodynamic tracking, could improve dialysis treatment by allowing continuous fluid balance assessment and reducing the risk of complications. [7]

Accurately assessing the volume status of dialysis patients is of critical importance, with fluid overload being associated with left ventricular hypertrophy and cardiovascular mortality. [1] [2] [8]

CHAPTER THREE

METHODOLOGY

3.1 Study Design

A quantitative cross-sectional analysis investigated a potential relationship between eGFR and BIA parameters in haemodialysis patients. The approach was selected to observe the two parameters at one point in time. The design was suitable for running and identifying correlations between kidney function and body composition in end-stage renal disease patients undergoing haemodialysis.

3.1.2 Participants

The study sample consisted of 25 patients from the haemodialysis clinic of Tartu University Hospital. Patients ranged from ages 34 to 99. The following were the criteria for recruiting patients:

- Inclusion Criteria:
 - Adult patients aged 18 years and above.
 - Patients are currently undergoing haemodialysis.
 - Patients who had been on haemodialysis for at least 6 months.
- Exclusion Criteria:
 - Patients with pacemakers or implanted defibrillators (contraindication for BIA).
 - Pregnant patients.
 - Acute illnesses or recent surgeries that affect hydration or nutritional status.

3.1.3 Consent and Ethical Approval

A convenience sampling method was used to select participants who met the inclusion criteria and were available for participation during the study period. An application was submitted to the Research Ethics Committee of the University of Tartu for ethical approval. The application reference no. 397/T-10 was approved on 10 February 2025. [Appendix C]

All participants provided informed consent before taking part in the study.

3.2 Data Collection

Data was collected in two primary stages:

1. eGFR Measurement:

eGFR values were obtained from each patient's online health system eHL records. Routine clinical blood tests were used for the CKD-EPI formula, which is widely used to estimate kidney function based on serum creatinine, age, sex, and race. The eGFR values were recorded within one week of taking the BIA measurements to ensure accuracy.

1. BIA Measurement:

Body composition analysis was performed using a QuadScan 4000 BIA tool, which measures parameters such as phase angle, total body water, fat mass, and lean mass. The apparatus is a portable, multi-frequency BIA device that measures nutritional parameters using four frequencies. The measurements were taken under standardised conditions, ensuring that participants were in a rested state. The measurement was recorded pre-dialysis.

The main researcher conducted all measurements to minimise errors in data collection. The BIA device was calibrated according to the manufacturer's guidelines before use.

3.3 Data Analysis

The data collected from eGFR and BIA parameters were analysed using IBM SPSS (Statistical Package for Social Sciences Statistics) 21. The tool allowed for data management, descriptive and inferential statistics, regression, and graphical visualization.

Descriptive statistics were first computed to summarise the characteristics of the sample, including means and standard deviations for continuous variables (e.g., age, eGFR, BIA parameters). T-scores were calculated for BFMI and FFMI to standardise the values.

For normally distributed data, Pearson's correlation coefficient was used to assess the relationship between eGFR and BIA parameters. The significance level was set at $p < 0.05$ for all statistical tests. Regression analysis was conducted to explore the potential predictive value of BIA parameters for eGFR.

CHAPTER FOUR

RESULTS

4.1 Descriptive Statistics

The sample consists of 25 patients, ages 34 to 99 (Mean= 68.96, SD= 16.035). 76% of the population was male (19 participants), and 24% was female (6 participants). BMI scores spanned from 18.0 to 36.3 (Mean= 27.05, SD= 5.05). The eGFR values in the patient group ranged from 4.0 to 12.0 (Mean= 6.8, SD=2.14). Phase angle measurement showed wide variability, ranging from a minimum of -10.0 to 5.9 (Mean= 1.832, SD= 4.37).

