

The Reliability of Ultrasound Assessment of Muscle Mass in End-Stage Renal Disease Patients
Receiving Hemodialysis

Delight Adri

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Abstract

Introduction: Muscle wasting is a major complication of end-stage renal disease (ESRD) particularly for patients undergoing hemodialysis. Muscle wasting is associated with morbidity, increased hospitalization, and mortality in ESRD patients. With the increasing prevalence of ESRD disease, it is important to routinely assess and monitor changes in muscle size to guide interventions and monitor disease progression in this population. Ultrasound is a reliable tool for muscle thickness assessment, however, its routine application in ESRD population undergoing hemodialysis is limited by the higher rate lower limb amputation. This often makes the rectus femoris muscle, which is commonly used as a surrogate for overall muscle mass inaccessible. Therefore, there was a need to explore different muscle sites for potential ultrasound muscle thickness assessment in this population. This study aimed to explore upper limb muscles including the biceps brachii and the triceps brachii muscles as potential and reliable alternative ultrasound muscle thickness assessment sites to the rectus femoris muscle and further explore the perception of healthcare professionals and patients on the integration of ultrasound assessment of muscle thickness into routine renal care.

Methods: This study was a convergent parallel design. The quantitative aspect was a longitudinal design with 50 ESRD patients (30 males and 20 females) recruited for baseline ultrasound muscle thickness measurement with recruited patients reducing to 45 (27 males and 18 females) at 3 months follow up measurements. Muscle thickness, measured in centimeters (cm) of the rectus femoris muscle, biceps brachii muscle, and triceps brachii muscle A and B were performed by two dietitians. Measurements were performed during patients' hemodialysis session by the first dietitian and immediately by the second dietitian blinded to the results of the first rater. Interclass correlation coefficient (ICC) was conducted to assess the inter-rater reliability of ultrasound-derived muscle thickness between the raters (dietitians) across timepoint. Pearson's correlation and Spearman's correlation were conducted to assess the association between the thickness of the rectus femoris muscle and the biceps brachii muscle thickness and the triceps brachii muscle A and B thickness. The qualitative aspect was conducted through a semi-structured interview. Nine participants (three dietitians, two nurses, a nephrologist, and three patients) were recruited and interviewed with guided interview scripts. Interviews were analysed using the Braun and Clarke (2006) approach to thematic analysis.

Results: At baseline, inter-rater reliability of rectus femoris muscle thickness was excellent (ICC (2,1)=.91, 95% CI [.83, .96], $n=33$), good for biceps brachii muscle thickness (ICC (2,1)=.87, 95% CI [.76, .93], $n=38$), moderate for triceps brachii muscle A thickness (ICC (2,1)=.53, 95% CI [.27, .73], $n=38$), and moderate for triceps brachii muscle B thickness (ICC (2,1)=.66, 95% CI [.44, .81], $n=38$). At 3 months, the biceps brachii muscle thickness retained good inter-rater reliability (ICC (2,1)=.84, 95% CI [.68, .92], $n=30$), and the rectus femoris muscle thickness declined to good inter-rater reliability (ICC (2,1)=.75, 95% CI [.27, .91], $n=21$). Both triceps brachii muscle A thickness and triceps brachii muscle B thickness declined to poor inter-rater reliability (ICC (2,1)=.32, 95% CI [-.02, .60], $n=30$); and (ICC =.41, 95% CI [.05, .67], $n=30$) respectively. There was a moderate, positive, and significant association between the rectus femoris muscle and the biceps brachii muscle thickness for rater 1 at baseline ($r=.44$, 95% CI [.16, .66], $n=42$, $p=.004$), at 3 months ($p=.42$, 95% CI [.10, .67], $n=36$, $p=.01$). There was a moderate, positive, and significant association between the rectus femoris muscle and the biceps

brachii muscle thickness for rater 2 ($r=.53$, 95% CI [.12, .77], $n=22$, $p=.01$) and triceps brachii muscle B thickness ($r=.45$, 95% CI [-.06, .67], $n=22$, $p=.04$) at 3 months. The themes identified in the interviews included (1) current assessment of muscle status, (2) ultrasound as a valuable clinical instrument, (3) competency, (4) application of ultrasound in hemodialysis care, (5) patients' experience and acceptance, and (6) ultrasound data as potential motivational evidence.

Conclusion: The biceps brachii muscle is a potential alternative muscle site for muscle thickness assessment but future validation with gold standard criterion is warranted for the hemodialysis population. Also, healthcare professionals and patients are receptive to the integration of ultrasound muscle thickness assessment into routine care as they perceive it to improve education, communication, and motivation.

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List of Abbreviations

BIA – Bioimpedance analysis
B-mode – Brightness mode
CKD – Chronic kidney disease
cm – Centimeter
CSA – Cross-sectional area
CT – Computed tomography
DEXA – Dual-energy x-ray absorptiometry
ESRD – End-stage renal disease
EWGSOP – European working group in sarcopenia
g – Gram
ICC – Interclass correlation coefficient
ICU – Intensive care unit
kg – Kilogram
L - Liter
m² - Squared meter
MDC - Minimal detectable change
mg – Milligram
mL/min – Milliliter per minute
RRT – Renal replacement therapy
SEM – Standard error of measurement
USA – United States of America
LoA – Limit of Agreement

Chapter 1: Introduction

Background

The prevalence of chronic kidney disease (CKD) has been increasing steadily worldwide, with notable increases in the percentage of patients diagnosed with specific stages of CKD (Kampmann et al., 2023). Over 850 million people worldwide are estimated to have progressive renal disease (Francis et al., 2024) of which nearly 10 million are in the final stage (Fiseha & Osborne, 2023). According to The Kidney Foundation of Canada (2023), one in 10 Canadians have kidney disease and over 53,000 people in the final stage of this disease nationwide. End-stage renal disease (ESRD) is the final stage of CKD (stage 5) characterized by a significant decline in kidney function and clinically defined as glomerular filtration rate of less than 15 mL/min/1.73m² (Hashmi et al., 2023). As CKD progresses to ESRD, the kidney is unable to filter waste, excess salt, and fluid from the blood to meet the body's need (Bentz & Bailey, 2023).

ESRD patients require renal replacement therapy (RRT) such as kidney transplantation or dialysis to survive (Groth et al., 2022). It was estimated in 2017 that about 3.9 million patients with ESRD received one form of RRT worldwide (Bello et al., 2022). Although kidney transplantation is the ideal RRT option, most ESRD patients are treated with dialysis due to factors such as availability of donor kidneys, patients' eligibility for transplantation, and the collaborative decision-making between healthcare providers and patients in choosing alternative or the best treatment options available (Wouk, 2021). Nearly 61% of ESRD patients in Canada were treated with dialysis in 2023 and about 80% of these patients received hemodialysis (Canadian Institute for Health Information, 2024).

Hemodialysis is a life-sustaining treatment performed outside of the body to remove metabolic bi-products in the body, imitating but not completely replacing kidney function (Clinical Pharmacist, 2015; Vadakedath & Kandi, 2017). Despite its life-sustaining nature, hemodialysis is associated with muscle wasting (Cheng et al., 2022; Sabatino et al., 2021). Muscle wasting is strongly linked to poor health-related quality of life, increased hospitalization, mortality depression, and a higher risk of cardiovascular events in ESRD patients (Cheng et al., 2022; Sabatino et al., 2021).

It is clinically imperative to accurately and routinely assess muscle mass in ESRD patients to guide nutritional interventions, physiotherapy interventions, and monitor disease progression in this population. The traditional muscle mass assessment modalities include bioelectrical impedance analysis (BIA), dual energy x-ray absorptiometry (DEXA), computed tomography (CT), and magnetic resonance imaging (MRI) which are highly labour and cost intensive and not easily accessible to rural patients (Matsuzawa et al., 2020; Sabatino et al., 2021). However, ultrasound imaging modality offers a bedside alternative in clinical settings for muscle assessment. This imaging modality possesses several advantages over the traditional modalities including its low cost, portability, absence of radiation exposure, faster image processing time, and the ability to be operated by non-specialist staff (Matsuzawa et al., 2020; Sabatino et al., 2021). Also, ultrasound is widely available in the hemodialysis centres to guide peripheral intravenous cannulation (Iglesias et al., 2021). This readily availability of this tool hemodialysis centres also provides potential for easy repurposing to muscle assessment.

Notwithstanding the numerous advantages of ultrasound, its application in ESRD patients undergoing hemodialysis is still influenced by the context where care is delivered. In Canada, hemodialysis is predominantly delivered in the hospital settings (Canadian Institute for Health

Information, 2024). This requires the patients to attend a facility for treatment at least two to four times per week with sessions spanning for three to five hours (Lewis et al., 2023). Patient care at these facilities follows a tightly structured workflow including preparation and monitoring of dialysis machines, cannulation of vascular access, leaving limited time for additional clinical tasks (Ellis, 2010; Plantinga et al., 2024). Workflow in these facilities is further compromised by staff shortages, high patient-to-staff ratios, and availability of equipment (Bello et al., 2024; Plantinga et al., 2024). Introducing any new assessment procedure, such as ultrasound for muscle mass assessment, in these facilities for ESRD patients therefore requires that it be feasible within the existing workflow and acceptable to both providers and patients without adding undue burden.

Problem Statement

A major challenge with the application of ultrasound in ESRD population is the higher rate of lower limb amputation partly due to higher rate of diabetes (Franz et al., 2018). Reported rates of amputation in ESRD population is more than 20 times higher than in the general population. (Franz et al., 2018). Lower extremity amputation particularly above knee amputation in ESRD population does not always allow the assessment of quadriceps femoris muscle commonly used as a surrogate for overall muscle mass. The inaccessibility of the quadriceps femoris muscle with ultrasound in some ESRD patients necessitates the exploration of a reliable alternate muscle site, such as muscle sites in the upper limb (i.e., biceps brachii and triceps brachii) for comprehensive patient care and to monitor change in health status and/or treatment effect. The inaccessibility of the quadriceps muscles is particularly due to the positioning of patients during hemodialysis therapy sessions. Patients are often seated in semi-fowler to fowler position with the knees in partial flexion. This position does not allow the full relaxation of the

quadriceps muscles but rather introduces tension and muscle architectural change (De Sousa et al., 2023).

Also, ultrasound has demonstrated strong evidence of inter-rater reliability of ultrasound muscle mass assessment in various populations (Hashida et al., 2022; Ogawa et al., 2023; Smerilli et al., 2023). However, patient related factors including dialysis chair positioning may affect the reliability in ESRD population undergoing in-centre hemodialysis. The inter-rater reliability of ultrasound muscle mass assessment has not been fully established particularly in Canada. Furthermore, no study has comprehensively assessed the inter-rater reliability of ultrasound and its validity for assessing upper limb muscle mass particularly in the ESRD hemodialysis population. Finally, to successfully implement ultrasound as a routine muscle mass assessment tool in clinical practice, it is critical to understand the determinants of its feasibility such as healthcare professionals and patients' perceptions, workflow integration, and patients' acceptance.

Purpose of the Study

The purpose of this study was to address the above-mentioned gaps by identifying a reliable and valid alternate muscle site for muscle mass assessment in ESRD population undergoing hemodialysis. Also, the feasibility of implementation of ultrasound in routine care was explored based on the perspective of the healthcare providers and the patients to inform health policy decision making and practice.

The following objectives and guiding question directed the design, data collection, and data analysis for this study:

- A. To examine the reliability of ultrasound measurement of muscle thickness in ESRD patients undergoing hemodialysis. The guiding research question is:
1. What is the inter-rater reliability of ultrasound-derived muscle thickness of the biceps brachii, triceps brachii, and rectus femoris muscles across various healthcare providers in hemodialysis setting?
- B. To provide evidence of validation for the use of ultrasound to measure muscle thickness in the upper limb as an alternative muscle mass assessment site. The guiding research question is:
2. Is there correlation between rectus femoris muscle thickness and the thickness of biceps brachii and triceps brachii in hemodialysis patients?
- C. To explore the feasibility of integrating ultrasound muscle thickness assessment into routine care for ESRD patients undergoing hemodialysis. The guiding questions are:
3. What are the experiences/perceptions of healthcare providers with the use of ultrasound as a muscle assessment tool in hemodialysis care?
 4. How can ultrasound muscle assessment be incorporated into the workflow of multidisciplinary team?
 5. How do hemodialysis patients perceive ultrasound application for routine muscle assessment in their care?

Chapter 2: Review of Literature

Introduction

This chapter provides an overview of ESRD particularly its prevalence globally and regionally. It further discusses how ESRD is managed with hemodialysis therapy and the adverse effect of muscle wasting associated with the disease. In addition, the chapter also discusses the use of ultrasound as a muscle assessment tool focusing on its validity and reliability.

End-Stage Renal Disease

Global and Regional Prevalence

There is a significant global disproportion of CKD prevalence (Duff et al., 2024). A recent study assessing the prevalence and global health inequalities of CKD in 2024 gathered 119 studies from 54 countries around the world (Duff et al., 2024). The study reported Asia as the continent with the highest prevalence of stages 1 (i.e., glomerular filtration of 90 mL/min/1.73m² and above) to stage 5 of CKD (15.5%); Australia and Oceania had the highest prevalence of stages 3 (i.e., glomerular filtration between 30-59 mL/min/1.73m²) to stage 5 CKD (8.1%); Europe experienced the lowest prevalence of stages 1-5 CKD (10%); and Africa had the lowest prevalence of stage 3-5 CKD (5.7%). After classifying countries based on their economic statuses, high-income countries recorded the lowest overall prevalence of stages 1-5 CKD, and low-income countries recorded the lowest overall prevalence of stages 3-5 CKD (4%; Duff et al., 2024).

A major reason attributed to the low prevalence ESRD in low-income countries is the higher mortality rate in patients in stages 3-5 CKD due to the inability to easily access one form of RRT (Ashuntantang et al., 2017). About 32% of CKD patients living in low-income countries

and 45% of patients in low- to medium-income countries requiring one form of RRT have no access to these services (Bello et al., 2024). According to a study in sub-Saharan Africa by Ashuntantang et al. (2017), only 51% of newly diagnosed ESRD patients have access to dialysis. Also, out of the patients who had access to dialysis treatment, only 10% continued dialysis after three months and 1% after 12 months (Ashuntantang et al., 2017). The limited access to dialysis was attributed to the associated financial cost for accessing dialysis in this region (Ashuntantang et al., 2017). The study also reported a 95% mortality rate among newly diagnosed patients as they could not afford dialysis, leading to low reported prevalence ESRD in the region (Ashuntantang et al., 2017).

The prevalence rate of ESRD in North America has also seen significant increases in the past decades. According to the 2024 United States of America (USA) Annual Data Report, the prevalence of ESRD has increased from 429,051 in 2002 to 815,896 in 2022, representing an increase of 90.2% in two decades (U.S. Department of Health and Human Services, 2024). In Canada, 71.9 per 1000 persons in primary care settings are diagnosed with stage 3-5 CKD (Bello et al., 2019). In 2023, over 49,000 Canadians in all provinces, excluding Quebec, lived with ESRD (Canadian Institute for Health Information, 2024). This number compared to 2018 has shown an overall 100% increase in the prevalence over the half decade. Rural communities in Canada recorded higher ESRD prevalence compared to urban cities (Bello et al., 2019). This trend was attributed to limited access to healthcare and the high rates of diabetes experienced by Indigenous people in these communities (Slater et al., 2019).

In the local context of Northwestern Ontario region, where the Indigenous population constitute only about 20% of the total population (Domonkos, 2021), Kelly et al. (2019) found that Indigenous adults living in this region are two times more affected by CKD stage 3-5 than

the general population. The study also found that 71% of these CKD patients were diabetic highlighting the disease burden in this population.

Risk Factors and Causes

Globally, diabetes and hypertension are the leading risk factors and causes of CKD and ESRD (Paidí et al., 2021). However, their relative contributions vary by country and region. According to the Canada Organ Replacement Registry, diabetes is the leading cause of ESRD, accounting for approximately 33.3% of all recorded cases, while hypertension, the second most common cause, contributes to about 12.2% (Canadian Institute for Health Information, 2024). Though data from the Center for Disease Control and Prevention in the USA indicate that diabetes (38%) and hypertension (27%) are the two leading causes of ESRD (Centers for Disease Control and Prevention, 2023), the prevalence of hypertension is considerably higher compared to the Canadian dataset (Canadian Institute for Health Information, 2024).

Notably, over 11 million people living in Canada are diabetic or pre-diabetic, with over 1.6 million diabetic patients residing in Ontario (Costa et al., 2023). The prevalence of diabetes is higher in the Indigenous population than in the non-Indigenous population, with a higher prevalence rate in remote areas compared to rural areas (Kelly et al., 2019). Diabetic patients living in these remote communities face greater negative outcomes because of food insecurity and access to healthcare services and resources, increasing the risk of complications such as non-traumatic amputation, CKD, and ESRD (Costa et al., 2023).

In contrast to USA and Canada, the prevalence of diabetes as the primary cause of ESRD in South Korea is even higher. According to the Korean Renal Data system, 48.4% of the total cause of ESRD is attributed to diabetes (Hong et al., 2021). This result could stem from the

higher rate of albuminuria observed in the Asian population compared to Caucasians, as albuminuria (i.e., microalbuminuria and macroalbuminuria) is a marker for diabetic nephropathy and progression to ESRD (Gheith et al., 2015). The presence of albumin, a plasma protein found in urine, is termed albuminuria (Barzilay et al., 2024). This occurs when the endothelial layer of the glomerulus, which serves as the kidney's filtration barrier, is damaged, often due long-term hyperglycemia (Barzilay et al., 2024). In healthy individuals, this barrier prevents significant loss of albumin into urine. However, an albumin level exceeding 30 mg in a 24-hour urine sample indicates damage to the filtration barrier, thus, it is a biomarker of diabetic nephropathy (Barzilay et al., 2024).

In recent years, there has been an increased rate of ESRD disease without any known underlying cause. This outcome is more prevalent in low-income and low- to medium-income countries (Fiseha & Osborne, 2023). The early stages of CKD of unknown etiology are thought to be asymptomatic until it progresses to ESRD requiring emergent RRT (Khadda et al., 2024). CKD of unknown etiology is widely attributed to heat stress or dehydration and exposure to agriculture and environmental toxins such as fertilizers, herbicides, pesticides, and fungicides (Khadda et al., 2024). CKD of unknown etiology is remarkably prevalent in Central America, Latin America, South Asia, (Khadda et al., 2024), and Africa (Fiseha & Osborne, 2023).

Over half of all new ESRD cases in Mexico and El Salvador are due to unknown causes and mostly prevalent in young male agriculture workers in rural regions (Fiseha & Osborne, 2023; Strasma, et al., 2025). In Africa, the prevalence of ESRD of unknown origin ranges from 8% to 45% of all recorded cases (Fiseha & Osborne, 2023). Also, young male adults in rural regions of Africa exposed to pesticides, unsafe drinking water, and limited healthcare facilities are disproportionately affected (Fiseha & Osborne, 2023).

Treatment Options for End-Stage Renal Disease

Renal Replacement Therapy

Preparation for the initiation of one form of RRT (i.e., kidney transplantation or dialysis) begins as CKD reaches stage 4 (i.e., glomerular filtration rate of 15-29 mL/min/1.73m²; Vaidya & Aeddula, 2024). The selection of the right RRT is made through collaborative decision making between patients and clinicians (Wouk, 2021). Kidney transplantation is the ideal RRT (Abramyan & Hanlon, 2023; Groth et al., 2022) due to the lower risk of mortality and improved quality of life in recipients. (Sawinski & Poggio, 2021). Naylor et al. (2021) showed that kidney transplant recipients in Canada have higher survival rates. They found that male kidney transplant recipients have a median survival time of 18.7 years compared with prostate (15.6 years), lung (0.6 year), colorectal (6.9 years), and pancreatic cancer (0.4 years). This finding underscores the efficacy of kidney transplantation as the ideal RRT for ESRD patients.

In 2023, only 1,800 patients received kidney transplantation in Canada, while about 2,400 were wait-listed (Canadian Institute for Health Information, 2024). In the USA, 44,560 new patients were added to the kidney transplant waiting list in 2023, but only 27,332 patients received transplantation (Cron et al, 2025), perhaps due to the scarcity of kidney donors (living and diseased). Some patients were also ineligible for transplantation due to the high risk associated with surgery, the presence of active malignancy, or uncontrolled psychiatric disease (Abramyan & Hanlon, 2023). Therefore, patients who choose to receive transplantation, ineligible transplant recipients, and patients waiting for kidney transplantation are treated with one form of dialysis (i.e., peritoneal dialysis or hemodialysis).

Vascular Access Creation

Prior to initiating hemodialysis, a vascular access is created to form a connection between the circulatory system of the patient and the dialysis machine. Arteriovenous fistula, arteriovenous graft, and central venous catheter are the available traditional vascular accesses used (Lok et al., 2024). Arteriovenous fistulas are the most common vascular access ways for hemodialysis patient (Arasu et al., 2022), as it is associated with higher patency and lower complications compared to arteriovenous graft and central venous catheter (Lok et al., 2020). Despite the higher patency and lower complication rate of arteriovenous fistula, the rate of maturation failure is still high (Lok et al., 2020). The maturation of arteriovenous fistula is achieved when the arteriovenous fistula is ready for cannulation and hemodialysis by developing a diameter of at least 0.6 cm, a depth of 0.6 cm or less from the surface of the skin, and blood flow of at least 600 mL/min (Oliver, 2018). However, some arteriovenous fistulas fail to mature due to early thrombosis (Arasu et al., 2022). The maturation failure, thus, prevents cannulation, leading to a delay in commencing hemodialysis.

The creation of arteriovenous graft is considered when all arteriovenous fistula options are exhausted including interventions to prevent maturation failure (Arasu et al., 2022). Standard arteriovenous grafts can be used between two to four weeks after creation, and early cannulation can be done within 24 to 72 hours after creation (Lok et al., 2024). However, the associated cost of creation and maintenance of arteriovenous graft is high in all aspects compared to arteriovenous fistula, and, thus, arteriovenous fistula is mostly used. A study by Sorber et al. (2021) on the cost of creating and maintaining hemodialysis vascular access in the USA, revealed that the associated cost in all aspects including the initial creation of vascular access was significantly higher in arteriovenous grafts compared to arteriovenous fistulas. The average

cost of initial creation of arteriovenous graft access was \$9,213 compared to \$6,504 in arteriovenous fistula access creation. The average vascular access maintenance cost for the first year of creation was \$4,535, for arteriovenous graft and \$3,001 for arteriovenous fistula (Sorber et al., 2021).

Central venous catheter for hemodialysis is the option used for the ESRD patient without permanent, or with dysfunctional existing arteriovenous fistula and arteriovenous graft, but require emergent hemodialysis (Sohail et al., 2021). Central venous catheters are usually inserted in the internal jugular vein, femoral vein, or subclavian vein (Sohail, 2021). Central venous catheter is associated with complication such as mispositioning of the catheter, arterial injury, pneumothorax, venous air embolism, central venous stenosis, thrombosis, and catheter related infections (Sohail et al., 2021). Thus, arteriovenous fistula and arteriovenous graft are the preferred vascular accesses over central venous catheter for initiating hemodialysis.

Furthermore, cannulation of vascular access for the initiation of hemodialysis has been extensively aided by ultrasound (Iglesias et al., 2021). The use of ultrasound in dialysis units to guide vascular access cannulation highlight the availability of ultrasound machines in the dialysis units and the familiarity of with the use by both clinicians and patient. This supports the feasibility of extending its application to routine bedside muscle thickness assessment in hemodialysis patients.

Basic Principles of Hemodialysis

Hemodialysis works on the principles of diffusion and ultrafiltration (Clinical Pharmacist, 2015). Based on the needs of patients, diffusion and ultrafiltration can be performed concurrently or separately (Flythe & Watnick, 2024). Diffusion is defined as the movement of

particles from a region of higher concentration to a region of lower concentration through a semi-permeable membrane (Kalsi & Balani, 2016). In hemodialysis, the diffusion process involves the movement of waste particles from the blood into the dialysate through a dialyzer membrane (Flythe & Watnick, 2024). However, electrolytes in dialysate also move across the semi-permeable membrane into the blood until equal concentration between the blood and dialysate is obtained (Ellis, 2010).

The dialysate is a carefully prepared fluid with electrolytes including sodium, potassium, calcium, magnesium, bicarbonate, phosphate, and chloride to mimic the body's extracellular fluid composition (Ellis, 2010). Ultrafiltration is utilized to remove fluid from the blood through pressure gradient against the dialyser membrane (Ellis, 2010). The hemodialysis machine (see Figure 1) works in a countercurrent flow direction (Clinical Pharmacist, 2015). As the circuits connected to the hemodialysis machine take blood from the patient towards the semi-permeable membrane, prepared dialysate is pushed in the opposed direction of the blood toward the semipermeable membrane to create a concentration gradient.

Figure 1.

Hemodialysis Machine



Prevalence and Outcome of Hemodialysis

Hemodialysis accounts for about 61% of all RRT worldwide (Bello et al., 2022). According to the 2024 annual data report of the United States Renal Data System, 483,567 ESRD patients representing about 59.6% of prevalent ESRD in 2022 were receiving hemodialysis (U.S. Department of Health and Human Services, 2024). Similarly, about 46% of ESRD patients in Canada requiring RRT were treated with hemodialysis as of December 2023, representing about 81% of ESRD patients receiving dialysis (Canadian Institute for Health Information, 2024). Similar data from Europe shows that hemodialysis is the most utilized RRT. Stel et al. (2021) aimed to determine the frequency of dialysis and transplantation in 33 European countries through the European Renal Association-Dialysis and Transplant Registry report. This result revealed that the overall average prevalence of RRT as of 2016 was 985 per million population and the average incidence of hemodialysis was 502 per million population. This outcome suggests that the delivery of hemodialysis is not uniform. Hemodialysis may be administered at a healthcare centre or at home (Flythe & Watnick, 2024)

In-centre hemodialysis is the most common form of dialysis used worldwide and is performed intermittently, usually for four hours per session and two to four days per week (Groth et al., 2022). However, patients with severe fluid overload receiving less optimal fluid clearance through intermittent hemodialysis are treated with prolonged intermittent hemodialysis for six to 12 hours per session and four to seven days a week (Clark & Vijayan, 2023). According to a study by Htay et al. (2020) on the use of hemodialysis across 154 countries in the world, 129 (84%) of the countries had in-centre hemodialysis services available to patients and only 69 countries (45%) had home-based hemodialysis services available.

The reliance on hemodialysis as the major treatment modality for ESRD patients comes at a profound physical cost, including severe fatigue, cardiovascular complications, and risk of vascular infection. Also, ESRD patients undergoing hemodialysis are at a higher risk of severe muscle wasting. One study showed that patients who could not receive kidney transplantation due to comorbidities and were receiving chronic hemodialysis had a 17% decrease in lean body mass after 20 weeks (Visser et al., 2020). Another study showed that hemodialysis patients can lose 9.5% of lean body mass annually (Kitamura et al., 2021). These studies revealed the drastic rate of muscle mass loss in the hemodialysis population. It is, therefore, important to explore the underlying mechanisms of muscle loss in ESRD and understand the severity of this phenomenon.

Muscle Mass Loss in End-Stage Renal Disease

Pathophysiology

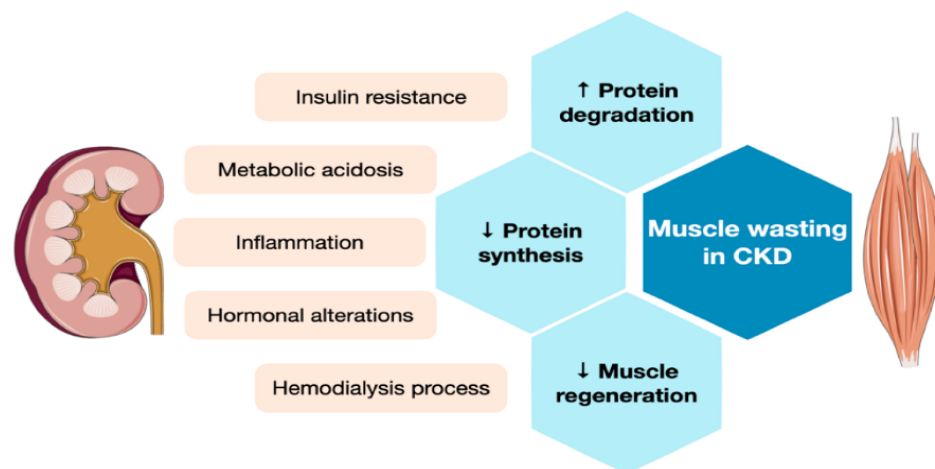
Natural aging-induced muscle loss begins at around the age of 30 years with about 3-8% loss of muscle mass, increasing to about 12% by the age of 60 and 30% by the age of 80 years (Ju & Hi, 2023). However, individuals with comorbidities such as ESRD experience a more rapid loss of muscle mass (Kitamura et al., 2020). Muscle mass is maintained by the balance of protein metabolism, with a small and continuous imbalance between protein degradation and protein synthesis causing muscle wasting over time (Cheng et al., 2022; Robinson et al., 2020). Current studies have identified that muscle wasting in ESRD patients is a result of accelerated protein degradation, suppressed protein synthesis (Robinson et al., 2020), and impaired muscle regeneration (Cheng et al., 2022).

Skeletal muscle is the largest reservoir for protein in the body, accounting for approximately 50% of total body protein (Stenvinkel et al., 2015). Protein plays an important

role for survival, and muscle mass represents the most reliable reserve called upon to maintain protein homeostasis (Stenvinkel et al., 2015). Naturally, protein homeostasis is maintained by the ubiquitin-proteasome system through controlled degradation of misfolded, damaged, and unneeded proteins, leaving behind only functional proteins (Jana, 2012). Catabolic factors associated with ESRD such as metabolic acidosis, insulin resistance, chronic inflammation, and hormonal alterations upregulate the ubiquitin-proteasome system (Cheng et al., 2022). This leads to accelerated protein degradation and consequent loss of muscle mass (see Figure 2).

Figure 2.

Illustration of Muscle Wasting Inducing Factors



From "Muscle wasting in chronic kidney disease: mechanism and clinical implications – a narrative review" by Cheng et al., (2022), International Journal of Molecular Sciences, 23(11), 6047.

Nutritional Drivers

Individuals with ESRD may experience appetite loss leading to reduced intake of protein and calories (Nitta & Tsuchiya, 2016). One of the causes of appetite loss in ESRD patients is the disruption of leptin and ghrelin hormones (Wang et al., 2022). Leptin suppresses appetite and ghrelin stimulates appetite. In ESRD patients, the plasma levels of leptin and ghrelin are elevated

significantly, leading to ghrelin resistance and causing a loss of appetite (Mak & Cheung et., 2011). A single center study in Nigeria by Mamven and Amira (2022) assessed the dietary protein and energy intake of 35 CKD patients (i.e., pre-dialysis patients and dialysis patients) and 35 healthy controls. They found a significant lower protein and energy intake level in CKD patients than in the control group. A concerning 69% of CKD patients had inadequate energy intake and 60% of pre-dialysis patients and all dialysis patients consumed less than the recommended daily intake of 0.8 g/kg/day (Mamven & Amira, 2022).

Appetite loss is also a major risk factor for malnutrition. Kiesswetter et al. (2019) investigated the association between appetite loss and malnutrition among older adults. A statistically significant association between appetite loss and malnutrition was found after univariate analysis with the odds ratio (OR) of malnutrition ranging from 2.55 to 7.82. Their finding indicates that older adults with appetite loss were more likely and, in some cases, nearly eight times more likely to be malnourished than other older adults with normal appetite. This demonstrates that appetite loss is a significant risk factor for malnutrition. In ESRD patients undergoing hemodialysis, the prevalence of malnutrition is estimated to be between 20-61% (Guner et al., 2023). Malnutrition is characterized by loss of fat and muscle mass due to the inadequate intake of protein and calories. As ESRD patients consume less protein and calories, the body begins to break down its protein reserves in skeletal muscles and body fat to meet the body's resting expenditure (Khor et al., 2021).

Hemodialysis' Impact on Muscle Loss

Furthermore, the hemodialysis procedure itself has been established as a major protein catabolic process. Ikizler et al. (2002) found out in their study energy aimed to determine if hemodialysis stimulates whole body and protein loss that, whole body protein breakdown after

hemodialysis increased by 10% while whole body protein synthesis remained the same. A major driver of catabolism during hemodialysis is the loss of amino acids into dialysate (Hendriks et al., 2020). Besides the efflux of waste, metabolic products from the blood during hemodialysis, small-sized nutrients including amino acids are also removed (Hendriks et al., 2020).

During a single hemodialysis session, about 8-12 g of amino acids are lost into dialysate (Hendriks et al., 2020; Ikizler et al., 2002). As amino acids are building units of protein, an increase in plasma amino acids concentration after ingestion stimulates muscle protein synthesis and inhibits protein degradation to maintain skeletal muscles (Hendriks et al., 2020). The dialytic amino acids loss leads to a significant decline in circulating amino acids concentration in plasma stimulating muscle protein degradation while inhibiting muscle protein synthesis (Hendriks et al., 2020). Ikizler et al. (2002) explained that amino acid lost into dialysate is compensated for by an increased breakdown of muscle protein into constituent amino acids into plasma causing a net negative protein balance and, subsequently, muscle wasting.

Clinical Implication of Muscle Mass Loss

Low muscle mass has been identified as an independent risk factor for mortality in ESRD. Choi et al. (2024) conducted a national study in South Korea enrolling 2,072 CKD patients from the National Health and Nutrition Examination Survey to investigate the association between low muscle mass and risk mortality in CKD patients. They found low muscle mass to be an independent risk factor for mortality in these patients. They indicated that that CKD patients with low muscle mass had 60% higher mortality risk (HR=1.60, 95% CI [1.32, 1.94], $p<.001$) compared to CKD patients without low muscle mass. Low muscle was defined as appendicular skeletal mass index $<7 \text{ kg/m}^2$ in men and $<5.5 \text{ kg/m}^2$ in women based on the criteria set by the European Working Group on Sarcopenia in Older People 2. After

propensity score matching, the association between low muscle mass and mortality remained statistically significant (HR=1.82 95% CI [1.42, 2.33], $p<.001$) underscoring the critical role of low muscle mass in the risk of death among CKD patients.

Notably, low muscle mass is not only a mortality risk factor in CKD and ESRD patients but also in critically ill patients with and without intensive care unit (ICU) admission (Maluf et al., 2025). Also, it is a significant short and long-term mortality risk factor (Maluf et al., 2025). However, in the older general population, low muscle strength and declined physical function were found to be larger contributors to mortality than muscle mass (Beaudart et al., 2025). Although this contradicts the findings from diseased populations, muscle mass may still be a strong predictor of strength and function among diseased and older populations. Matsuzawa et al. (2021) demonstrated that low muscle mass was independently associated with decreased handgrip strength, decreased gait speed, and increased chair stand time. The authors also reported a high degree of agreement between variables even after adjusting for patients' characteristics indicating that low muscle mass is predictor of decreased strength and poor function. Therefore, to be able to identify ESRD patients that are risk of mortality, morbidity, and response to treatment, it is important to accurately and reliably assess muscle mass. The findings of Choi et al. (2024) and Matsuzawa et al. (2021) further deepen the need for a reliable and readily available tool to enable clinicians to routinely assess muscle mass and integrate muscle status into nutritional and rehabilitative assessment and care.

Current Assessment Methods

The gold standard modalities available for muscle mass assessment are CT and MRI due to their ability to differentiate between tissues and high level of accuracy; however, the high financial cost, longer time of execution, and general patient access make their application

impractical as routine assessment tools (Sabatino et al., 2021). DEXA is considered the reference method for estimating muscle mass through the measurement of the appendicular skeletal muscle mass (Ju & Yi 2023; Sabatino et al., 2021). DEXA accurately estimates bone mineral density, the amount of fat, and the amount of lean mass in the body but its application in routine assessment is limited due to radioactive exposure to the patient (Barone et al., 2022).

Similar to DEXA, BIA is used to estimate muscle mass by measuring appendicular skeletal muscle mass (Ju & Yi, 2023). BIA is a non-invasive and inexpensive that relies on electric impedance of an electric current passing through the body to estimate the muscle mass (Walter-Kroker et al., 2011). BIA estimates many muscle parameters including fat-free mass, soft lean mass, lean body mass, skeletal muscle mass, skeletal muscle mass index, and segmental values (Moonen & Van Zanten, 2021). BIA parameters are greatly dependent on the subject's hydration status, therefore, abnormalities in fluids and electrolytes may lead to error in muscle mass estimation (Walter-Kroker et al., 2011).

Hemodialysis is associated with rapid fluid and electrolyte shift and directly influences the accuracy of BIA muscle mass estimates. Bellafronte et al. (2021) conducted a study on the accuracy of BIA predictive equations for estimation of muscle mass in non-dialysis CKD patients, hemodialysis patients, peritoneal dialysis patients, and kidney transplant recipients, comparing them to DEXA as the reference method. Fat free muscle and appendicular fat free muscle was estimated using four predictive equations (i.e., Sergi, Kyle, Jansen, and MacDonald) developed for different population (Bellafronte et al., 2021). The Sergi equation was developed for healthy elderly Caucasians above the age of 60 years. The Kyles equation was developed for healthy Caucasians from age of 24 to 94 years. The Jansen equation was developed for Caucasians between age 18 and 86 years. The MacDonald was developed for non-dialysis

dependent CKD patients. Sergi's equation for appendicular fat free mass estimation demonstrated the highest diagnostic agreement for diagnosing low muscle mass ($\kappa=.68, p<.001, n=266$), demonstrating substantial agreement with DEXA (Bellafronte et al., 2021). Despite demonstrating substantial overall agreement, it performed moderately in hemodialysis patients ($\kappa=.46, p<.001, n=79$). After multiple linear regression model analysis for factors associated with measurement bias between Sergi's predictive equation for appendicular fat free mass estimation and DEXA derived appendicular fat free muscle mass, total body water emerged as a statistically significant independent predictor of measurement bias $\beta=-0.33, p<.001$ after controlling for other variables such as sex, resistance index, and fat mass. The negative regression coefficient indicates that as total body water increases, overestimation of appendicular fat free mass by Sergi's equation also increased. This shows how BIA-based muscle mass estimations is distorted by fluid shifts in hemodialysis patients but not an actual increase in muscle mass ((Bellafronte et al., 2021).

Ultrasound imaging is currently a widely adopted tool for bedside muscle mass measurement for different patient profiles in clinical settings. This modality offers several advantages including portability, cost-effectiveness, non-radiation exposure, and the possibility of being administered by any other healthcare professional besides a radiologist or sonographer (Sabatino et al., 2021). Also, ultrasound muscle mass parameters may be less influenced by a patient's hydration status giving it a key potential advantage over BIA as a bedside optional assessment tool. However, evidence on this point is conflicting. Sabatino et al. (2017) found no statistically significant differences between quadricep muscle thickness values measured before and after hemodialysis in critically ill patients with acute kidney disease. Contrary to the findings of Sabatino et al. (2017), Cheng et al. (2023) found a statistically significant decrease in both

rectus femoris muscle cross-sectional area (CSA) and muscle thickness measurement values post hemodialysis with more significant decreases in CSA measures compared to muscle thickness measures. These conflicting findings highlight the need for further exploration into the effects of hydration status in ESRD patients receiving hemodialysis on ultrasound muscle mass measurement. With all the advantages of ultrasound as a bedside modality for routine assessment of muscle mass in ESRD patients, it is essential to understand the basic principles on which it works.