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age_years	25	34	99	68.96	16.035
Height_m	25	1.44	1.91	1.7372	.12445
Weight_kg	25	52.0	110.9	81.760	17.8265
PHASEANGLE	25	-10.0	5.9	1.832	4.3705
eGFR	25	4.0	12.0	6.800	2.1409
Valid N (listwise)	25				

Table 1 Descriptive Statistics

	Gender	N	Mean	Std. Deviation	Std. Error Mean
BMI	male	19	26.689	5.2358	1.2012
	female	6	28.200	4.6712	1.9070
PHASEANGLE	male	19	1.416	4.9598	1.1378
	female	6	3.150	.6221	.2540
eGFR	male	19	7.105	2.3069	.5292
	female	6	5.833	1.1690	.4773

Table 2 T-Test Group Statistics

4.2 Standardisation by T-score

The Body Fat Mass Index (BFMI) was measured at 2.5 at minimum and 14.8 at maximum (Mean= 8.648, SD= 3.56). The Fat-Free Mass Index (FFMI) ranged from 12.7 to 22.9 (Mean=18.396, SD=2.61). Both were standardised using T-scores.

	N	Minimum	Maximum	Mean	Std. Deviation
BodyFatMassIndexBFMI	25	2.5	14.8	8.648	3.5611
FatFreeMassIndexFFMI	25	12.7	22.9	18.396	2.6087
Valid N (listwise)	25				

Table 3 T-Scores

4.3 Pearsons Correlation Test [Appendix A]

4.3.1 Fat-Free Mass Index

FFMI t-scores expressed a strong positive correlation with extracellular water (ECW) ($r = 0.867^{**}$, $p < 0.01$) and intracellular water (ICW) ($r = 0.804^{**}$, $p < 0.01$), showing that both body water compartments were closely related to FFMI. On the other hand, BFMI showed a negative correlation with water ($r = -0.780^{**}$, $p < 0.01$), indicating that an increase in body fat decreases the total body water content. A similar relationship was seen with ECW ($r = -0.780^{**}$, $p < 0.01$)

4.3.2 Extracellular Water

ECW has a strong positive correlation with ICW ($r = 0.827$, $p < 0.01$) and dry weight ($r = 0.670$, $p < 0.01$).

4.3.3 Body Mass Index

BMI showed a strong negative correlation with water ($r = -0.669^{**}$, $p < 0.01$), ECW ($r = 0.513^{**}$, $p < 0.01$), and ICW ($r = 0.513^{**}$, $p < 0.01$), suggesting that higher BMI is associated with more extracellular and intracellular water in the body. BMI also has a strong association with FFMI ($r = 0.746^{**}$, $p < 0.01$) and BFMI ($r = 0.872^{**}$, $p < 0.01$), which was expected since both are body composition measures.

4.3.4 eGFR

eGFR, in isolation, has no strong correlations with body parameters. The strongest relationship was a weak negative relation with phase angle ($r = -0.354$, $p = 0.082$) and a weak positive relationship with dry weight. ($r = 0.244$, $p = 0.240$).

4.3.5 Phase Angle

Phase angle showed a moderate positive correlation with ICW observed ($r = 0.493$, $p = 0.012$).

4.4 Correlations with Hydration Ratios [Appendix B]

4.4.1

FFMI showed strong positive correlation with ECW/TBW and ICW/TBW ($r = 0.702^{**}$, $p < 0.01$ and $r = 0.729^{**}$, $p < 0.01$). It showed a negative correlation with ECW/ICW ($r = -0.430^*$, $p < 0.05$), indicating that lean people might have better overall water distribution. A positive correlation was seen between ECW/Lean mass ($r = 0.667^{**}$, $p < 0.01$), again indicating better fluid distribution with higher lean mass.

4.4.2

BFMI showed a strong positive correlation with ECW/TBW ($r = 0.641$, $p < 0.01$) and moderate positive with ICW/TBW ($r = 0.516$, $p < 0.01$). A negative correlation was found with ECW/ICW ($r = -0.546$, $p < 0.01$). Higher fat mass was associated with total body water, especially in the extracellular space. This could be due to fluid imbalance. A robust positive correlation was found with ECW/Lean mass ($r = 0.829$, $p < 0.01$), further suggesting the relationship between higher body fat and higher ECW relative to lean body mass.

4.4.3

eGFR/TBW has a moderate positive correlation with ECW/TBW ($r = 0.508$, $p < 0.01$). This suggests a positive relationship between eGFR and the proportion of extracellular water. A negative correlation was with ECW/ICW ($r = -0.440^*$, $p < 0.05$) and a positive correlation with

ECW/Lean mass ($r = 0.402^*$, $p < 0.05$), linking kidney function to better hydration status, particularly in lean individuals.