Ultrasound Imaging Technology

Basic Principles

Ultrasound imaging relies on the principles of sound wave propagation and medium interaction. Images are produced by the reflection of high frequency sound waves passing through subcutaneous body structures. A typical diagnostic ultrasound operates with a frequency range of 2 MHz to 18 MHz (Carovac et al., 2011). Sound waves are propagated into the body through a transducer coupled with a water-based gel. The gel prevents air from forming between the skin and the transducer head, which can prevent the sound waves from reaching the body. Transducers contain piezoelectric crystals that produce the piezoelectric effect (Poggi & Palavecino, 2024). The piezoelectric effect is the conversion of electrical energy applied to the transducer into sound waves and back to electrical energy once they reach a targeted tissue to form an ultrasound image (Poggi & Palavecino, 2024).

In ultrasound imaging, linear array transducers (see Figure 3) are the most utilized for evaluating musculoskeletal structures (Bianchi & Martinoli, 2007; Jacobson, 2018) due to their high frequency (i.e., 7-18 MHz) and shorter penetration range (Poggi & Palavecino, 2024). A

variety of linear array transducers are available in different sizes and within the frequency range suitable for musculoskeletal evaluation as these structures are superficial and require high frequencies and shorter penetration range to achieve good image quality. The large and medium linear probes are used to image large body parts without contour (Bianchi & Martinoli, 2007). However, in evaluating musculoskeletal structures in parts of the body that permits limited contact with the probe surface such as in the distal extremities, a small footprint linear transducer may be used (see Figure 4; Bianchi & Martinoli, 2007; Jacobson, 2018).

Figure 3.

Linear Transducer



From "Fundamentals of Musculoskeletal Ultrasound" by Jacobson J, A, 2018, Elsevier, 3, p. 2. Copyright 2018 by Elsevier Incorporation.

Figure 4.



Small Footprint Linear Transducer

From “Fundamentals of Musculoskeletal Ultrasound” by Jacobson J, A, 2018, Elsevier, 3, p. 2. Copyright 2018 by Elsevier Incorporation.

The quality of the image produced is influenced by the interaction between the propagating sound waves and the media (e.g., body tissue) (Grogan & Mount, 2023). This interaction is influenced by the acoustic properties (i.e., density and elasticity) of the media (Grogan & Mount, 2023). The acoustic properties of a tissue determine how much sound wave is reflected or transmitted at the tissue boundaries for image creation which is a crucial characteristic known as impedance. High liquid composition tissues such as urinary bladder have low impedance, resulting in no to few waves reflected back to the transducer and appear black in the display (i.e., anechoic); whereas, solid tissues such as bones have high impedance resulting in more sound waves reflected back to the transducer and appears bright (echoic) on grayscale on the display (Grogan & Mount, 2023; Poggi & Palavecino, 2024).

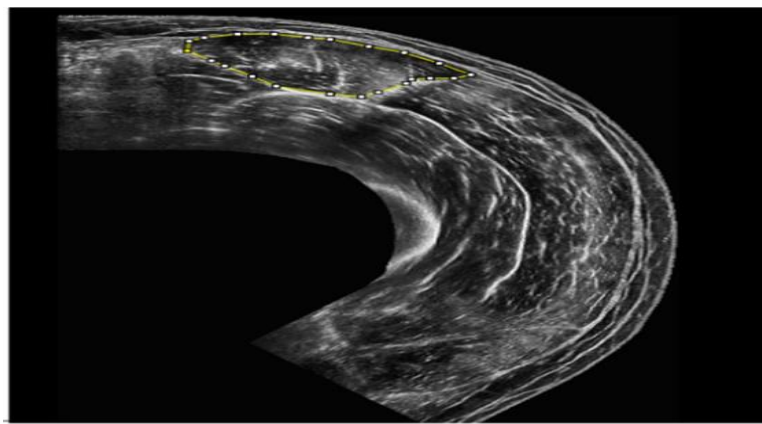
Muscle Parameters

Ultrasound being a versatile modality, can be used to assess muscle quality and quantity (Sarto et al., 2021). Muscle quantity in the context of ultrasound measurement is often used interchangeably with muscle mass as both refers to the physical size of muscle tissue. Muscle quantity may be assessed as muscle thickness or CSA (Sarto et al., 2021). The CSA of a refers to the circumference of the muscle (Van den Broeck et al., 2023). The assessment of muscle CSA (see Figure 5) is complex, involving stitching of single scans of a muscle using contour matching in B-mode or by extended field of view techniques to obtain the dimension of a muscle (Sarto et al., 2021). Muscle thickness (see Figure 6), however, is simply determined through the perpendicular linear distance between skeletal muscle aponeuroses (Sarto et al., 2021). Though

CSA accurately depicts muscle quantity, the relatively simple method of recording muscle thickness makes it the most employed method to quantify muscle (Klein et al., 2021). Moreover, depending on the muscle to be quantified, the transducer can be placed longitudinally or transversely to measure the thickness (Sarto et al., 2021).

Figure 5.

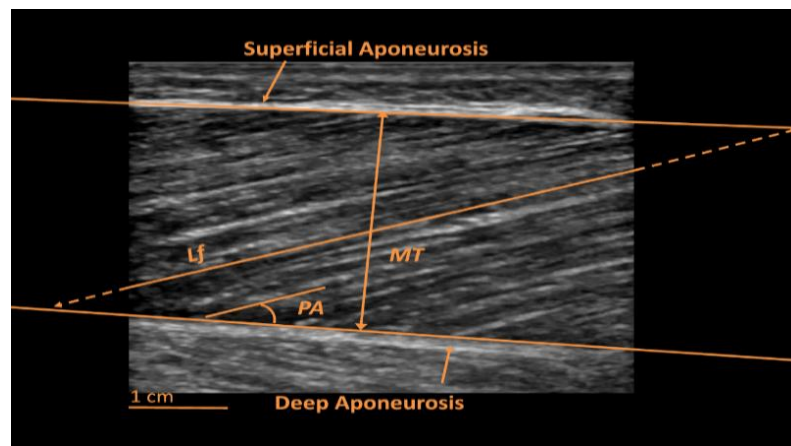
Illustration of Muscle Cross-Sectional Area Measurement



From “Implementing ultrasound imaging for the assessment of muscle and tendon properties in elite sports: practical aspects, methodological considerations and future directions” by Sarto et al. (2021), Sports Medicine, 51, 1151 – 1170.

Figure 6.

Illustration of Muscle Thickness Measurement



From “Implementing ultrasound imaging for the assessment of muscle and tendon properties in elite sports: practical aspects, methodological considerations and future directions” by Sarto et al. (2021), Sports Medicine, 51, 1151 – 1170.

The quality of the muscle is, however, measured as the echo intensity (Sarto et al., 2021; Taniguchi, 2024). Echo intensity is the brightness of muscle tissues as a result of the amount of fat and fibrous tissue infiltration in muscle (Taniguchi, 2024). High echo intensity presenting as high brightness on the images displayed suggest low muscle quality and impairment while low echo intensity suggests high muscle quality (Taniguchi, 2024). High brightness of muscle on grayscale image indicates a large amount of adipose and fibrous tissues deposited in a muscle.

Application of Ultrasound in Muscle Mass Assessment

The rectus femoris muscle has been the most extensively studied muscle in musculoskeletal ultrasonography for evaluating muscle mass across different populations (Naruse et al., 2022; Sabatino et al., 2021). A comprehensive review by Naruse et al. (2022), which included 627 articles examining 107 skeletal muscles found that the rectus femoris muscle was the most commonly investigated muscle across diverse populations and conditions. The rectus femoris muscle was either solely examined or with other muscles in 207 of the total articles included (Naruse et al., 2022). The use of this muscle compared to other muscles is due to its critical role in hip flexion, knee extension, and as a dynamic stabilizer of the knee (Murdock et al., 2019). Thus, making it more susceptible to atrophy and wasting compared to the other quadriceps muscles. Also, the rectus femoris muscle is superficial, and its nearly vertical orientation makes it more distinguishable (Murdock et al., 2019).

Guner et al. (2023) identified ultrasonography of the rectus femoris muscle's thickness and CSA as predictors of sarcopenia in hemodialysis patients independent of age, sex, and body mass index. Guner et al. (2023) used the European Working Group on Sarcopenia in Older

People 2 algorithm (Cruz-Jentoft et al., 2018) which includes a five-item questionnaire for initial screening, handgrip strength for muscle strength, and BIA for whole body skeletal muscle mass to assess sarcopenia. Skeletal muscle index was calculated with a threshold of 7.4 kg/m² for women and 9.2 kg/m² for men denoting low muscle mass. The result indicated a positive significant Spearman's correlation between rectus femoris muscle thickness and skeletal muscle index $\rho=.527, p<.001$ and rectus femoris CSA and skeletal muscle index $\rho=.366, p=.014$.

The application of ultrasound in muscle mass measurement among patients does not only provide healthcare providers the extent of muscle loss to guide interventions but also whether patients are responding to prescribed treatments. Gould et al. (2019) demonstrated that ultrasound derived rectus femoris CSA is sensitive to change in the quadriceps muscle mass over time in response to exercise training. The study recruited CKD stage 3b patients (i.e., patients with glomerular filtration rate between 30-49 mL/min/1.73m²) and CKD stage 5 patients not undergoing dialysis. They found a moderate positive correlation ($\rho=.44, CI [.09, .70], p=.02$) between ultrasound rectus femoris CSA and MRI total quadriceps volume (i.e., rectus femoris, vastus lateralis, vastus intermedius, and vastus medialis muscles) after a 12-week exercise intervention. The findings of this study suggest that ultrasound is a sensitive tool for detecting change in muscle mass over time in response to exercise interventions and may be a valid muscle mass assessment tool in ESRD population.

Validity of Ultrasound for Muscle Assessment

When conducting muscle assessment in clinical populations such as patients undergoing hemodialysis, it is critical to use measurement tools with strong evidence of validity. Ultrasound has recently gained attention as a non-invasive tool for assessing muscle mass in hemodialysis population. Although several studies support the validity of ultrasound, establishing its validity

remains important in the hemodialysis population, as ultrasound measures depend on the consistency of measurement technique, probe placement, and image interpretation.

Traditionally, the validity of a measuring tool or instrument has been described as the degree to which the measuring tool or instrument measures what it is intended to measure (Andersson et al., 2024). The definition of validity, however, has evolved in the last two decades to a more profound and empirical concept under the rationale that it is about the validity of the score interpretation rather than the tool itself. Kane (2006) described validity as an argument-based framework and not just a property of a test or instrument but the degree to which evidence and theory support the interpretation or use of test scores. The argument-based framework for standardized measures by Kane (2006) explained that in order to validate a proposed interpretation or use of test scores, four inferences must be justified including scoring, generalization, extrapolation, and implication. Scoring refers to the accurate and consistent translation of observed scores from the observed performance. Generalization refers to the how observed scores generalize to a universal score (i.e., assessed tasks). Extrapolation refers to how the observed scores reflect real-world target scores or domains. Finally, the implication inference refers to the appropriateness of the interpretation of observed scores.

In establishing evidence of validity based on score interpretations from a tool, researchers evaluate several types of validity, including criterion validity, which is the most evaluated in the context of ultrasound as a tool for assessing muscle mass. Criterion validity is the degree to which a measurement of tool correlates with an established measure (Chiang et al., 2015). Criterion validity is divided into concurrent validity which measures the agreement with an established criterion at the same time and predictive validity which measures the agreement with a criterion measured at some point in the future (Chiang et al., 2015). Since traditional muscle

mass assessment modalities (i.e., CT and MRI) have been established as the gold standard, researchers have focussed on establishing concurrent validity of ultrasound. However, this justifies only the extrapolation inferences within the argument-based framework of Kane (2006) by supporting the interpretation that ultrasound muscle mass measures correlate with measure of established gold standards. The following studies provide strong evidence that support the concurrent validity of ultrasound for assessing muscle mass.

Fetterplace et al. (2020), Peres et al. (2023), and Betz et al. (2021) all concluded that ultrasound measurement of muscle mass correlated well with already established methods. Fetterplace et al. (2020) and Peres et al. (2023) compared ultrasound with CT in evaluating muscle mass in patients in the ICU. Both studies evaluated the quadriceps femoris muscle (combined vastus lateralis and rectus femoris) thickness. The time of ultrasound evaluation differed between both studies. Fetterplace et al. (2020) took ultrasound measurements at two different time points. The initial measures were taken within 72 hours of ICU admission, and the second measures were taken between days five and seven of ICU admission. Peres et al. (2023) performed three measurements with the initial measure taken within 24 hours of ICU admission. This highlights the variation between both studies although ultrasound was compared to CT imaging techniques in both studies.

While Fetterplace et al. (2020) defined the specific landmarks of ultrasound measurement (i.e., the midpoint between the anterior superior iliac spine and the upper pole of the patella and at the point two-thirds between the anterior superior iliac spine and the top of the patella), Peres et al. (2023) did not clearly define the points of ultrasound measurement. Different methodologies were used to access the muscle mass by CT. Peres et al. (2023) measured the quadriceps femoris muscle thickness of the patient with CT by having them positioned in supine

lying with the leg extended and relaxed. The landmarks for measurement were clearly outlined as the lower-third between the anterior superior iliac spine and the proximal edge of the patella. The measurements were performed with a maximum interval of 6 hours after ultrasound measurements, as well. Furthermore, Fetterplace et al. (2020) performed abdominal CT on patients taking a single CT slice with 5 mm thickness at the level of third lumbar vertebrae and identifying, analyzing, and recording the CSA.

Also, Betz et al. (2021) compared ultrasound measurement with MRI measurements. Vastus lateralis muscle thickness and CSA of physically active healthy participants were measured. Betz et al. (2021) performed three different thickness measurements at three different reference points. At 10, 15, and 20 cm distances from the middle of the upper patella pole towards the anterior superior iliac spines was marked and measured. Extended fields of view were used to evaluate the CSA by reconstructing panoramic images of the belly of vastus lateralis. The same reference points were used in MRI imaging measurements. They found out that measurement at the 20 cm reference points showed very good correlation between the two tools (interclass correlation coefficients, $ICC=.895$ $p<.001$) and also a statistically significant strong positive correlation ($R^2=.807$, $p<.001$).

Despite the methodological variation presented in these studies, they provided robust evidence that ultrasound muscle mass parameters (i.e., CSA and muscle thickness) strongly correlate with gold standard modalities across healthy and diseased populations. The consistency of the results demonstrated across the different methodological protocols suggests that ultrasound is a flexible and adaptable assessment tool. While the validity of ultrasound has been established, it is important to establish its reliability for its clinical utility.

Reliability

Types of Reliability

Reliability is defined as the stability and consistency of measures across time, item, or raters (Andersson et al., 2024). The concept of reliability is a critical criterion to justify the quality of research and measurement tools (Nha, 2021). Reliability ensures that under similar circumstances, findings of a research instrument/measurement tool can be replicated. In clinical settings, reliability of a tool does not only instill confidence in clinicians but also enables sound decision making. The measure of reliability is an estimate, and perfect reliability is usually unattainable due to a variety of errors (e.g.,....). .

Rater reliability (i.e., intra-rater and inter-rater) and test-retest reliability are the common types of reliability used in clinical settings (Scheel et al., 2018). Rater reliability is subdivided into two types including intra-rater reliability and inter-rater reliability. Intra-rater reliability assesses the consistency of measurements by the same rater over a period of time across multiple measures. Similar to test-retest reliability which assesses consistency of measurements over time but focuses on the stability of the assessment tool, intra-rater reliability assesses the consistency of the rater. Inter-rater reliability assesses the consistency of measurements by two or more raters over a single measure. Therefore, intra-rater and inter-rater reliability are important for replicability of clinical measurements (Gwet, 2008).

Measurement Error in Clinical Measurement

No measurement is entirely free from error, however, in clinical research and clinical practice, the ability of a tool to produce accurate and precise measures is of a high importance. Measurement error is how much an observed score deviates from the true score. Measurement

errors can be generally classified as systematic or random (Stoker, 2008). Systematic errors produce consistent deviation of observed scores from true scores resulting in poor accuracy. Random error on the other hand relates to unpredictable variation that occurs among repeated measurements, leading to poor precision. The sources of error may be due to the natural variation in patients, variations in the measurement process, or both (Bland & Altman, 1996).

The need for reliable measurement is of critical importance in the ESRD population as these patients present unique challenges including fluid shifts and body composition alterations. These coupled with comorbidities pose significant risks of errors in measurements. Also, there is no standardized protocol for assessing muscle mass using ultrasound currently (Perkisas et al., 2021). Methodological approaches, landmark identification, scan sites, patient positioning, and probe pressure all differ across studies (Gould et al., 2019). While some studies perform measurements on patients in a supine lying position, others prefer seated positioning. Identification of landmarks and the site of scan can also differ. An example is in evaluating the quadriceps femoris muscle, the measurement point has been reported to be in either the mid-point or two-thirds point on the muscle. These challenges introduce variability that threatens both the validity and reliability of observed measures.

Reliability of Ultrasound Muscle Mass Assessment

Many studies have examined the intra and inter-rater reliability of ultrasound assessment of muscle mass across different populations and conditions and have found good to excellent reliability. Hashida et al. (2022) concluded that ultrasound is a reliable tool for evaluating and detecting changes in muscle mass. The study investigated three muscles including the biceps brachii, quadriceps femoris, and suprahyoid muscles of patients who received their first allogeneic hematopoietic stem cell transplantation by three healthcare professionals (physician,

physiotherapist, and speech therapist). Biceps brachii and quadriceps femoris muscle thickness were measured while the CSA of the suprahyoid muscle was measured, and all measurements taken before transplantation, and on days 30, 90, and 180 after transplantation. Results indicated that there was strong evidence of inter-rater reliability between the three healthcare professionals with ICC ranging from .90 to .98, $n=62$, $k=3$ across all four measurement times. Another study by Ogawa et al. (2023) investigated the intra-rater and inter-rater reliability of muscle assessment using ultrasound. The thickness of the quadriceps femoris muscle was evaluated by three assessors (two physicians and a physiotherapist) in healthy males. The result of this investigation found strong evidence of intra-rater reliability of ultrasound imaging with an ICC ranging from .98-.99. Also, strong evidence of inter-rater reliability was found with ICC=.90-.97.

Recently, Smerilli et al. (2023) examined the inter-rater reliability of a newly developed multimodal ultrasound technique for muscle assessment in rheumatic and musculoskeletal disorders and concluded that ultrasound is a reliable tool. The multimodal ultrasound techniques combined and integrated data from ultrasound modalities including B-mode, elastography, and contrast-enhanced ultrasound to provide a more comprehensive and simultaneous assessment of different aspects of muscle, such as the quantity (thickness), quality (echogenicity), and stiffness. Two rheumatologists with 11- and 5-years experience in musculoskeletal ultrasound performed the ultrasound assessment of the bilateral quadriceps femoris muscles in 45 rheumatic and musculoskeletal disorder patients blinded to each others assessment. They found strong evidence of inter-rater reliability, ICC=.97, 95% CI [.95 .98], $n=45$, $k=2$ for the bilateral quadriceps muscle thickness, excellent reliability ICC=.92, 95% CI [.88, .94], $n=45$, $k=2$ for echogenicity, and good reliability, ICC=.76, 95% CI [.71, .80], $n=45$, $k=2$ for stiffness. While ultrasound presents as a reliable tool for muscle mass assessment, its reliability in the ESRD hemodialysis

population has not been fully established, necessitating further investigation in this diverse population.

Chapter 3: Methodology

Design

A convergent parallel mixed-methods design was used for this study (Creswell & Plano Clark, 2018). The quantitative and the qualitative data were collected independently. The quantitative aspect focused on the measurement of muscle thickness using ultrasound in hemodialysis patients and the qualitative phase explored the feasibility of ultrasound application for routine muscle mass assessment using interviews to help explain and complement the initial quantitative phase. Findings from the quantitative and qualitative aspects were analyzed separately and integrated in the discussion chapter by combining the interpretation of the two sets of results. The details of both aspects are presented as follows:

Quantitative Phase

Participants

Recruitment

Ethical approval to conduct this study was obtained from the Lakehead University Research Ethics Board and the Thunder Bay Regional Health Sciences Centre Research Ethics Board. Following approval, participants receiving hemodialysis at the renal unit of the Thunder Bay Regional Health Sciences Centre were recruited through purposive sampling. Participants were included in the study if they were:

1. 18 years and above;
2. Undergoing hemodialysis scheduled three times weekly with no more than 4.5 hours per session; and

3. Willing to provide informed consent to undergo the study protocol including ultrasound measurement during dialysis.

Participants were excluded from the study if they:

1. Have a known disease of the musculature (e.g., muscular sclerosis, muscular dystrophy);
2. Have a bilateral below the knee amputation;
3. Are undergoing concurrent peritoneal dialysis; and
4. Are a new hemodialysis patient. For this study, a new hemodialysis patient is defined as a patient who is on hemodialysis for less than three months.

Based on a previous study (Sabatino et al., 2017) and determined by a priori power analysis for reliability studies, 24 participants were needed to achieve an expected ICC of .80, a 95% confidence level, and an expected precision of $\pm .10$ (Bonett, 2002). After informed consents were provided, participants were assigned a date for ultrasound assessment in alignment with their regular scheduled hemodialysis therapy date and time. However, 50 participants were recruited for this study.

Instrumentation

SonoSite® S II Ultrasound Machine

Muscle thickness measured in centimeters (cm) and was the parameter included for this aspect of the study. Muscle thickness was selected as the primary parameter for quantifying muscle due its feasibility during hemodialysis session as it is relatively easy to assess and less time intensive (Klein et al., 2021). This parameter was measured using the SonoSite® S II ultrasound machine. Ultrasound is a commonly used non-invasive tool in medical imaging to visualize tissues and internal organs allowing multi-dimensional imaging (i.e., two-dimensional

and three-dimensional). A typical ultrasound machine is comprised of a generator, transducer (probe), control user interface, and display unit. The ultrasound is commonly used in muscle mass measurement because of its portability and ease of use. Muscle images are produced in grayscale using the B-mode system. The distance between the aponeuroses of the muscle boundaries is measured to obtain the thickness of the muscle (cm). The application of ultrasound in measuring muscle mass has been validated against gold standard as described previously (Betz et al., 2021; Fetterplace et al., 2020, Peres et al., 2023). For this study, a SonoSite® S II ultrasound unit was used (see Figure 7).

Figure 7.

SonoSite® S II.



Procedures

Demographic and Anthropometric Variables

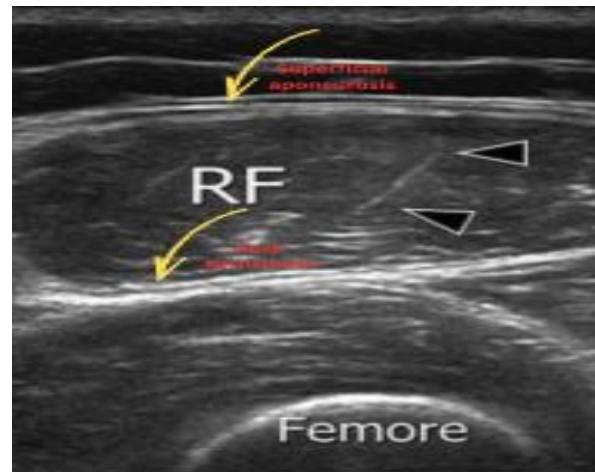
Baseline demographic data including age (years), sex (male/female) and amputation status (left / right / bilateral / none) were collected via the hospital's record. Anthropometric measurements including prescribed dialysis body mass (kg), and post hemodialysis body mass (kg) corresponding to the date of ultrasound measurement were collected and recorded using a demographic information collection sheet (see Appendix 1). Body mass index was calculated and recorded by dividing the prescribed dialysis body mass in kilogram (kg) by height in squared meters (m²).

Ultrasound Measurement

The ultrasound measurements were performed by a two dietitians (i.e., $k=2$) under the supervision of a radiologist during the participant's regular dialysis session after a day of formal training. B-mode ultrasound and a 50 mm width linear array probe (5-14 MHz, S II; SonoSite®, Bothell, Washington, USA) was used on standard default settings (depth, gain, and focus) to assess the thicknesses of the rectus femoris, biceps brachii, and triceps brachii. Muscle images were captured, and a built-in caliper tool was used to measure the distance between the deep and superficial aponeuroses of each muscle of interest (see Figure 8). All measurements were taken with conventional amount of ultrasound gel between the transducer and the skin. Minimum pressure was applied and maintained to the transducer without indentation throughout the scanning. All measurements were taken 3 months from the initial measurement dates. No formal rater re-training was conducted between baseline and 3 months follow up assessment.

Figure 8.

Illustration of the Superficial and Deep Aponeuroses of the Rectus Femoris Muscle



From "Sonography of the quadriceps muscle: Examination technique, normal anatomy, and traumatic lesions" by Pasta et al., (2010), Journal of Ultrasound, 13(2), 76-84

Rectus femoris muscle thickness measurement was performed first while the participant was seated in a high Fowler position in a dialysis chair connected to the dialysis machine. The backrest of the dialysis chair was adjusted between 60-90° based on the participant's need and the leg rest was angled at 45°. After successfully positioning the patient in the dialysis chair, the landmarks bordering the rectus femoris muscle (i.e., the anterior superior iliac spine and the superior patellar border) on the dominant leg were palpated and identified. However, these landmarks were identified on the non-dominant leg of any participant with an above-knee amputation of the dominant leg. The transducer head was placed steadily at the midpoint between the identified landmarks perpendicular to the long axis of the belly of the rectus femoris muscle to capture the muscle image.

Next, the thickness of the biceps brachii and triceps brachii muscles were measured. All measurements were taken on the non-fistula arm (opposite fistula) of the participants. To measure the thickness of the bicep brachii muscle, a Flexion Test was performed to palpate and

identify the belly of the bicep brachii muscle while patient is still seated in high Fowler position in the dialysis chair. The participant was instructed to supinate the elbow of his/her non-fistula arm and then flex the elbow to 90° against resistance. The belly of the biceps brachii muscle was palpated and the transducer steadily placed perpendicular to the long axis of the muscle belly to capture the muscle image. The participant was instructed to fully extend the non-fistula arm while he/she is still seated in a high Fowler position in the dialysis chair. The belly of the triceps brachii muscle was palpated and identified. The transducer head was placed perpendicular to the long axis of the triceps brachii muscle to capture the image of the muscle. Two measures were captured at the triceps brachii muscle region labelled triceps brachii muscle A (the perpendicular distance between the superficial aponeurosis and the deep fascial layer) and triceps brachii muscle B (the perpendicular distance between the superficial aponeurosis and the humeral cortex). A total of 4 measurements were taken by the first dietitian comprising of a measurement for each muscle (i.e., rectus femoris, biceps brachii, and triceps brachii A and B) on each participant. All measurement protocols were repeated immediately on the same participant by the second dietitian blinded to the results of the first dietitian except the initial positioning of the patient in the dialysis chair. After 3 months measurements were repeated by the same dietitians.

Data Processing

The thickness of rectus femoris, biceps brachii, and triceps brachii muscles captured by each assessor was recorded into Microsoft® Excel® for each respective participant. The dependent variables were the ultrasound parameters captured and recorded including the thickness of the rectus femoris, biceps brachii, and triceps brachii A and B. The independent variables were the assessors (i.e., dietitians).

Statistical Analysis

Statistical analysis was conducted using IBM© SPSS 31. Each of the previously stated research questions was used to guide the statistical analysis. Descriptive statistics were conducted for the variables of interest and presented in means and standard deviations for continuous variables, and percentages for categorical variables

To answer question one, a two-way random effect ICC for absolute agreement was used to analyze inter-rater reliability. An ICC <.50 was interpreted as a poor, .50–.75 as a moderate, .75–.90 as a good, and >.90 as an excellent correlation based on the proposed threshold by Koo and Li (2016). Measurement errors were also calculated using standard error of measurement (SEM) and minimal detectable change at 95% confidence level (MDC₉₅). SEM at each timepoint was calculated using the formula $SEM = SD \times \sqrt{(1 - ICC)}$, where SD is the pooled standard deviation of measurements across raters. MDC₉₅, which is the smallest change of a measurement that is not attributable to measurement error and calculated as $SEM \times 1.96 \times \sqrt{2}$.

Bland-Altman analysis was conducted and plot was to visualize the systematic bias between the two assessors and measures in timepoint. Statistical significance level was set at $\alpha=.05$. For each comparison, the assumption of normality of between rater differences was assessed using the Shapiro-Wilk Test. Where rater differences were normally distributed, parametric Bland-Altman analyses were conducted. Where rater differences violated the assumption of normality, log-transformation was performed and Shapiro-Wilk Tests were once again conducted to assess the assumption of normality on the log-differences. Where log-differences satisfied the assumption of normality, parametric Bland-Altman analyses were conducted on the log scale and the bias and then log back-transformed to ratios for interpretation. Where log-differences

violated the assumption of normality, non-parametric Bland-Altman analysis was performed. LoA at 2.5th and 97.5th percentiles if the differences were used and the central tendency reported with the median. Linear regression was conducted by regressing the mean of scores on their difference to assess proportional bias for parametric Bland-Altman analyses. For non-parametric Bland-Altman analysis, proportional bias was assessed using the Spearman's Correlation analysis between the absolute difference and the mean.

To answer question two, a Shapiro-Wilk Test was conducted to determine if the data is normally distributed. Pearson's Correlation Coefficient (r) was used to analyze the correlation between the independent variables (biceps brachii and triceps brachii muscle thickness) and the dependent variable (rectus femoris muscle thickness) for normally distributed data. Spearman's Correlation Coefficient (ρ) was used when the assumption of normality was violated. Correlation values were interpreted as follows: $r < .30$ weak correlation; $r > .30 < .70$ moderate correlation; and $r > .70$ strong correlation. A 95% confidence interval was reported.

Qualitative Aspect

This section describes the methods that was used in the qualitative aspect of the study exploring the feasibility of implementing ultrasound as routine muscle mass assessment tool in clinical practice. The qualitative aspect addressed the third objective of this study which aimed to explore the feasibility of integrating ultrasound muscle thickness assessment into routine care for ESRD patients undergoing hemodialysis. Unlike quantitative studies where terms such as validity and reliability are used to assess rigour, trustworthiness is used in qualitative study to assess rigour (Forero et al., 2018; Lincoln & Guba, 1985). Trustworthiness is the quality criteria

in qualitative research that encompasses credibility, dependability, transferability, and confirmability of findings (Forero et al., 2018; Lincoln & Guba, 1985).

Credibility is the ability to establish confidence not only against the perspective of the participants but also the perspective of the reader that the interpretation of the findings is accurate (Lincoln & Guba, 1985). To achieve credibility in this study, investigator triangulation was done. Interview transcripts and generated themes were independently read and reviewed by the researcher and a clinician. Also, verbatim quotations from participants were used throughout the study findings to allow the reader to judge the correspondence between the data collected and the themes reported. Dependability pertains to the traceability and consistency of the research process (Forero et al., 2018). Dependability was achieved in this study by preparing rich and detailed documentation of the study protocols, approaches to data collection and analysis. Furthermore, comprehensive record of the data collection process was developed and also, records of codes and themes development. This process established an audit trail. Finally, analysis of data was done in line with established standard six-phase thematic analysis approach by Braun and Clarke (2006). Transferability is the extent to which the finding of a study can be generalized to other settings (Lincoln & Guba, 1985). In order to ensure transferability, detailed outline of inclusion and exclusion criteria were be laid out. Also, participant characteristics including role of participants (i.e., physician, nurse, dietitian, and patient), Additionally, a step-by-step description of the data collection process including how participants were recruited (i.e., the sampling strategy), the number of participants recruited, the location of the interview, the nature of the interview question, how rapport was established during the interviewing process, and any adaptations made during the interviewing process. This assists readers to determine if the findings of this study might be applicable to similar populations and setting outside of this

study context. Finally, confirmability pertains to the impartiality and authenticity of findings, ensuring findings are clearly based on participants narrative and not researcher's bias (Lincoln & Guba, 1985). Confirmability was achieved by regular debriefing session with research team members and committee members on the progress and challenges of the study and also seek feedback on results interpretation to reduce researcher biases. Also, reflexive journaling was done by keeping record of all evolving thought, ideas, and biases during the research process to enhance transparency.

Participants

Recruitment

A purposive sampling method was used to recruit participants for the qualitative aspect of this study. Participants included:

1. Nine healthcare professionals (i.e., three nurses, two dietitians, and a nephrologist) and three hemodialysis patients.
2. Healthcare professionals and patients who spoke English and were willing to give informed consent.
3. Patients who were alert and able to converse for over 30 minutes.

Participants were excluded from this study if they:

1. Were student healthcare professionals.
2. Were nephrologist, nurses, and dietitians who do not directly work in the renal department of the Thunder Bay Regional Health Services Centre.

Instrumentation

Semi-Structured Interview

A semi-structured interview is a data collection method used to explore the thought, feelings, and beliefs of a participant on a particular topic of study. This method is typically a dialogue between a researcher and participant guided by interview questions. Interview questions are structured to allow the researcher and participant to shape the conversation through supplemented follow-up questions and probes while maintaining the key themes of the topic under study (DeJonckheere & Vaughn, 2019). A major advantage of an interview is the ability to build rapport with participants, which makes it possible to obtain information that would probably not be revealed by other data collection methods (Hill, 2016). Two separate interview scripts have been prepared to guide the interviewing process for this aspect of the study. One script was used for the healthcare professionals and the other for the patients. Interview scripts for healthcare professionals explored domains including the applicability of ultrasound in the dialysis unit, understanding of potential clinical values, and integration of ultrasound into normal workflow (see Appendix 4). For patients, the main domains explored include their experience with ultrasound as a measurement tool and their preferred assessor among the healthcare team (see Appendix 5). The interview scripts were pre-tested through expert review to improve the credibility of the semi-structured interviews (Bhalla et al., 2023). Expert review requires that individual experts with experience in survey methodology and practical field work give their opinions of the questions in an interview script in relation to content, wording, the number of questions, sensitivity of the question, and relevance of the questions to the topic under study (Bhalla et al., 2023). The expert review for the developed interview scripts was undertaken by four experts (i.e., two academic experts and two healthcare providers). Finally, interview scripts

were validated through face validation after incorporating suggestions from expert reviewers. Face validity is the extent to which a measurement tool (i.e., the interview scripts) appears to measure what it is intended to measure (Price et al., 2015). The face validation of the interview scripts was done by engaging healthcare providers who are familiar with the dialysis environment of the Thunder Bay Regional Sciences Centre to provide feedback on the appropriateness of each question on the scripts.

Procedures

Interview

After obtaining ethics approval from the Lakehead University Research Ethics Board and the Thunder Bay Regional Health Sciences Centre Research Ethics Board, 9 participants were recruited for this aspect of the study. The participants included two nurses, three dietitians, a nephrologist, and three patients. The healthcare professionals (i.e., nurses, dietitians, and physicians) were approached directly during rounds at the renal unit of Thunder Bay Regional Health Sciences Centre and presented with the option of participating in the study. Also, posters were circulated at the renal unit to encourage patient and healthcare provider participation (see Appendix 2). Patients were recruited through poster circulation at the renal unit. Recruitment posters were posted in the renal unit, and patients were also handed posters directly during their hemodialysis sessions (see Appendix 3). Interested participants were given information letters explaining the purpose, the potential risk and benefits of the study, and the confidentiality of their participation if they chose to participate. After informed consent was obtained, semi-structured interviews were scheduled based on the days and times requested by the participants. Interviews were conducted behind a closed door in the office of the dietitian at the renal department of Thunder Bay Regional Health Sciences Centre to safeguard confidentiality. The

interviews lasted an average 25 minutes. Recruitment of participants continued until information richness across healthcare professionals and patients was sufficient, balancing the feasibility and timelines of this thesis project . (Malterud et al., 2015).

Informed written consents from the prospective participants were obtained on the day of the interview. Permission was sought from each prospective participant to audio record the interviews for the purposes of data analysis. At the beginning of each interview, a preamble was read to the participant describing the background and the relevance of the study (See Appendix 6). Each interview started with an opening question and ended with a closing question. For participants who are healthcare professionals, their opening question was, “*What is your understanding of the relationship between ultrasound and nutritional status?*” and the interview ended with the question, “*What helps ensure the technique or protocol is applied the same way across team members?*” Most questions during the interview were probed further by asking follow-up questions to elicit more detailed information from the participant. For example, “*What are your thoughts about implementing muscle ultrasound routinely or as a standard of care?*” was probed further by asking them, “*What barriers, if any, are there to implementing muscle ultrasound into practice?*”, “*What do you consider the benefits to be?*”, and “*Could these benefits outweigh the potential impact it may have on workload?*”

The interview with patients followed the same pattern, starting with an opening question and finishing with a closing question. The opening question for patients was, “*Can you describe your experience with ultrasound?*” and the closing question was, “*Would you want healthcare professionals to continue using this ultrasound method on other patients or in other hospitals?*” Also, questions for patients were probed further. For example, the question “*Would you be willing to have routine measurements of your muscle if the results could help to improve delivery*

of care provided by your renal healthcare team?” were followed by asking, *“Have you had this ultrasound assessment done on you more than once by the same healthcare professional?”*, *“Did the test feel the same?”*, *“Did different healthcare professionals perform the ultrasound test on you?”*, and *“Did it feel the same regardless of who performed it?”* These follow-up questions encouraged participants to elaborate on their initial responses. Although follow-up questions are prepared to be asked during the interviewing process, some spontaneous questions emerged during the interview. These spontaneous questions were recorded into a notebook for reference. After each interview, the participant was thanked and reassured that their participation will not affect their role as employees and the care they receive as patients.

Data Processing

Each audio-recorded interview was uploaded into REV AI© for transcription. REV AI© is an online tool that uses artificial intelligence models to transcribe audios and videos. This tool is compliant with the Health Insurance Portability and Accountability Act of the USA. This implies that REV AI©’s application programming interface has been safeguarded to protect the security and confidentiality of any protected health information data that may emerge in any uploaded audios and videos. However, to further protect the privacy of our participants, no identifying information was recorded during the interview. Each transcript generated was saved as a Microsoft® Word® document and identified with made up names. The researcher read each transcript multiple times while listening to the recorded audios to correct all errors that may occur during transcription. The transcripts and the audio recordings were also be reviewed independently by a trained research assistant. All corrected transcripts were compared to ensure rigour.