Dry mass/eGFR has a moderate positive correlation with ICW/TBW ($r = 0.680^{**}$, $p < 0.01$) and a negative correlation with ECW/ICW ($r = -0.614$, $p < 0.01$), suggesting that higher mass weight tends to be associated with better fluid distribution.

Phase angle negatively correlates with ECW/ICW ($r = -0.546$, $p < 0.01$), meaning a higher phase angle also correlates with better water distribution, which is less ECW and more ICW. A negative relationship was found when correlated against eGFR/TBW ($r = -0.440^*$, $p < 0.05$). This indicates that as phase angle increases, the eGFR ratios become less favourable, which is another testament to the complex relationship between kidney function and body composition in dialysis patients.

4.5 Multiple Linear Regression

Multiple linear regression showed the extent to which phase angle, ECW/TBW ratio, BFMI t-score, and FFMI t-score predicted eGFR. The regression model was not statistically significant. Among the predictors, phase angle showed the strongest association with eGFR ($\beta = -0.427$). It has a negative relationship with eGFR ($\beta = -0.427$) and is nearly significant ($p = 0.087$). This suggests that eGFR decreases as phase angle increases, which can't be claimed at the standard $p < 0.05$ level. Other variables, including ECW/TBW ratio ($p = .691$), BFMI t-score ($p = .766$), and FFMI t-score ($p = .588$), were not significantly associated with eGFR.

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	22.049	4	5.512	1.253	.321 ^b
	Residual	87.951	20	4.398		
	Total	110.000	24			

a. Dependent Variable: eGFR

b. Predictors: (Constant), FFMI_tscore, BFMI_tscore, PHASEANGLE, ECW_TBW_RATIO

Table 4 Anova

Coefficients^a

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	4.439	2.707		1.640	.117
	PHASEANGLE	-.209	.116	-.427	-1.802	.087
	ECW_TBW_RATIO	4.371	10.844	.154	.403	.691
	BFMI_tscore	-.017	.057	-.081	-.301	.766
	FFMI_tscore	.040	.073	.188	.550	.588

a. Dependent Variable: eGFR

Table 5 Regression Coefficients

CHAPTER 5

DISCUSSION

5.1 Aim of the Study

This study explored the relationship between body composition and residual kidney function in 25 haemodialysis patients. The demographic profile included a predominantly male group (76%). The mean BMI was 27.05 kg/m², indicating that most of the patients were overweight. As expected in this population, the mean eGFR was low (6.8 mL/min/1.73m²), indicating advanced kidney disease.

5.2 Body Composition and Fluid Distribution

The analysis revealed significant associations between body composition and fluid compartments. FFMI had a strong positive association with ECW ($r = 0.867$, $p < 0.01$) and ICW ($r = 0.804$, $p < 0.01$), indicating that individuals with higher lean mass carry more water. These findings support physiological understanding, as muscle tissue contains more water than adipose tissue. [11]

Similarly, BFMI was positively correlated with ECW/TBW ($r = 0.641$, $p < 0.01$) and ICW/TBW ($r = 0.516$, $p < 0.01$) and negatively with ECW/ICW ($r = -0.546$, $p < 0.01$). Although seemingly contradictory, the data suggests that individuals with higher fat mass have proportionally more extracellular water, possibly due to fluid imbalance commonly seen in dialysis patients. This was further supported by the strong positive correlation between BFMI and ECW/lean mass ($r = 0.829$, $p < 0.01$), indicating that increased fat mass is associated with a disproportionate increase in ECW compared to muscle mass. An increase in ECW relative to ICW could signal a pathological fluid distribution that affects overall health. The obesity study highlights how weight loss can reduce ECW, which might be of interest when considering fluid management strategies for overweight or obese dialysis patients. [12] The obesity study also emphasised that lean tissue, particularly muscle, plays a significant role in maintaining fluid balance. This research, in conjunction with ours, explores how changes in muscle mass during haemodialysis or post-transplant impact fluid status and kidney function over time.