Qualitative Analysis

Altas.ti© was used to analyze the qualitative data guided by research question three, four, and five. This analysis followed the thematic analysis approach developed by Braun and Clarke (Braun & Clarke, 2006). Thematic analysis is a method for identifying, analyzing, and reporting patterns found within qualitative data (Braun & Clarke, 2006). The Braun and Clarke approach for thematic analysis has six phases which includes familiarization with the data, generating initial codes, generating themes, reviewing potential themes, defining and naming themes, and producing the report. Analysis started by uploading all transcripts to Altas.ti© workspace. Transcripts were read multiple times by the reviewers to immerse themselves in the collected data and become familiar with the data. This forms the first phase of data familiarization. Since there were no pre-generated codes prior to the analysis, relevant information was highlighted and labelled by systematically reading through each transcript to summarize the data into codes keeping in mind the relevant research questions. Generated codes were reviewed and codes with similar meanings were grouped to generate meaningful patterns related to the research questions. This process completed the phase of themes generation. Initially generated themes were reviewed by reading over the data, and summarized into codes, to ensure accurate representation of the themes. At this phase of reviewing the themes, some the initially generated themes were discarded, split, or merged. Next, each theme was named to be reflective of the research questions. Detailed descriptions of these themes were generated to enhance the clarity of each theme. Finally, a coherent report was written to interpret the data, providing a detailed account of the themes and extracts from the data.

Quantitative and Qualitative Aspects Integration

After the analysis of the quantitative and the qualitative aspects of this study, the findings of both aspects were merged together at the discussion section to develop a comprehensive understanding of the applicability of ultrasound. The qualitative aspect was set out to compliment and contextualize the quantitative reliability findings by explaining the feasibility of implementing ultrasound as a routine muscle mass assessment tool in the renal unit of Thunder Bay Regional Health Sciences Centre.

Chapter 4: Results

The results of this study are divided into two separate parts, the quantitative part and the qualitative part. The quantitative part of the analysis provides insight into the reliability of ultrasound assessment of rectus femoris, biceps brachii, and triceps brachii muscle thickness in ESRD patients undergoing hemodialysis and if the biceps brachii and triceps brachii could be a potential alternative muscle thickness assessment site in this population. Specifically, it sought to find the inter-rater reliability of ultrasound-derived muscle thickness of the biceps brachii, triceps brachii, and rectus femoris muscles across various healthcare providers in hemodialysis setting and the correlation between rectus femoris muscle thickness and the thickness of biceps brachii and triceps brachii in hemodialysis patients. The qualitative part of the analysis provides insight into the perspectives of patients and clinicians on the integration of ultrasound muscle thickness assessment to routine care of hemodialysis patients. Specifically, it explored the experiences/perceptions of healthcare providers with the use of ultrasound as a muscle assessment tool in hemodialysis care; how can ultrasound muscle assessment be incorporated into the workflow of multidisciplinary team; and how do hemodialysis patients perceive ultrasound application for routine muscle assessment in their care?

Quantitative Aspect

Demographic Information

A total of 50 participants (30 males and 20 females) undergoing standard (three times per week and four hours per session) hemodialysis treatment completed the baseline assessment (see Table 1). In the follow-up assessment afterwards, 45 completed (27 males and 18 females) the assessment (see Table 2). Five participants were lost between timepoints due to hospitalization,

death, and withdrawal from the study. Sample sizes varied across individual analyses due to missing ultrasound measurements as a result of patient discomfort, probe position constraints due to patient positioning in the dialysis chair, and lower limb amputation; therefore, sample size may have differed by muscle, rater, and timepoint.

Table 1

Participant Demographic Information at Baseline

Characteristic	<i>n</i>	%	<i>M</i>	<i>SD</i>
Male	30	60		
Female	20	40		
Age (years; whole group)			59.80	17.63
Amputation status				
None	41	82		
Right	4	8		
Left	3	6		
Bilateral	2	4		
Pre-dialysis Body Mass (kg; whole group)			82.68	17.62
Post dialysis Body Mass (kg; whole group)			83.06	18.20
Pre-dialysis Body Mass Index (kg/m ² ; whole group)			29.08	5.33
Post dialysis Body Mass Index (kg/m ² ; whole group)			29.19	5.50

Table 2*Participant Demographic Information at 3 months*

Characteristic	<i>n</i>	%	<i>M</i>	<i>SD</i>
Male	27	60		
Female	18	40		
Age (year; whole group)			59.93	17.59
Amputation status				
None	38	84.4		
Right	2	4.4		
Left	3	6.7		
Bilateral	2	4.4		
Pre-dialysis Body Mass (kg; whole group)			80.70	18.62
Post dialysis Body Mass (kg; whole group)			81.24	18.37
Pre-dialysis Body Mass Index (kg/m ² ; whole group)			29.00	5.63
Post dialysis Body Mass Index (kg/m ² ; whole group)			29.14	5.64

Research Question 1: *What is the inter-rater reliability of ultrasound-derived muscle thickness of the biceps brachii, triceps brachii, and rectus femoris muscles across various healthcare providers in hemodialysis setting?*

Intraclass Correlation Coefficient

An ICC was conducted to assess the inter-rater reliability of ultrasound-derived thickness of the biceps brachii muscle, triceps brachii muscle A (i.e., the perpendicular distance between the superficial aponeurosis and the deep fascial layer), triceps brachii muscle B (i.e., the perpendicular distance between the superficial aponeurosis and the humeral cortex), and rectus femoris muscle between 2 raters at baseline and at 3 months follow up. For each muscle thickness measurement, ICC two-way random-effect model for absolute agreement with single

measure was conducted. Descriptive statistics for ultrasound derived muscle thickness at baseline and 3 months separated by raters are presented in Table 3 and Table 4, respectively.

At baseline, rectus femoris muscle thickness yielded an ICC (2,1)=.91, 95% CI [.83, .96], $n=33$, $k=2$, and biceps brachii muscle thickness, ICC (2,1)=.87, 95% CI [.76, .93], $n=38$, $k=2$. Triceps brachii muscle A and triceps brachii muscle B thickness produced ICC (2,1)=.53, 95% CI [.27, .73], $n=38$, $k=2$; and ICC (2,1)=.66, 95% CI [.44, .81], $n=38$, $k=2$, respectively.

At 3 months, rectus femoris muscle thickness produced an ICC (2,1)=.75, 95% CI [.27, .91], $n=21$, $k=2$. The biceps brachii muscle thickness yielded an ICC (2,1)=.84, 95% CI [.68, .92], $n=30$, $k=2$. Both triceps brachii muscle A thickness and triceps brachii muscle B thickness yielded an ICC (2,1)=.32, 95% CI [-.02, .60], $n=30$, $k=2$; and ICC =.41, 95% CI [.05, .67], $n=30$, $k=2$ respectively.

Table 3

Descriptive Statistics for Ultrasound-derived Muscle Thickness Measurements at Baseline by Both Raters

Muscle	N	Rater 1	Rater 2
		<i>M (SD)</i>	<i>M (SD)</i>
Rectus femoris	33	2.73 (0.88)	2.64 (0.86)
Biceps brachii	38	2.89 (0.75)	2.88 (0.68)
Triceps brachii A	38	1.69 (0.60)	1.51 (0.44)
Triceps brachii B	38	2.89 (0.66)	2.76 (0.52)

Table 4

Descriptive Statistics for Ultrasound-derived Muscle Thickness Measurements at 3 Months by Both Raters

Muscle	N	Rater 1	Rater 2
		<i>M (SD)</i>	<i>M (SD)</i>
Rectus femoris	21	2.49 (0.74)	2.15 (0.70)
Biceps brachii	30	2.72 (0.69)	2.61 (0.70)
Triceps Thickness A	30	1.65 (0.50)	1.36 (0.30)
Triceps brachii B	30	2.92 (0.53)	2.90 (0.49)

Standard Error of Measurement

At baseline, rectus femoris and the biceps brachii muscle thickness yielded a SEM of 0.26 cm and 0.26 cm, respectively. These measures represent a percentage error of 9.7% for the rectus femoris and 9.0% for biceps brachii muscle thickness. The SEM of triceps brachii muscle A thickness was 0.35 cm representing a percentage error of 22.1%. Triceps brachii muscle B thickness yielded an SEM of 0.34 cm representing a percentage error of 12.1%. At 3 months, the

SEM for biceps brachii muscle thickness was 0.28 cm, 0.33 cm for triceps brachii muscle A thickness, and 0.39 cm for triceps brachii muscle B thickness. The measures for the biceps brachii muscle thickness represent a percentage error of 10.5%, 22.0% for triceps brachii muscle A thickness, and 13.5% for triceps brachii muscle B thickness. The SEM for the rectus femoris muscle at 3 months was 0.36 cm representing a percentage error of 15.5%.

Minimum Detectable Change

Minimum detectable change (MDC) values were also calculated. At baseline, MDC_{95} values ranged from 0.72 cm to 0.98 cm across all muscles. The MDC values for the rectus femoris muscle thickness was $MDC_{95}=0.72$ cm, biceps brachii muscle thickness, $MDC_{95}=0.71$ cm, triceps brachii muscle A thickness, $MDC_{95}=0.98$ cm, and triceps brachii muscle B thickness, $MDC_{95}=0.95$ cm. At 3 months, the MDC_{95} values ranged from 0.77 cm to 1.09 cm across all muscles. The MDC values for the rectus femoris muscle thickness was $MDC_{95}=1.00$ cm, biceps brachii muscle thickness, $MDC_{95}=0.77$ cm, triceps brachii muscle A thickness, $MDC_{95}=0.91$ cm, and triceps brachii muscle B thickness, $MDC_{95}=1.09$ cm.

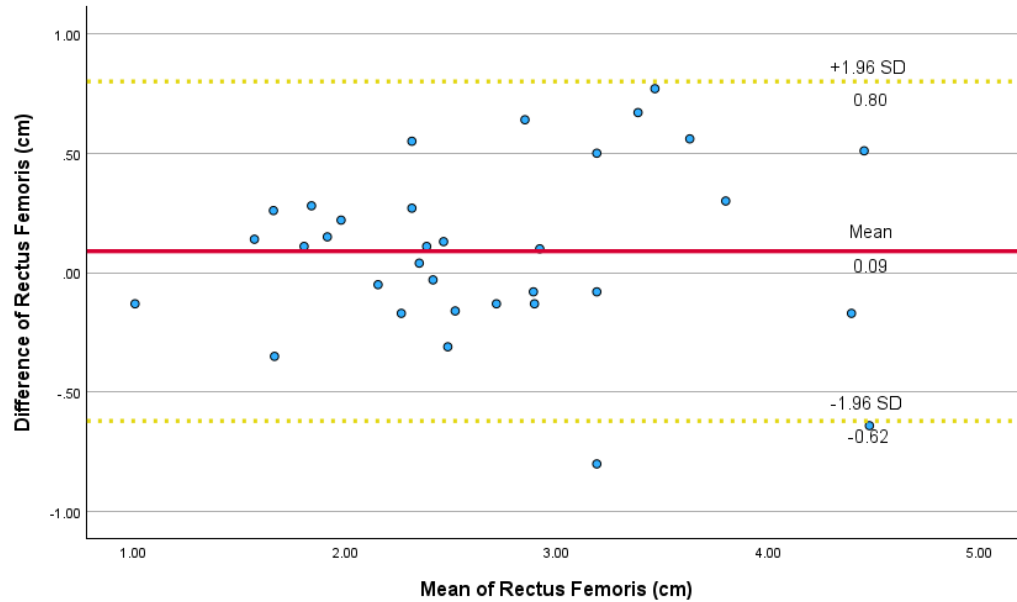
Bland-Altman Analyses

Baseline Measurements: A Shapiro-Wilk Test was conducted to assess the assumption of normality on rater difference for rectus femoris muscle thickness. Results showed that the normality assumption was satisfied, $W(33)=.97$, $p=.55$ and, therefore, parametric Bland-Altman analysis was conducted. Rectus femoris muscle thickness revealed a mean bias of 0.09 cm (see Figure 9). The 95% limits of agreement (LoA) ranged from -0.62 cm to 0.80 cm. Linear regression analyses was conducted to assess the proportional bias of the difference on the mean.

The result indicated that there was no statistically significant proportional bias, $B=0.03$, 95% CI $[-0.13, 0.18]$, $p=.37$.

Figure 9

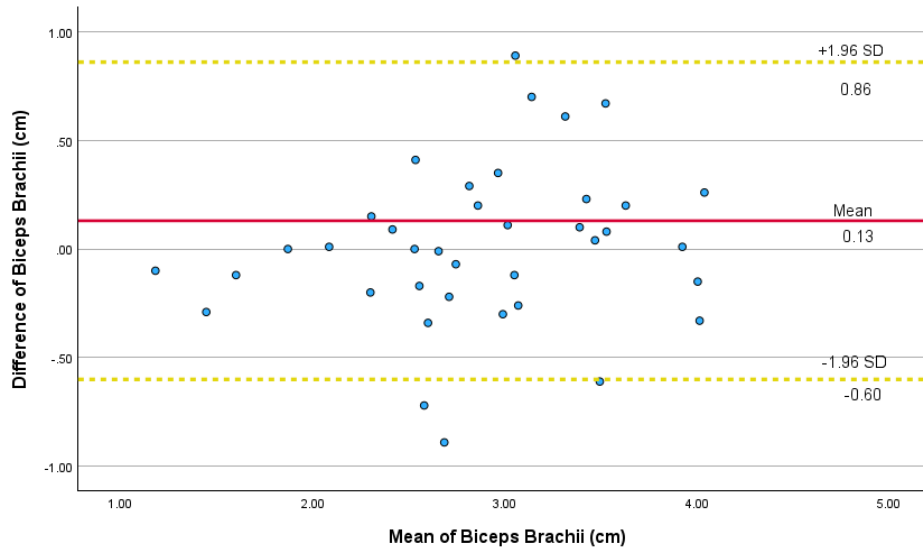
Bland-Altman Plot for Agreement Between Raters for Rectus Femoris Muscle Thickness at Baseline



For biceps brachii muscle thickness, a Shapiro-Wilk Test indicated that normality assumption was satisfied, $W(38)=.98$, $p=.61$. Parametric Bland-Altman analysis was conducted for biceps brachii muscle thickness and showed a mean bias of 0.13 cm which did not statistically significantly differ from 0, $t(37)=0.22$, $p=.83$ (see Figure 10). The 95% LoA ranged from -0.60 cm to 0.86 cm. Linear regression analysis was conducted to assess the proportional bias of the difference on the mean. The result indicated that there was no statistically significant proportional bias, $B=0.11$, 95% CI $[-0.07, 0.28]$, $p=.23$.

Figure 10

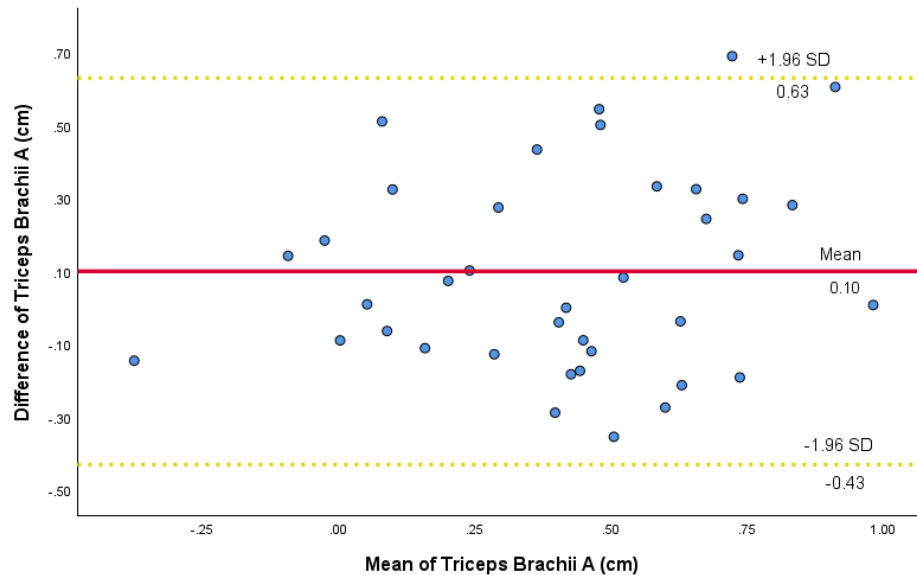
Bland-Altman Plot for Agreement Between Raters for Biceps Brachii Muscle Thickness at Baseline



For triceps brachii muscle A, a Shapiro-Wilk Test indicated the assumption of normality on rater difference was violated, $W(38)=.93$ $p=.03$. Log transformation was conducted and log transformed differences satisfied the assumption of normality, $W(38)=.96$ $p=.18$. Parametric Bland-Altman analysis was conducted and the geometric mean ratio of triceps brachii muscle A thickness of Rater 1 to Rater 2 was 1.11 (see Figure 11). The 95% LoA, back transformed to ratios ranged from 1.01 to 1.20. Linear regression analysis of the log-transformed difference on the log-transformed mean to assess the proportional bias indicated that there was no statistically significant bias, $B=0.16$, 95% CI $[-0.14, 0.46]$, $p=.28$.

Figure 11

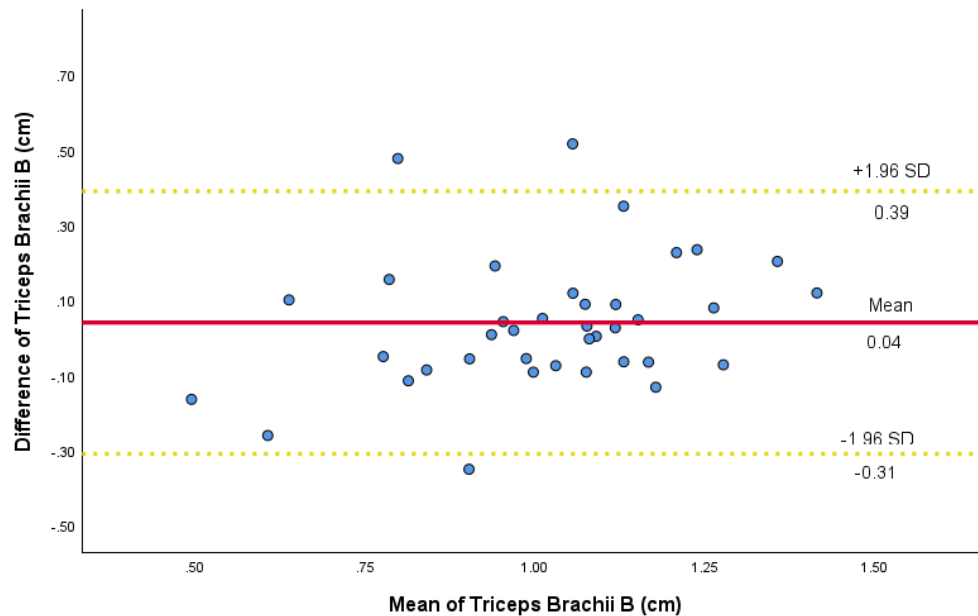
Bland-Altman Plot for Agreement Between Raters for Triceps Brachii Muscle A thickness at Baseline



For triceps brachii muscle B, a Shapiro-Wilk Test indicated the assumption of normality on rater difference was violated, $W(38)=.94, p=.04$. After log transformation, the assumption of normality was satisfied, $W(38)=.95, p=.09$ and Parametric Bland-Altman analysis was conducted. The geometric mean ratio of triceps brachii muscle B thickness of Rater 1 to Rater 2 was 1.04 (see Figure 12). The 95% LoA, back transformed to ratios ranged from 0.98 to 1.11. Linear regression analysis of the log-transformed difference on the log-transformed mean to assess the proportional bias indicated that there was no significant bias, $B=0.24, 95\% \text{ CI } [-0.05, 0.52], p=.10$.