FFMI, on the other hand, had a positive association with both ECW/TBW ($r = 0.702$, $p < 0.01$) and ICW/TBW ($r = 0.729$, $p < 0.01$) and a negative association with ECW/ICW ($r = -0.430$, $p < 0.05$). This indicates that higher muscle mass contributes to a more favourable water distribution. A more significant proportion of water held intracellularly is a sign of healthier tissue and better fluid regulation. These results align with a study demonstrating that the ICW/lean mass ratio is a reliable indicator of muscle function and hydration status in elderly individuals. The study concluded that better cellular hydration within lean tissue is associated with greater muscle strength and lower frailty. This reinforces the observation in our data that leaner individuals have more favourable water distribution and stronger functional capacity. [12]

5.3 Phase Angle as a Marker of Cellular and Nutritional Health

Phase angle is often used as an indicator of cellular integrity and nutritional status, and it demonstrated several noteworthy relationships in our study. It had a moderate positive correlation with ICW ($r = 0.493$, $p = 0.012$) and a negative correlation with ECW/ICW ($r = -0.546$, $p < 0.01$), suggesting that higher phase angle is linked to better fluid distribution, with less extracellular and more intracellular water. This reflects healthier cell membranes and metabolic status, consistent with prior studies linking higher phase angle with lower morbidity and mortality in CKD populations. [12] [13]

Phase angle also negatively correlated with eGFR/TBW ($r = -0.440$, $p < 0.05$), suggesting that patients with better cellular health might not necessarily have better residual renal function. This complex relationship may reflect the confounding effects of dialysis, body composition, and inflammation on both variables. This correlation suggests increased ECW dilutes TBW, causing overhydration and worsening kidney function.

Monitoring PhA and ECW/TBW via bioimpedance provides important prognostic information and could help guide individualised fluid and nutrition management in dialysis care. Our study supports the clinical relevance of ECW/TBW and PhA as markers of poor outcomes.

Despite similar eGFR levels indicating severely reduced kidney function in both groups the PhA differences suggest variations in cellular health and nutritional status among patients. A low PhA ($< 4.5^\circ$) may reflect poor cell integrity, muscle wasting, or malnutrition, even if kidney function (eGFR) is comparable to those with a normal PhA. The normal PhA ($\geq 4.5^\circ$) group, despite having

similarly low eGFR, might have better-preserved muscle mass or hydration, possibly due to differences in diet, inflammation, or metabolic health. This implies that eGFR alone does not capture overall patient health. PhA may provide additional insight into frailty, nutritional deficits, or survival prognosis in advanced kidney disease. Further research should explore whether improving PhA could benefit patients, even when eGFR remains critically low.