Figure 12

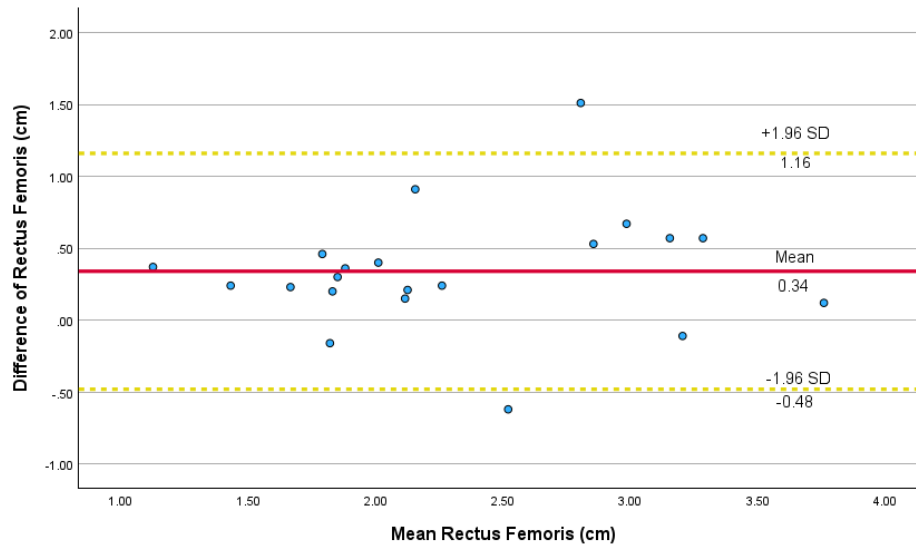
Bland-Altman Plot for Agreement Between Raters for Triceps Brachii Muscle B Thickness at Baseline



3-Months Measurements: For rectus femoris muscle thickness, a Shapiro-Wilk Test was once again conducted to assess the assumption of normality on rater difference. Results showed that the normality assumption was satisfied, $W(21)=.93$, $p=.12$. Parametric Bland-Altman analysis indicated that the mean bias of rectus femoris muscle thickness was 0.34 cm (see Figure 13). The 95% LoA ranged from -0.48 cm to 1.16 cm. Linear regression analysis was conducted to assess the proportion bias of the difference on the mean. The result indicated that there was no statistically significant proportional bias, $B=0.80$, 95% CI [-0.21, 0.37], $p=.58$.

Figure 13

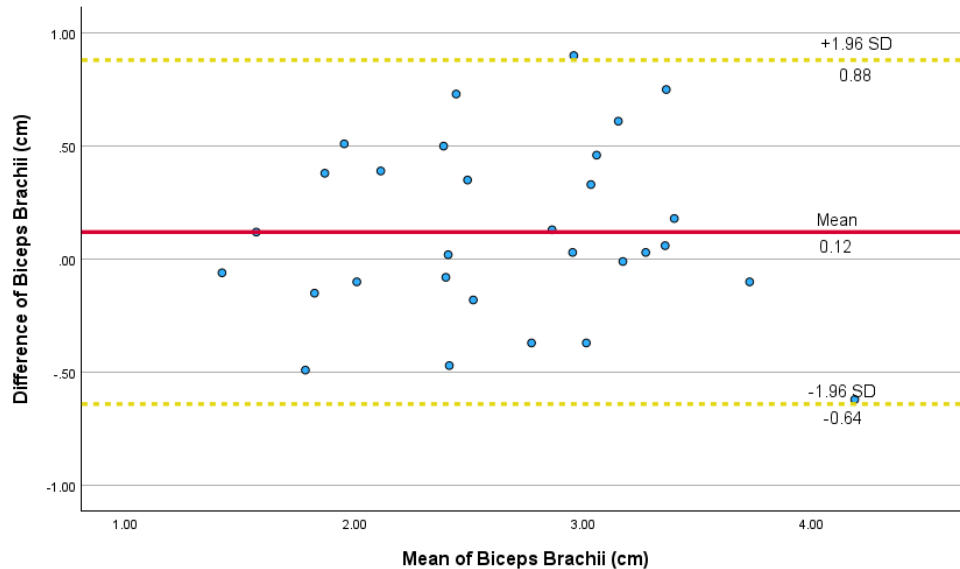
Bland-Altman Plot for Agreement Between Raters for Rectus Femoris Muscle thickness at 3 months



For biceps brachii muscle thickness, a Shapiro-Wilk Test was conducted to assess the assumption of normality on rater differences. The analysis indicated that the assumption of normality on rater differences was satisfied, $W(30)=.98$, $p=.82$. A parametric Bland-Altman analysis was conducted, and the results showed a mean bias of 0.12 cm for biceps brachii muscle thickness (see Figure 14). The 95% LoA ranged from -0.64 cm to 0.88 cm. Linear regression analysis was conducted to assess proportional bias of the difference on the mean. The result showed that there was no statistically significant proportional bias, $B=0.01$, 95% CI [-0.23, 0.22], $p=.94$.

Figure 14

Bland-Altman Plot for Agreement Between Raters for Biceps Brachii Muscle Thickness at 3 Months



A Shapiro-Wilk Test was completed and the analysis indicated that the assumption of normality was violated for the triceps brachii muscle A differences, $W(30)=.87, p=.002$. The violation remained consistent after log transformation, $W(30)=.87, p=.002$, square root transformation, $W(30)=.88, p=.003$, and inverse transformation, $W(30)=.84, p<.001$. Therefore, empirical non-parametric Bland-Altman analysis was conducted, and the median rater difference was 0.23 cm with 2.5th percentile at -0.39 cm and 97.5th percentile at 1.89 cm (see Figure 15). Spearman's Correlation was conducted between the absolute difference and the mean of the triceps brachii muscle A thickness to assess proportional bias. The result indicated a statistically significant proportional bias, $\rho=.53, 95\% \text{ CI } [.19, .75], p=.003$.

Figure 15

Bland-Altman Plot for Agreement Between Raters for Triceps Brachii Muscle A Thickness at 3 Months

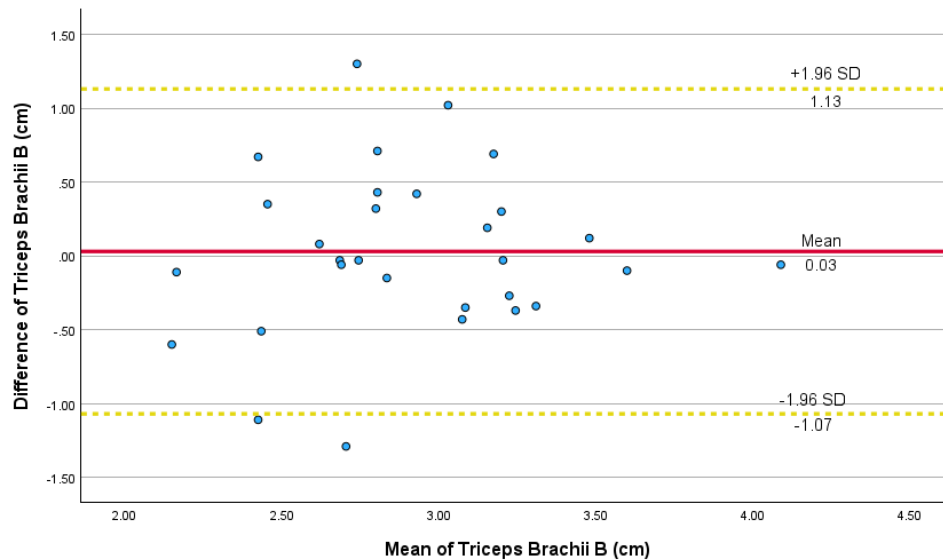


Note. The regression line indicates proportional bias. ** Indicates statistically significant proportional bias at $p < .01$.

For triceps brachii muscle B thickness, a Shapiro-Wilk Test was conducted to assess the assumption of normality on rater difference. The result showed that the assumption of normality was satisfied, $W(30) = .98$, $p = .79$. Therefore, a parametric Bland-Altman analysis was conducted. Results indicated that the mean bias of the triceps brachii muscle B thickness was 0.03 cm which did not significantly differ from 0, $t(29) = 0.25$, $p = .81$ (see Figure 16). The 95% LoA ranged from -1.07 cm to 1.13 cm. A linear regression analysis was conducted to assess the proportional bias of the difference on the mean. The result revealed that there was no statistically significant proportional bias, $B = 0.12$, 95% CI [-0.39, 0.62], $p = .64$.

Figure 16

Bland-Altman Plot for Agreement Between Raters for Triceps Brachii Muscle B Thickness at 3 Months



Research Question 2: *Is there correlation between rectus femoris muscle thickness and the thickness of biceps brachii and triceps brachii in hemodialysis patients?*

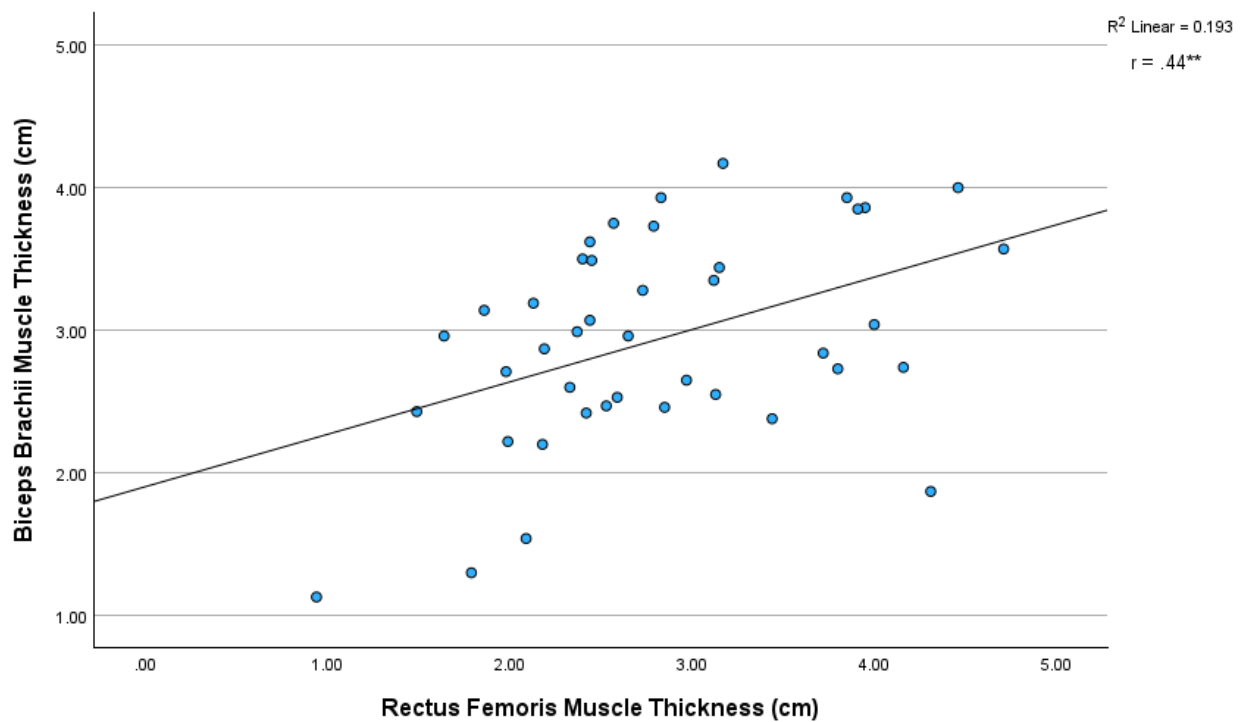
Correlational Analysis

Baseline Measurements by Rater 1: A Shapiro-Wilk Test was conducted to assess the assumption of normality and suggested that the rectus femoris, $W(42)=.97, p=.33$, biceps brachii $W(42)=.97, p=.26$, triceps brachii A $W(42)=.96, p=.14$, and triceps brachii muscles B $W(42)=.99, p=.89$ were normally distributed. A Pearson's Correlation analysis was conducted to assess the association between the thickness of the rectus femoris muscle and the thickness of the biceps brachii, triceps brachii A, and triceps brachii B muscles. The results indicated that there was a moderate, positive, and statistically significant correlation between rectus femoris muscle thickness and biceps brachii muscle thickness, $r=.44$, 95% CI [.16, .66], $n=42, p=.004$ (see

Figure 17). No statistically significant correlation was found between the rectus femoris muscle and the triceps brachii A muscle thickness, $r=.27$, 95% CI $[-.03, .53]$, $n=42$, $p=.08$ and triceps brachii B muscle thickness, $r=.19$, 95% CI $[-.12, .47]$, $n=42$, $p=.22$.

Figure 17

Association Between Thickness of Rectus Femoris Muscle and Biceps Brachii Muscle for Rater 1 at Baseline



Note. ** Indicates statistically significant association between rectus femoris muscle and biceps brachii muscle thickness at $p<.01$.

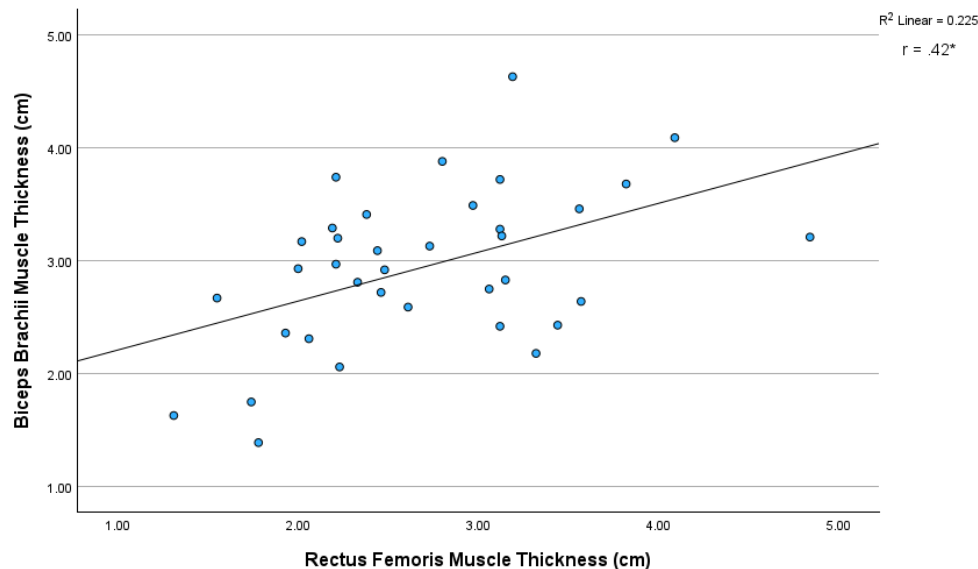
Baseline Measurement by Rater 2: A Shapiro-Wilk Test was conducted to assess the assumption of normality in the data between rectus femoris, biceps brachii, triceps brachii A, and triceps brachii B muscle thickness measured by the second rater. It was determined that there was no violation of the assumption of normality in the rectus femoris $W(34)=.96$, $p=.25$, biceps brachii $W(34)=.98$, $p=.78$ triceps brachii A $W(34)=.97$, $p=.48$, and triceps brachii muscle B

thickness $W(34)=.98, p=.74$. A Pearson's Correlation analysis was conducted to assess the correlation between the thickness of the rectus femoris muscle and the thickness of the biceps brachii, triceps brachii A, and triceps brachii B muscles. No statistically significant correlation was found between rectus femoris muscle and biceps brachii muscle thickness $r=.30, 95\% \text{ CI } [-.04, .58], n=34, p=.08$ (see Figure 20), triceps brachii muscle A thickness $r=.17, 95\% \text{ CI } [-.18, .48], n=34, p=.35$ (see Figure 21), and triceps brachii muscle B thickness $r=.18, 95\% \text{ CI } [-.17, .49], n=34, p=.31$ (see Figure 22).

3 months Measurement by Rater 1: A Shapiro-Wilk Test was conducted to assess the assumption of normality between the data of the rectus femoris, biceps brachii, triceps brachii A, and triceps brachii muscle B thickness. It was determined that there was violation of the assumption of normality for the triceps brachii muscle A, $W(36)=.91, p=.005$. Spearman's Correlation was conducted to examine the association between the thickness of rectus femoris muscle and the thickness of biceps brachii, triceps brachii A, and triceps brachii B muscles. There was a positive, moderate, and statistically significant correlation between the rectus femoris and biceps brachii muscle thickness, $\rho=.42, 95\% \text{ CI } [.10, .67], n=36, p=.01$ (see Figure 18). There was no statistically significant association found between the rectus femoris muscle and triceps brachii muscle A thickness, $\rho=.14, 95\% \text{ CI } [-.21, .46], n=36, p=.42$ and triceps brachii muscle B thickness, $\rho=.26, 95\% \text{ CI } [-.09, .55], n=36, p=.13$.

Figure 18

Association Between Thickness of Rectus Femoris Muscle and Biceps Brachii Muscle for Rater 1 at 3 Months



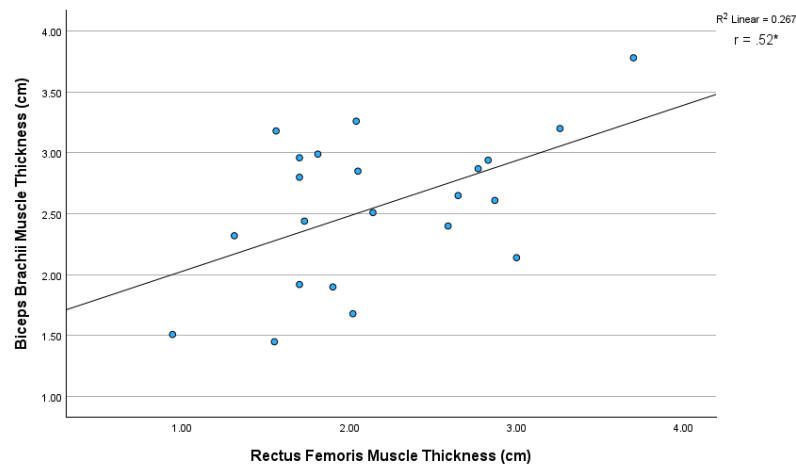
Note. * Indicates statistically significant association between rectus femoris muscle and biceps brachii muscle thickness at $p < .05$.

3-month Measurement by Rater 2: A Shapiro-Wilk Test was conducted to assess the assumption of normality of the data between the rectus femoris, biceps brachii, triceps brachii A, and triceps brachii muscle B thickness. The Shapiro-Wilk Test revealed no violation of assumption of normality for each muscle (rectus femoris muscle thickness $W(22)=.96$, $p=.43$, biceps brachii muscle $W(22)=.97$, $p=.72$; triceps brachii muscle A $W(22)=.94$, $p=.22$, and triceps brachii muscle B $W(22)=.96$, $p=.40$). Pearson's Correlation was conducted to examine the association between the thickness of the rectus femoris muscle and the biceps brachii, triceps brachii A, and triceps brachii B muscles. A positive, moderate, and statistically significant correlation was found between rectus femoris muscle thickness and biceps brachii muscle thickness $r=.52$, 95% CI [.12, .77], $n=22$, $p=.01$ (see Figure 19) and triceps brachii muscle B thickness $r=.45$, 95% CI [-.06, .67], $n=22$, $p=.04$ (see Figure 20) . No statistically significant

association was found between the rectus femoris muscle thickness and triceps brachii muscle A thickness $r=.37$, 95% CI [.04, .60], $n=22$, $p=.09$.