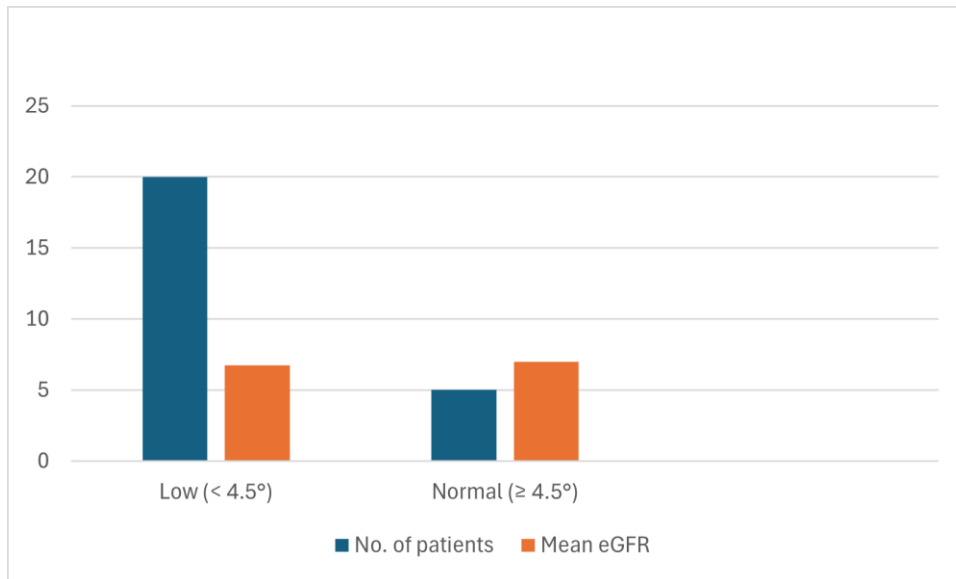


Diagram 1 eGFR in Low vs High Phase Angle Groups

5.4 eGFR and Its Relationship with Hydration Ratios

eGFR alone showed weak direct associations with most body composition parameters, but additional patterns emerged when expressed as a ratio to TBW. eGFR/TBW had a positive correlation with ECW/TBW ($r = 0.508$, $p < 0.01$) and a negative correlation with ECW/ICW ($r = -0.440$, $p < 0.05$). These findings show that better kidney function is associated with improved water balance, specifically a healthier distribution between extracellular and intracellular compartments.

A further relationship was observed between eGFR and ECW/lean mass ($r = 0.402$, $p < 0.05$), linking better residual renal function with leaner body composition and possibly more efficient

fluid handling. This supports the clinical notion that muscle mass and hydration status are interconnected with kidney function, though causality remains challenging to determine in this cross-sectional context. [14]

An elevated ratio of measured ECW to expected TBW is independently associated with worse renal outcomes in CKD patients. This suggests that fluid overload, as indicated by a higher percentage of ECW/TBW, may contribute to the progression of kidney disease. Monitoring and managing extracellular fluid volume is crucial in the care of CKD patients to improve renal outcomes. [14] ECW/ICW ratio is independently associated with both the presence and progression of albuminuria in Type 2 Diabetes Mellitus (T2DM) patients without kidney failure. This suggests that fluid imbalance, as indicated by an elevated ECW/ICW ratio, maybe an early marker for diabetic kidney disease. Monitoring fluid status using BIA could be a valuable tool in detecting and managing renal complications in diabetic patients. [15]

Dry mass/eGFR also showed relevant patterns, being positively correlated with ICW/TBW ($r = 0.680$, $p < 0.01$) and negatively correlated with ECW/ICW ($r = -0.614$, $p < 0.01$). These results further emphasise that patients with higher dry mass tend to exhibit more favourable fluid distribution, which may be clinically protective. Comparing eGFR to dry mass could help interpret whether a person has relatively more or less filtration capacity per kg of metabolically active body mass. A person with a high dry mass but a low eGFR might indicate that their kidneys are under greater strain to support a larger metabolic load. Patients with high fat mass might have lower creatinine production, which can lead to an overestimation of eGFR. If dry mass includes a large proportion of adipose tissue, eGFR per kg might be misleadingly high. [16] Dry Mass Index (DMI) has been used to assess body composition in haemodialysis patients. This index compares total body water measured by bioelectrical impedance analysis (BIA) to that estimated by the Watson formula for nutritional assessment. [17]

Mendelian randomisation research has provided causal evidence linking increased whole-body water mass to reduced kidney function, measured by a significant decrease in eGFR and elevated risk for CKD progression. Their findings support a growing body of literature suggesting that excess total body water, particularly when associated with extracellular water expansion, can negatively impact renal outcomes. These results align with our observations that patients with higher hydration ratios (ECW/TBW) tend to have lower eGFR values. The genetic evidence

presented by this study adds strength to the physiological link between fluid overload and kidney function decline, reinforcing the clinical importance of precise fluid management in both pre-dialysis and dialysis populations. Furthermore, it underscores the potential value of using body composition metrics, such as BIA-derived hydration indices and phase angle, as predictive markers in nephrology practice. [18]

5.5 Regression Analysis

To explore whether body composition and hydration parameters could predict kidney function, a multiple linear regression was conducted with eGFR as the dependent variable and phase angle, ECW/TBW ratio, BFMI t-score, and FFMI t-score as predictors. The overall model was not statistically significant ($F = 1.253$, $p = .321$), suggesting that these variables, taken together, did not significantly explain the variance in eGFR within this sample.