Figure 19

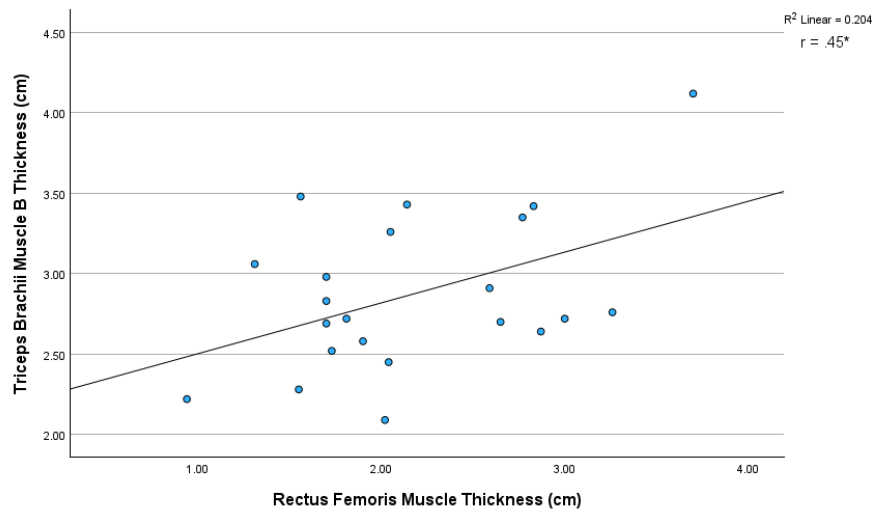
Association Between Thickness of Rectus Femoris Muscle and Biceps Brachii Muscle for Rater 2 at 3 Months



Note. * Indicates statistically significant association between rectus femoris muscle and biceps brachii muscle thickness at $p<.05$.

Figure 20

Association Between Thickness of Rectus Femoris Muscle and Triceps Brachii Muscle B for Rater 2 at 3 Months



Note. * Indicates statistically significant association between rectus femoris muscle and triceps brachii B muscle thickness at $p<.05$.

Qualitative Results

Thematic analysis of interviews ($n=9$) resulted in six prominent themes, including (1) current assessment of muscle status, (2) ultrasound as a valuable clinical instrument, (3) competency (4) application of ultrasound in hemodialysis care, (5) patients' experience and acceptance, and (6) ultrasound data as potential motivational evidence. These themes were further grouped under the three research questions guiding this aspect of the study. Excerpts were quoted verbatim, except when brackets were used to provide more clarity.

Research Question 3: *What are the experiences/perceptions of healthcare providers with the use of ultrasound as a muscle assessment tool in hemodialysis care?*

Two themes emerged under this question. The first theme described how muscle status is currently assessed among hemodialysis patients. The second theme described the perceived importance of ultrasound for clinical decision-making and communication support.

Theme 1: Current Assessment of Muscle Status

All the clinician participants described their assessment of muscle status in hemodialysis patients as relying primarily on subjective information and physical observations. The clinicians identified one particularly important gap i.e., the absence of a direct, objective tool to measure muscle thickness in ESRD patients at the renal unit. The nurses relied mostly on physical observation of the patient by comparing their current physical state to their memory baseline physical state. RN_01 stated, "how they'll start of dialysis walking in and six months later they're in an electric wheelchair." RN_02 acknowledged the physical deterioration of patients over time but noted that there was no objective way to confirm this changes in patient. RN_02 stated:

Oh, they definitely decline over time, but there's no way to look at that. You know, I come in especially, uh, coming in intermittently, you see that, oh, this person looks a lot thinner than the last time I saw them a couple of weeks ago, a couple of months ago. But there's no real objective way to assess that.

(RN_02)

The dietitians also described their assessment as predominantly subjective. RD_02 described the assessment of muscle status as: "by like talking to the patient how they feel. You know, if they feel like they've had weight loss. Kind of like mostly just like asking them what their experience is as opposed to like anything more, um, objective." When further questioned about the objective tool they mostly relied on for muscle status assessment, RD_02 responded: "I don't know to be honest with you" which only show how heavily the assessment of nutritional status and physical status of patient undergoing hemodialysis relies on laboratory values and diet history of patients. The only physician in the study described his position as focusing on acute markers rather than directly assessing nutritional and muscle status. MD_01 stated: "I do lean on our dietitian staff for, you know, those pieces and then us, specifically, it's things that might be life threatening or might require dialysis. So, potassium, high phosphorus, calcium durations, blood pressure control, fluid intake, and so forth. And it obviously sugar control in the sense that it might accelerate kidney disease along the way."

While participants' assessment is predominantly subjective, they perceived these current muscle status assessment methods as not sufficient. RN_02 stated: "just being able to eyeball somebody is not good enough" and further expressed a desire for an objective measurement tool to assess muscle mass changes in patient: "we actually get a measurement on that [muscle mass] that would be great." MD_01 also described the acute markers available to him as "very

unreliable”. MD_01 specifically stated that, “there is a lot of noise in what we see you know, fluid status, weight, and all that, that’s very unreliable. Yeah, in terms of markers and nutrition, sugar control, even that too.”

Theme 2: *Ultrasound as a Valuable Clinical Instrument*

Clinician participants perceived ultrasound as a clinically valuable tool and described the ultrasound as a potential objective data point that could enhance communication with patients, patient education, and influence clinical decision-making:

The ultrasound results in addition to all the other components of the assessment and you have somebody who's losing weight, muscle wasting, potentially not meeting protein needs because of increased needs for like wound healing or just the dialysis or they just have, or that's even like food security, food choices, cost of food, all of those factors, we could, you know, we just have additional evidence that maybe we need to intervene more aggressively or sooner.

(RD_01)

Participants also highlighted some perceived importance of the ultrasound. RD_2 stated that: “[ultrasound] kind of gives you a better picture in terms of like if there’s any education needed or any other intervention.” RD_01 also stated: “[ultrasound is] actually giving them something that’s like no, this changed happened, this is so important, [it] can really compliment the education we’re giving.” RD_03 added: “it may speed up or cause me to offer interventions like supplemental enteral nutrition and where it maybe wouldn't otherwise.”

In the context of communication with patients, RN_02 described ultrasound as tool that could complement observations and better explain patients true state to them. RN_02 stated:

So, if I say saw somebody who looks a little thinner, we will then do the muscle, uh, ultrasound and say, hey, they're 6% thinner that are less stents or whatever the term than previous. So yes, we've actually objectively tied them or sorry, subjectively they look thinner and now tied it to an objective measure that they are six to eight, 10%, whatever the mystical number would be and it would allow for contextualizing.

(RN_02)

The value of the ultrasound was also echoed as RN_01 cited that the data from ultrasound imaging of a patients' muscle status could influence the decision of escalating patient cases to the appropriate professional for further management. RN_01 stated that "I would call the dietitian. I would call the social worker, like tell them that their, what their issues is with them." RN_01 further stated that: "if it was something where there was a big enough change, I would involve a physician too. Like if I think they needed albumin or something more."

Research Question 4: *How can ultrasound muscle assessment be incorporated into the workflow of multidisciplinary team?*

In addressing the question of how ultrasound assessment could be integrated into workflow, two themes were reported. The first theme addressed workforce training on the use of ultrasound. The second theme described the practical application of ultrasound within the hemodialysis unit, role delegation, and muscle site selection for measurement

Theme 3: *Competency*

This theme described the training needs of clinicians to confidently perform ultrasound measurement in a hemodialysis setting and how standardized protocols would be sustained over time. The need for training was acknowledged by participants with training specifically targeting the operation of the ultrasound machine and interpretation of the results or measurement. The

word training surfaced in most interview when clinicians were asked what it would take for them to be comfortable with the use of the ultrasound machine for assessment. RD_03 stated this clearly: “definitely some introduction to how to use an ultrasound machine. So, like training. Training on the interpretation of data.” RD_02 also stated:

I would just say like, um, if I guess any literature that's kind of relevant. As well as just like hands-on experience. Being that it's not something I've ever really done before, and I wouldn't really know what I would be looking for or like kind of how to assess anything. So, I guess just like training with the tool as well as like just the literature of anything that's relevant.

(RD_02)

One participant (RN_01) also cited that ultrasound could be performed once clinicians were trained.

Probably with training. I don't know if our current ultrasounds would be able to measure that sort of thing, but okay. I think with training and showing nurses or dietitians what to look for and how to make those measurements, that's something that could be doable.

(RN_01)

Some participants also suggested that training on the use of ultrasound should be conducted by an external formal trainer/instructor with expertise in that field. RD_01 stated that “I'd rather have someone who has like a fair bit of background in it as opposed to like me getting trained and then training someone else a month later.” A concern was raised by RN_02 about the uncompensated training at the workplace which could potentially create resistance for the training roll out.

I would not want to have to come in when I'm not supposed to be here to do it. Right. So taking somebody out of the day to train them and or having dedicated days paid would be ideal for training, which is not your area, but it's No, but facet because, we just had a conversation about this the other day about coming in for unpaid training and quote unquote being required and not being paid and the frustrations that come with that. And there is a number of people who will absolutely refuse to do it if it's not something that we'll be compensated for.

(RN_02)

Theme 4: *Application of Ultrasound in Hemodialysis Care*

This theme concerned with who should perform the ultrasound assessment in the hemodialysis unit, which muscle site they perceived to be appropriate for assessment, and the cadence of assessment. On the question of who should perform the assessment among the multidisciplinary team in the unit, participants universally agreed that the role of the clinician is less important provided that there is adequate training. Most participant expressed similar views on who performed the assessment. RN_01 said “it could be conducted by a variety of people. Um, I feel like it doesn't necessarily matter like exactly who's doing that, especially just if there's proper training involved.” Despite MD_01 acknowledging this point, “I think we're all part of the same team, and I think we try to find the right information,” their stance was different when asked if they saw themselves performing the assessment, they said:

It's hard to see it in the current workload for that to happen, I think. But it might make sense for someone like, like our dietitian to are looking at nutrition more in more detailed fashion. It might make sense for them. I think for us is having the information, are they

losing muscle mass over time and what's our sort of the theory behind that? Those are sort of things I'm looking at high level stuff. So, um, it may not make sense for that.

(MD_01)

Regarding the site selection for muscle assessment, no consensus emerged on a single site for assessment. Participants expressed flexibility to selection of the site based on accessibility. RD_03 stated: “probably upper arm, mostly because it's more accessible to me.” RN_01 stated that: “either way [leg or arm] I wouldn’t have problem doing either of those.” RN_01 further stated that: “it would depend on how they're sitting and it depend on what type of clothing they're wearing. Like if they're wearing a hoodie that's impossible for me to get their arm out of. I probably prefer to do their lower leg.” RN_02 also based their stance on the health status of the patient and also the settings in the dialysis unit.

I think it would be patient by patient basis because of all the amputations things that we have. So, somebody with AKA is going to have wasted muscle mass at baseline on that stump, right? versus the upper arms or like, it would really be patient, patient specific. So, you could have a multifaceted intervention where it's up to the provider to determine where, as long as it's standardized, so it would be again, provider dependent on patient, dependent on where specifically. But I don't see a problem either with upper arm, middle arm or lower leg. Perhaps thigh would not be the most appropriate with the openness of the setting, but there are curtains everywhere, so you could take five minutes and do it that way too.

(RN_02)

On the question of perceived measurement interval, clinician participants recommended different assessment intervals. The proposed interval ranged from weekly to annually. RD_01 proposed that assessment of patient should be done at baseline and at regular intervals:

maybe make it more integrated on an ongoing basis, which might take time, but if patients were agreeable to it to, you know, try and get a baseline when they first start and maybe check it like, you know, looking every six month or so or more often if there's more obvious visual concerns.

MD_01 also proposed that intervals should be triggered by the health status of the patient:

I'm probably looking at intervals monthly and then I then looking at a distribution or histogram of patients' muscle mass change over time. And then just trying to figure out where, you know, how we, what's the right optimal frequency without adding too much work. Right? I think that's the balance you guys have to figure out. So, you know, practically speaking, is it quarterly? is that a good way? As you know, we conclude patients are on chronic dialysis after 90 days, technically speaking. Right. But I, and maybe that's good for muscle, maybe it's too infrequent, I don't know. Are you just doing it like, are you doing more frequently than someone who just came out of hospital or was in ICU? Or is it context situational dependent.

(MD_01)

Research Question 5: *How do hemodialysis patients perceive ultrasound application for routine muscle assessment in their care?*

Two themes were reported for this research question with the first theme describing the experiences of the patients with ultrasound as a diagnostic or therapeutic tool and their

acceptance of ultrasound for muscle assessment within their routine care. The second theme described the motivational potential of the ultrasound data as visual evidence to support engagement in lifestyle changing activities.

Theme 5: *Patients' Experience and Preference*

This theme described the different types of experience patients had with ultrasound, whether they were willing to accept ultrasound muscle mass assessment into routine care, and their preferred muscle site for measurement. All three patients interviewed had some level of past experience with ultrasound diagnostic imaging for either cannulation in the hemodialysis unit or for medical diagnosis. One patient said:

I've had various ultra ultrasounds. I've had my, I think the femoral artery, ultrasound to see if there's a clot. Um, that was initially when I first had edema and they were concerned about a clot. I've had kidney ultrasounds I think, I think a chest ultrasound, bladder ultrasound.

(Patient_03)

Another patient also cited their previous experience with ultrasound, and they stated “I’m trying to get on the list for a kidney transplant, and you have to go through all this stuff. So, I’ve had a lot of ab abdominal ultrasounds and stuff like that.” Another patient shared their experience on how the ultrasound is used for cannulation. The patient stated that: “only when they put the fistula in. some nurses use the ultrasound on my arm.”

On the issue of who among the healthcare professionals performed the measurement on them, all the patients expressed indifference, however, their acceptance was conditional on the person being trained appropriately. Patient _03 stated that “so long as they, I’m assuming that

they have sufficient training to understand and like education to understand what structures they [would] be like seeing.” Patient_03 further stated that: “I would trust that the unit ensure [that] the people handling that specific equipment would have sufficient training, like to understand it.” Patient_01 said “usually whoever knows how to do ultrasound. Okay, it doesn’t really matter.” Patient_02 cited: “I think anybody can do it. I guess that they have the training and they’re a nice person, I’m all for it.”

On the question of muscle measurement during the scheduled dialysis sessions, participants agreed to in-session assessment as they expressed the burden of additional appointments. Patient_01 stated that “probably, yeah. Because if I go home, you tell me, come back two weeks’ time, I won’t go.” Patient_02 also stated that: “a lot of people that are here like to have it when we’re here. Because we don’t really want to come back when we’re not here”

Patients had mixed preferences for muscle measurement sites. Patient_01 cited preference for the leg due to weakness: “probably my leg mostly ... it just that they get, they feel heavy at time.” Patient_03 expressed indifference: “I don’t think it matters.” However, Patient_03 later expressed preference for arm assessment: “if the, I guess the ultrasound would require like moving clothing, so it’d be easier probably to do the arm.” Patient_01 stated: “I think they are just as important.”

Theme 6: *Ultrasound Data as Potential Motivational Evidence*

This theme described how patients perceived ultrasound imaging to influence active engagement with their own muscle health. Patient interviews confirmed the findings of the clinicians that ultrasound imaging may influence lifestyle changes. Patient_03 cited that:

I would imagine like if for example, like it was discovered that like I was losing a lot of muscle mass or something like that. Right. Um, I would want to know that and like if it was determined that like one of the best, one of the best ways to address that was to like do exercise, I think that would, that would motivate me to exercise more.

(Patient_03)

Patient_03, on the dietary side expressed skepticism: “diet wise, I’m not sure what would help necessarily.” Patient_03 further acknowledged that: “I personally don’t consume a lot of protein. So, I would need to be convinced” and concluded: “[it] basically would be out of my normal habit. So, I would assume that, yeah, it would encourage me to change my habits.”

Patient_02 and Patient_01 replied, “I think it would” when asked whether protein recommendation related to their ultrasound data would feel different. However, Patient_02 later expressed skepticism about diet being the driver for muscle change. Patient_02 stated that: “this machine running through your blood and everything all the time and you not producing what you do with your kidney might be more of what would make your muscle not be worse than just a diet.”

Table 5 provides a joint display of the convergence (expansion) and divergence between the qualitative and quantitative results of this study and the integrated meta-inferences.

Table 5.*Convergence and Divergence Between the Quantitative and the Qualitative Findings*

Quantitative Findings	Qualitative Findings	Pattern	Meta-Inference Focus
Ultrasound is reliable for the rectus femoris and the biceps brachii muscles.	Healthcare professionals focus on observation for muscle status assessment.	Convergence	The need for an objective measure. Ultrasound present as a muscle specific reliable objective to for muscle thickness assessment.
Inter-rater reliability of rectus femoris muscle declined with wide confidence interval. The minimum detectable change of the biceps brachii muscle did not exceed the expected changes.	Healthcare professionals want to be able to track changes and act on those changes. Patients also say changes would motivate lifestyle changes.	Divergence	Muscle change tracking. The changes healthcare professionals want to track may be smaller than what measurement can resolve.
Inter-rater reliability declined for most muscles and the standard error of measurement increased at 3 months	Healthcare professional requested training as the top requirement for ultrasound application. Patients said they would accept any trained professional to perform measurements.	Convergence	Feasibility. While the right muscle selection is important, standardized training for ultrasound use is necessary for routine use.
Biceps brachii muscle was found to be the most consistently reliable muscle and also the most consistent correlate of the rectus femoris muscle.	Healthcare professionals and patients want a flexible and most accessible muscle site for muscle thickness measurement.	Divergence	The choice of muscle measurement site. Muscle site selection based on accessibility is reasonable, but flexibility must be bounded.

Chapter 5: Discussion

The purpose of this study was to explore a reliable and valid muscle thickness assessment site for ultrasound muscle assessment in ESRD patients undergoing hemodialysis through a mixed method design. The mixed-methods design used in this study enabled a broader evaluation of diagnostic ultrasound imaging than would have been possible using either method alone. The first part of the study examined the inter-rater reliability of the rectus femoris, biceps brachii, triceps brachii A and B muscle thicknesses to provide evidence of reliability for the use of this measurement technique. This aspect of the study also examined whether the thickness of the biceps brachii muscle and the triceps brachii muscle A and B correlated with the thickness of the rectus femoris muscle, which is the most extensively studied muscle in muscle mass using ultrasound, to provide evidence of validity for the use of this measure (Naruse et al., 2022; Sabatino et al., 2021). The second part of the study explored the feasibility of integrating ultrasound assessment of muscle mass into routine renal care from the perspective of both healthcare providers and patients. This chapter interprets the findings through the methodological lens of reliability and validity of the quantitative measures, and the trustworthiness of qualitative findings. Each part is discussed separately and then integrated through the meta-inferences. Four key meta-inferences emerged from the integration of the findings: (1) ultrasound may help address the objectivity gap in muscle assessment, (2) the ability to track muscle changes over time remains constrained by measurement error, (3) successful implementation depends on feasibility factors such as training and standardization, and (4) flexibility in choice of measurement site (see Table 5 above).

Reliability

In clinical practice, a measurement tool becomes useful only if comparable measures or values on the same patient can be obtained by different healthcare providers. This makes reliability a fundamental requirement of any clinical measurement tool (Andersson et al., 2024; Nha, 2021). Reliability does not only satisfy the methodological criterion for a measurement tool but also instils confidence in healthcare providers' decision-making regarding therapy initiation and alteration, or care escalation (Koo & Li, 2016). Reliability further defines the threshold of change that can be considered real (Koo & Li, 2016). In this study, the reliability findings were interpreted according to the criteria established by Koo & Li (2016).