Despite the overall model insignificance, phase angle emerged as the strongest individual predictor ($\beta = -0.427$, $p = .087$), showing a negative association with eGFR. While this relationship did not reach statistical significance at the conventional $p < .05$ level, it approaches significance and may indicate a clinically relevant trend. Patients with higher phase angles are typically associated with better nutritional status and cellular integrity yet show lower eGFR values. At first glance, this seems counterintuitive since higher PhA is usually a marker of better health, but overhydration may mask kidney dysfunction in low PhA individuals. Patients with fluid overload may appear to have higher eGFR due to haemodilution despite worse actual kidney function. In advanced kidney failure, some patients retain better cellular health (PhA) but still have severely reduced eGFR due to irreversible damage. Lower eGFR may lead to changes in body composition, but those with better nutritional status remain relatively stable for longer, even with lower eGFR. If younger or more muscular patients have higher PhA and naturally lower eGFR due to higher creatinine, this could distort the direction of the association. [19]

ECW/TBW ratio, BFMI t-score, and FFMI t-score did not demonstrate significant associations with eGFR, with p-values well above the significance threshold. These findings reinforce the multifactorial nature of kidney function in haemodialysis patients, which may not be directly explained by body composition and fluid status alone.

5.6 Strengths and Limitations

5.6.1 Strengths

- A novel combination of parameters: This study uniquely integrated eGFR with detailed BIA-derived hydration and composition markers, offering insight into the interrelation of fluid balance and kidney function.
- Use of standardised scores (T-scores): Standardising FFMI and BFMI allowed more reliable comparisons across individuals with varying body sizes and sex differences.
- In-depth fluid analysis: Ratios such as ECW/TBW, ECW/ICW, and ECW/lean mass provided a more nuanced understanding of fluid distribution than simple volume measures.

5.6.2 Limitations

- Small sample size (N=25): The limited number of participants reduces statistical power and limits generalizability.
- Cross-sectional design: This prevents any conclusions about causality or the direction of observed relationships.
- Single centre and population: Given the high male predominance, the study population may not represent broader CKD or dialysis populations.
- Measurement variability: BIA measurements may be influenced by timing relative to dialysis, fluid overload, or inflammation, potentially affecting the accuracy of hydration status assessment.
- eGFR limitations in dialysis: eGFR is not always an accurate reflection of renal function in patients already on dialysis, as it is typically calculated based on creatinine, which is influenced by muscle mass and dialysis clearance.

CHAPTER 6

CONCLUSION

This study investigated the associations between body composition measured by BIA and kidney function estimated by eGFR in a population of haemodialysis patients, providing several important insights. The findings demonstrate that increased fat mass is associated with a disproportionately high ECW, while higher lean mass contributes to a more favourable fluid distribution with increased ICW. These observations reinforce physiological knowledge about the water-retaining capacity of muscle and low water-holding capacity of adipose tissue, as is highlighted by the notable role of dry mass and TBW ratios in evaluating hydration and nutritional status in CKD patients. [17]

Phase angle (PhA), a marker of cellular integrity and nutritional health, also showed significant correlations with fluid compartments. Lower PhA values were associated with elevated ECW/ICW ratios, supporting previous research that links low PhA to fluid overload and increased mortality in dialysis patients. [20] Although PhA did not show significant correlation with eGFR in regression analysis, its near-significant association suggests its potential as a clinical marker of altered physiology in renal failure, reflecting complex interactions between nutrition, inflammation, and body composition.

The novel use of eGFR/TBW and dry weight/eGFR ratios in this study revealed that fluid distribution plays a subtle but critical role in kidney function. Patients with better hydration balance, indicated by lower ECW/ICW and higher ICW/TBW ratios, tended to have higher eGFR values. [18]

While the multiple regression model did not achieve statistical significance, individual trends, particularly the inverse relationship between PhA and eGFR, provide direction for further research.

Despite similar eGFR levels indicating severe kidney dysfunction, differences in phase angle (PhA) highlight variations in cellular health, muscle mass, and nutritional status. PhA offers additional insight into frailty and prognosis that eGFR alone may miss, underscoring its potential clinical value.

In conclusion, the findings underscore the importance of integrating BIA-based metrics into clinical practice for a more comprehensive assessment of volume status, especially when managing residual renal function and dialysis adequacy. Body composition and hydration status are intricately linked to kidney function in haemodialysis patients. These relationships are complex, multifactorial, and potentially modifiable. The clinical use of hydration ratios, dry weight-normalised eGFR, and BIA-derived parameters may offer valuable tools in guiding individualised interventions to optimise fluid balance, nutritional status, and overall prognosis in this population.

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APPENDIX

		FFMI_tscore	BFMI_tscore	PHASEANGL E	BMI	eGFR	Water	ECW	ICW	Dry
FFMI_tscore	Pearson Correlation	1	.325	.373	.746**	.110	-.228	.867**	.804**	.586**
	Sig. (2-tailed)		.112	.066	.000	.600	.273	.000	.000	.002
	N	25	25	25	25	25	25	25	25	25
BFMI_tscore	Pearson Correlation	.325	1	-.051	.872**	.101	-.780**	.090	.136	.054
	Sig. (2-tailed)	.112		.809	.000	.632	.000	.668	.518	.798
	N	25	25	25	25	25	25	25	25	25
PHASEANGLE	Pearson Correlation	.373	-.051	1	.157	-.354	.225	.275	.493*	.023
	Sig. (2-tailed)	.066	.809		.455	.082	.279	.184	.012	.912
	N	25	25	25	25	25	25	25	25	25
BMI	Pearson Correlation	.746**	.872**	.157	1	.128	-.669**	.513**	.513**	.343
	Sig. (2-tailed)	.000	.000	.455		.542	.000	.009	.009	.093
	N	25	25	25	25	25	25	25	25	25
eGFR	Pearson Correlation	.110	.101	-.354	.128	1	-.191	.118	.085	.244
	Sig. (2-tailed)	.600	.632	.082	.542		.360	.575	.686	.240
	N	25	25	25	25	25	25	25	25	25
Water	Pearson Correlation	-.228	-.780**	.225	-.669**	-.191	1	-.143	-.310	-.507**
	Sig. (2-tailed)	.273	.000	.279	.000	.360		.497	.131	.010
	N	25	25	25	25	25	25	25	25	25
ECW	Pearson Correlation	.867**	.090	.275	.513**	.118	-.143	1	.827**	.670**
	Sig. (2-tailed)	.000	.668	.184	.009	.575	.497		.000	.000
	N	25	25	25	25	25	25	25	25	25
ICW	Pearson Correlation	.804**	.136	.493*	.513**	.085	-.310	.827**	1	.797**
	Sig. (2-tailed)	.000	.518	.012	.009	.686	.131	.000		.000
	N	25	25	25	25	25	25	25	25	25
Dry	Pearson Correlation	.586**	.054	.023	.343	.244	-.507**	.670**	.797**	1
	Sig. (2-tailed)	.002	.798	.912	.093	.240	.010	.000	.000	
	N	25	25	25	25	25	25	25	25	25

** . Correlation is significant at the 0.01 level (2-tailed).

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

Appendix A Pearsons Correlation Test

Correlations

		FFMI_tscore	BFMI_tscore	PHASEANGLE	ECW_TBW_RATIO	ICW_TBW_RATIO	ECW_ICW_RATIO	ECW_LEAN_RATIO	Dry	Lean	eGFR
FFMI_tscore	Pearson Correlation	1	.325	.373	.702**	.729**	-.430*	.667**	.586**	.041	.110
	Sig. (2-tailed)		.112	.066	.000	.000	.032	.000	.002	.846	.600
	N	25	25	25	25	25	25	25	25	25	25
BFMI_tscore	Pearson Correlation	.325	1	-.051	.641**	.516**	-.092	.829**	.054	-.914**	.101
	Sig. (2-tailed)	.112		.809	.001	.008	.663	.000	.798	.000	.632
	N	25	25	25	25	25	25	25	25	25	25
PHASEANGLE	Pearson Correlation	.373	-.051	1	-.009	.241	-.546**	.072	.023	.203	-.354
	Sig. (2-tailed)	.066	.809		.967	.246	.005	.731	.912	.330	.082
	N	25	25	25	25	25	25	25	25	25	25
ECW_TBW_RATIO	Pearson Correlation	.702**	.641**	-.009	1	.930**	-.454*	.893**	.764**	-.420*	.238
	Sig. (2-tailed)	.000	.001	.967		.000	.023	.000	.000	.036	.252
	N	25	25	25	25	25	25	25	25	25	25
ICW_TBW_RATIO	Pearson Correlation	.729**	.516**	.241	.930**	1	-.733**	.771**	.823**	-.280	.170
	Sig. (2-tailed)	.000	.008	.246	.000		.000	.000	.000	.175	.415
	N	25	25	25	25	25	25	25	25	25	25
ECW_ICW_RATIO	Pearson Correlation	-.430*	-.092	-.546**	-.454*	-.733**	1	-.235	-.635**	-.075	.015
	Sig. (2-tailed)	.032	.663	.005	.023	.000		.258	.001	.721	.944
	N	25	25	25	25	25	25	25	25	25	25
ECW_LEAN_RATIO	Pearson Correlation	.667**	.829**	.072	.893**	.771**	-.235	1	.411*	-.632**	.149
	Sig. (2-tailed)	.000	.000	.731	.000	.000	.258		.041	.001	.477
	N	25	25	25	25	25	25	25	25	25	25
Dry	Pearson Correlation	.586**	.054	.023	.764**	.823**	-.635**	.411*	1	.142	.244
	Sig. (2-tailed)	.002	.798	.912	.000	.000	.001	.041		.498	.240
	N	25	25	25	25	25	25	25	25	25	25
Lean	Pearson Correlation	.041	-.914**	.203	-.420*	-.280	-.075	-.632**	.142	1	-.063
	Sig. (2-tailed)	.846	.000	.330	.036	.175	.721	.001	.498		.766
	N	25	25	25	25	25	25	25	25	25	25
eGFR	Pearson Correlation	.110	.101	-.354	.238	.170	.015	.149	.244	-.063	1
	Sig. (2-tailed)	.600	.632	.082	.252	.415	.944	.477	.240	.766	
	N	25	25	25	25	25	25	25	25	25	25

** . Correlation is significant at the 0.01 level (2-tailed).

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

Appendix B Correlations with Hydration Ratios

Research Ethics Committee of the University of Tartu (UT REC)

Operating to all ICH GCP requirements

Approval: 397/T-10

Date of meeting: 20 January 2025

In the presence of:

Chairman

Aime Keis University of Tartu, Chairman of UT REC

Vice-chairman

Kristi Lõuk University of Tartu, Faculty of Arts and Humanities, Project Manager and Doctoral Student

Members

Diva Ensoo	National Institute of Health Development, researcher
Katrin Kaarna	University of Tartu, Faculty of Medicine, Head of Clinical Research Centre
Kalle Kisand	University of Tartu, Faculty of Medicine, Professor in Laboratory Medicine
Piret Koosa	Estonian National Museum, Researcher
Malle Kuum	University of Tartu, Faculty of Medicine, Lecturer in Pharmacology and Research Fellow in Pharmacology
Marje Oona	University of Tartu, Faculty of Medicine, Associate Professor in Family Medicine
Maire Peters	University of Tartu, Faculty of Medicine, Associate Professor in Genetics
Raivo Puhke	University of Tartu, Faculty of Medicine, Lecturer in Functional Morphology
Atko-Sulhan Rimmel	University of Tartu, Faculty of Arts and Humanities, Associate Professor in Religious Studies
Anna-Liisa Tamm	Tartu Health Care College, Head of Physiotherapy and Environmental Health
Maarja Torga	Counsellor to the Civil Chamber of the Supreme Court of Estonia

Resolution: Approval is given to conduct the study

Study titled: Integrating Bioelectrical Impedance Analysis (BIA) and Estimated Glomerular Filtration Rate (eGFR): A Novel Approach to Assessment of Nutritional Status of Hemodialysis Patients

Principal Investigator's name and address:

Alastair Forbes (Tartu University Hospital, Internal Medicine Clinic / University of Tartu, Faculty of Medicine, Institute of Clinical Medicine, L. Puusepa 8, Tartu Estonia)

Documents reviewed:

1. Application for the approval of the Ethics Committee, 10.02.2025
2. Approval of the Tartu University Hospital
3. Informed Consent Form
4. CVs of the investigators (A. Forbes, K. Kõlvald, A. Basit)

End of the study: June 2025

Chairman of UT REC: Aime Keis /digitally signed/

Secretary of UT REC: Kaire Kallak /digitally signed/

Date of issue in Estonian: date of the latest digital signature 10 February 2025

Date of issue in English: date of the latest digital signature

Appendix C Ethics Approval