The bicep brachii muscle at baseline and at 3 months follow up demonstrated good inter-rater reliability. The rectus femoris muscle demonstrated strong inter-rater reliability at baseline measurement. However, the inter-rater reliability of the rectus femoris muscle thickness decreased (ICC=.91, 95% CI [.83, .96]) to a moderate point estimate (ICC=.75, 95% CI [.27, .91]) at 3 months with wide and overlapping CIs and evidence of systematic bias. The wide CIs indicate uncertainty in this estimate, with the true inter-rater reliability of the rectus femoris muscle at 3 months potentially ranging from poor to strong (Koo & Li, 2016). A possible explanation to the widened CI is the drastic reduction in analysis sample size from n=33 at baseline to n=21 at 3 months due to missing measurements arising from patient fatigue, discomfort, and unsaved scan images. The evidence of systematic bias at 3 months and not at baseline may be because measurements were taken while fluid was being removed intradialytic fluid shifts may have affected the values. Whether ultrasound muscle measures are influenced by hydration status in hemodialysis is still not concluded (Cheng et al., 2023; Sabatino et al., 2017). The triceps brachii muscle which was measured at two levels, A and B declined from moderate

inter-rater reliability at baseline to poor inter-rater reliability at 3 months follow up, where triceps brachii A showed evidence of inter-rater systematic bias at baseline and significant proportional bias at 3 months follow up.

The reported inter-rater reliability for the biceps brachii muscle thickness, the rectus femoris muscle thickness, and the triceps brachii muscle A and B thicknesses at baseline and 3 months follow up are comparable with previous studies. The most comparable is Van den Broeck et al. (2023), they assessed the biceps brachii muscle thickness, the rectus femoris thickness, and the triceps brachii muscle thickness in healthy adults by two raters. The study reported good inter-rater reliability for the rectus femoris muscle thickness and excellent inter-rater reliability for the bicep brachii thickness but were unable to confirm inter-rater reliability for triceps brachii muscle thickness through their bootstrap analysis and its coefficient of variation exceeding 10% (Van den Broeck et al., 2023). The triceps brachii is a three-headed muscle (long, lateral, and medial) with fascicles travelling at different pennation angles, coupled with less sharply defined aponeurosis makes it difficult for straightforward assessment. Van den Broeck et al. (2023) attributed their findings of the triceps brachii muscle to the anatomical complexity of this muscle. It was expected to see similar results of moderate to poor inter-rater reliability with high error (12.1% -22.1%) across the triceps brachii muscle measurement due to the complexity of the muscle in addition to the posterior arm partly obstructed by the dialysis chair compromising probe orientation between raters.

Also, in the current study, there was a drastic increase in standard error of measurement from 9.7% of the mean to 15.5% of the mean at 3 months. A possible cause of this decline could be attributed to a drift in measurement between the two raters at 3 months follow up. The two raters in this study only had a day of formal diagnostic ultrasound imaging training with no

additional training between timepoints. Their little experience may have had influence on landmark identification, the amount of pressure applied to the probe, and patient fowler positioning in the dialysis chair (the backrest of the dialysis chair was adjusted between 60-90° based on the participant's need for comfort), rather than the muscle itself. Comparing our reliability finding to broader literature, it can be inferred that the reliability of ultrasound for muscle thickness measurement is dependent on the conditions of measurement such as the experience of the raters and the sets of protocols used. Hashida et al. (2022) used three trained raters to assess the thickness of the biceps brachii muscle and the quadriceps femoris muscle before and after (30 days, 90 days, and 180 days) allogeneic haematopoietic stem cell transplantation and found excellent inter-rater reliability across timepoints. Ogawa et al. (2023) also used three raters who had at least three years of experience with ultrasound examination to assess the quadriceps muscle thickness in healthy adults and found an excellent inter-rater reliability. Hashida et al. (2022) and Ogawa et al. (2023) performed their measurements under controlled conditions. Participants were measured in supine lying position at rest and landmarks were identified and marked (Hashida et al., 2022; Ogawa et al., 2023). In this study, assessments were performed under hemodialysis conditions (seated in dialysis chair and connected to the dialysis machine) and landmarks were only palpated and identified but not marked.

The biceps brachii muscle was the most stable muscle among all the muscles measured. An acceptable SEM was found at both baseline and 3 months follow up measurement. Therefore, the clinical interpretation can be inferred. The MDC of the biceps brachii muscle was 0.71 cm and 0.77 cm at baseline and 3 months, respectively, against a grand mean thickness of 2.78 cm across raters and timepoints. According to Kitamura et al. (2021), ESRD patients undergoing hemodialysis lose on average 9.5% of lean mass each year. Placing it against our finding,

hemodialysis patients would only lose about 0.26 cm of biceps brachii muscle over a year which is below the MDC values of 0.71 cm and 0.77 cm. This implies that it can take up to three years for ultrasound to detect real biological muscle changes in hemodialysis patients. An important implication of this finding is that muscle wasting over 3 months to years could still be considered measurement error and not prompt nutritional or physiotherapy intervention. However, this must not be overstated because the 0.26 cm estimate applies to whole body lean mass loss percentage to a linear muscle thickness measure and therefore, should be considered as illustration rather than a precise figure.

Validity

According to Kane's (2006) argument-based framework, validity of an instrument should not be treated as a fixed property but as interpretation built from what the scores mean and how these scores can be used. In clinical practice, this is particularly important because muscle thickness measures can be repeatable but also cannot fully support decision making in patients' care. In order for a clinical use of a tool to hold, it must be weighed and interpreted through the chain of inferences i.e., scoring, generalization, extrapolation, and implication (Kane, 2006). Validity evidence in this study was evaluated against these inferences. The correlational analysis between the rectus femoris muscle thickness and the thickness of the biceps brachii, and the triceps brachii A and B muscle partially supports the extrapolation inference. The biceps brachii muscle thickness demonstrated significant association with the rectus femoris thickness at baseline for rater 1 and 3 months for rater 1 and 2. The triceps brachii muscle A and B were poorly and non-significantly associated with the rectus femoris across timepoints, with the exception triceps brachii muscle B at 3 months for rater 2. It is important to not overstate the strength of the relationship. The significant association between the biceps brachii muscle

thickness and the rectus femoris muscle thickness was moderate in magnitude with shared variance between 19% and 28%. This explains that only a fifth to a quarter of the changes in the rectus femoris muscle thickness can be associated with biceps brachii muscle thickness. This makes the biceps brachii muscles thickness measurements not precise to directly replace the rectus femoris muscle thickness measurement. The magnitudes of correlation found in this study are similar to what Ogawa et al. (2023) found. Ogawa et al. (2023) found moderate and significant correlation between the thickness of the quadriceps muscle and the leg skeletal muscle index ($r=.36, p=.02$), a weak but significant correlation with handgrip ($r=.30, p=.04$), and maximum isokinetic strength ($r=.20, p=0.04$). With this, it can be said that the limited shared variance in our study represents an inherent characteristic of ultrasound methodology for isolated muscle rather than a flaw within the current study.

Interestingly, previous validity evidence for the biceps brachii muscle is more encouraging than the correlation findings of the current study suggested. Hashida et al. (2022) validated ultrasound biceps brachii muscle thickness against the CT measure of the cross-sectional area of the psoas muscle in allogeneic haematopoietic stem cell transplant patients and found a strong and significant correlation $r = .73, p<.001$. The finding of Hashida et al. (2022) is very important to this current study because, while the current study cannot establish the biceps brachii muscle as a proxy for muscle thickness assessment in the hemodialysis population yet, the muscle has already demonstrated good criterion validity against a gold standard in a different population. Also, the thickness of the biceps brachii muscle in their study significantly declined after 90 days (16.7 ± 2.9 mm, $P < 0.001$) and 180 days (16.9 ± 3.3 mm, $P < 0.001$) after transplantation from baseline (18.6 ± 3.6 mm), indicating that the biceps brachii muscle was sensitive to real change (Hashida, et al., 2022). And if the susceptibility of the rectus femoris

muscle to atrophy and wasting made it a favourite to be validated as proxy for muscle thickness assessment, then the sensitivity for the biceps brachii muscle to wasting and evidence of good criterion validity strengthens the need to further pursue the criterion validation of the biceps brachii muscle rather than to abandon it (Hashida, et al., 2022; Murdock et al., 2019).

Trustworthiness

In addition to reliability and validity evidence, methodological rigour of this study was established through trustworthiness. Because qualitative findings are heavily dependent on the interpretation of a researcher, trustworthiness relies on demonstrating that the themes derived from the findings truly reflects what participants actually said rather than the researcher's assumption, and this is established through trustworthiness criteria including credibility, dependability, transferability, and confirmability (Forero et al., 2018). Grounding this in the interpretive argument-based framework by Kane (2006), the qualitative findings of this study established through trustworthiness criteria supported the implication inference.

One of the major themes that evolved from qualitative finding was the clinician participants' inability to objectively measure muscle status in ESRD patients. Healthcare professionals across the various roles included in the study currently assess muscle mass/status in this population subjectively and also through physical observation. They described this approach as a dissatisfactory way of assessing muscle mass in ESRD patients. Nurses explained that they assess muscle mass based on visual memories of how the limbs of the patients used to look against their present appearance and showing dissatisfaction with this approach. One nurse explicitly stated that "*just being able to eyeball somebody is not good enough.*" The dietitians described that their assessment of muscle mass was based on the patient's reported feeling and the only physician who participated in the study described the biomarkers available to him as

“*very unreliable*”. The consistency of these concerns (i.e., the inability to objectively measure muscle status) across different healthcare professionals strengthens the credibility and dependability of this finding, as similar limitations were identified independently across clinical roles rather than being attributed to a single perspective. The use of direct participant quotations further enhances confirmability by demonstrating that interpretations were grounded in participants’ descriptions and experiences rather than researcher assumptions. All these descriptions presented a genuine need for direct measurement of muscle mass in the ESRD population that the current workflow does not provide. Against this, healthcare professional participants saw the ultrasound machine as an objective data point that can support their impressions made through patient observation. They described that they would escalate patients to the appropriate professional if changes were “*big enough*”. Some healthcare professionals also described that by taking baseline muscle thickness measurement at the start and reviewing the measurements at intervals will support how they educate and communicate with patients. Patients, too, saw the change tracking of muscle status as a motivational one. They believed that ultrasound data showing evidence of muscle loss might motivate them to exercise more or change their dietary habits, though one patient doubted if diet was really a driver of muscle loss.

The other themes when grouped together explains the conditions under which ultrasound for muscle mass assessment could be adopted into patient care. Training was the most frequently raised requirement by both healthcare professionals and patients for ultrasound application assessment. Healthcare professionals believed that they needed to be adequately trained on the use of diagnostic imaging and the use of the ultrasound machine and the interpretation of the results. Most healthcare professionals believed also that, the professional role of the person performing the ultrasound assessment whether a nurse, a dietitian, or physician mattered less

given that they were adequately trained. The patients also echoed this view by making their acceptance any assessor only on knowing that they had sufficient training. The emergence of training requirement independently from two participant groups (i.e., healthcare professionals and patients) reinforces the credibility of the theme through data-source triangulation. The finding that any healthcare professional can perform ultrasound assessment strengthens the argument by Sabatino et al. (2021) that ultrasound can be used by non-specialist healthcare providers, but with the condition of adequate training. This alignment with existing research reinforces some degree of transferability. Furthermore, healthcare professionals were flexible about the selection of the muscle site to assess. They explained that their measurement site preference depended on each patient and what was more accessible to them. A healthcare professional further acknowledged the prevalence of lower-limb amputations among patients and how that would influence their decision as well. Patients were also flexible but divided in their preference with some opting for any muscle that was accessible and others open to whatever needed to be assessed.

Quantitative and Qualitative Findings Integration

Combining the inferences drawn from quantitative and qualitative findings revealed insightful conclusions which neither the quantitative nor qualitative strand could achieve alone. This maps well into the main idea of Kane (2006) the argument-based validity framework, that interpretation and the use of scores should be justified through interpretive argument. Both the quantitative and the qualitative findings of this current study provide evidence to the chain of inferences (scoring, generalization, extrapolation, and implication) of Kane's framework. However, integrating these pieces of evidence allows a validity argument for ultrasound

measurement in ESRD patients to be judged as a whole. Four meta-inferences were drawn to argue the use of the ultrasound derived muscle thickness measures in ESRD population.

The first point of convergence between the quantitative and the qualitative finding is that ultrasound may help address the objectivity gap in muscle mass assessment. The healthcare professionals, through the qualitative findings described a gap in their current workflow, i.e., the inability to objectively measure muscle mass in ESRD patients and described their current muscle status assessment as inadequate. The quantitative findings revealed that ultrasound can reliably assess the biceps brachii muscle thickness and the rectus femoris muscle thickness but not the triceps brachii muscle thickness in ESRD. The ultrasound machine for muscle thickness assessment, therefore, partly fill this current gap in workflow. Because reliability held for only two out the three muscles assessed in this study, the objectivity healthcare professionals were seeking is only available for particular muscle sites and cannot be assumed for whichever muscle that happens to be convenient. This distinction matters because despite the need for an objective tool to close the objectivity gap, consideration must be given to the site of measurement.

The second meta-inference described clear divergence point between the qualitative and the quantitative findings which concerns tracking changes in muscle status of ESRD patients over time. Healthcare professionals wanted to be able to detect changes in the patients' muscle and be able to act on it. Patients, too, described the change tracking of their muscle status could motivate them to change their diet or exercise more. However, this aspiration to track muscle changes over time by healthcare professionals and its implication to motivate patients remains constrained by measurement error. For the biceps brachii muscle, which is the most stable muscle assessed in this study, measurement error analysis showed that true biological change that may occur over 3 months may fall below the MDC. This implies that the decline or changes

that healthcare providers in our qualitative finding want to track, and also the patients said would motivate them may be smaller than what the diagnostic ultrasound measurement can actually provide over a short period of time.

The third meta-inference concerns the feasibility of integrating diagnostic ultrasound imaging into the routine care of patients. Successful integration depends on feasibility factors such as training and standardization. The quantitative result of this study established that a reliable muscle site existed for muscle thickness assessment in ESRD patients. However, it also showed that reliability was dependent on the rater and the protocol. Gould et al. (2019) discussed that methodological issues such as the location of the scan, patient position, landmark identification, and probe placement may introduce heterogeneity in ultrasound parameters. In this current study, muscle measurements were taken during hemodialysis sessions while patient were seated in the dialysis chair and connected to the dialysis machine. This coupled with the fact that there was no retraining for the assessors between time point, and fact that the assessors were novice could be a possible explanation for the poor performance of the rectus femoris muscle and the triceps brachii muscle A and B particularly at 3 months follow up. This aligns with the training requirement on diagnostic ultrasound both the healthcare professionals and patients proposed for clinical adoption.

The fourth meta-inference concerns the flexibility in muscle site selection. A major clinical problem that motivated the search of an upper limb muscle as an alternative site for the measurement of muscle thickness in ESRD patients is the high rate of lower-limb amputations in the ESRD population (Franz et al., 2018). Franz et al. (2018) found that lower-limb amputation rate was five times higher in diabetic ESRD patients compared to non-diabetic patients. In the study, 18.0% of the participants at baseline measurement had an amputation (below-knee

amputation) and 15.6% of the participants at 3 months received an amputation. The challenge with using diagnostic ultrasound after a lower-limb amputation most often makes the rectus femoris muscle, the most used muscle for muscle thickness assessment/measurement, inaccessible (Naruse et al., 2022; Sabatino et al., 2021). The qualitative findings confirmed that accessibility is what shaped both healthcare professional's and patient's thinking about muscle site selection. These findings endorsed a model in which the healthcare provider determines and chooses whichever muscle site is most practical at the time of assessment but uses a patient centred approach to allow the patient to have some input as well and clearly be educated on why that site was chosen. The quantitative findings, however, cautioned against the full implementation of this model. The rectus femoris, biceps brachii, and the triceps brachii muscles were not interchangeable. When correlated against the rectus femoris muscle thickness, the biceps brachii muscle thickness had the most consistent association but with a small percentage of shared variance. The triceps brachii muscle thickness on the other hand was not reliable with evidence of systematic bias. Only the triceps brachii muscle B thickness for rater 2 at 3 months showed positive significant association with the rectus femoris muscle thickness. therefore, it can be said that selection of muscle site for ultrasound muscle thickness assessment based on accessibility to the site is reasonable, but it must be bounded. The flexibility to muscle site selection should only operate within validated muscle site rather than any muscle site a healthcare professionals find accessible.

Limitations

This study has several limitations that should be acknowledged. First, the initial sample size reduced from 50 at baseline, to 45 at 3 months follow up for the quantitative analysis. These participants were lost due to hospitalization, death, and withdrawal. Also, per analysis sample

sizes ranged from 21 to 38 due to missing data as a result of discomfort from participants during dialysis, probe positioning, and constraints from dialysis chair itself. This widened the CI for reliability estimates and reduced statistical power for the correlation analysis. Also, muscle thickness measurements were obtained during the dialysis sessions, and given the unresolved question on the effect of intradialytic fluid shift on muscle measurements, the systematic bias and the increased error at 3 months may have been due to hydration status in these patients (Cheng et al., 2023; Sabatino et al., 2017). For the qualitative analysis, only 9 out of the proposed 12 participants were recruited. Therefore, results from this study should be interpreted with caution and care taken when generalizing. Second, muscle measurement protocols for this study were not standardized. Currently no standardized ultrasound protocol for muscle thickness assessment exists for any population (Perkisas et al., 2021). The protocols used in this study required that measurements were performed in the dialysis chair during dialysis. This differs from previous studies that performed measurements on patients in supine or prone lying position, at rest, and in the laboratory (Hashida et al., 2022; Ogawa et al., 2023; Van den Broeck et al., 2023). This potentially limited the direct comparisons, and it may have shaped the different reliability findings. Furthermore, no rater retraining was conducted between the measurement timepoints. This may have contributed to the increased random error observed at 3 months and also the drift in mean bias for the rectus femoris muscle at 3 months. Finally, this study was a single center study. The quantitative aspect employed only two raters, both of which were dietitians. The qualitative aspects only included one nephrologist limiting the breadth of the nephrologist's and physician's perspective. All together, this may limit the generalizability of our findings to settings with different patient and institutional demographics, protocols, and staffing models.

Recommendation for Future Research

To our knowledge, this is the first study that aimed to explore an alternative upper limb muscle site for diagnostic ultrasound imaging muscle thickness assessment in ESRD patients undergoing hemodialysis. Additionally, this study aimed to explore the perspective of healthcare professionals and patients on the integration of ultrasound assessment into routine renal care. Further research is required through concurrent validation of the biceps brachii muscle thickness against an established criterion such as CT scan, MRI, or DEXA in the ESRD population to support the extrapolation inferences (Kane, 2006). The significant correlation between the rectus femoris muscle thickness and the biceps brachii muscle thickness does not establish biceps brachii muscle as a substitute muscle for muscle thickness assessment. However, Hashida et al., (2022) finding of a strong correlation between the biceps brachii thickness ultrasound and CT scan of CSA of the psoas muscle further strengthens the biceps brachii muscle as promising alternative muscle site. Furthermore, future research should be multi-center, including raters from different professions (i.e., nurses, dietitians, nephrologists, and/or physiotherapists). Also, detailed protocol specifying landmark identification and marking, probe orientation, and patient positioning during measurement should be developed and strictly followed for muscle thickness assessment in ESRD. This may show whether the triceps brachii muscle is not suitable in this population or simply lack standard approach to measurement. Lastly, rater retraining should be conducted at regular intervals and between timepoints for future longitudinal studies to allow novice assessors to gain more experience and reduce errors.

Chapter 6: Conclusion

The purpose of this study was to explore an upper limb muscle as a reliable alternative diagnostic ultrasound muscle thickness measurement site in ESRD patients undergoing hemodialysis. Furthermore, it aimed to explore the perception of healthcare professionals and patients on the possible integration of diagnostic ultrasound muscle thickness assessment/measurement into the routine care of patients. This study suggested that the biceps brachii muscle was the most promising upper limb muscle alternative to the rectus femoris muscle for ultrasound measurement of muscle thickness in ESRD patients undergoing hemodialysis. The biceps brachii muscle had consistently good inter-rater reliability across timepoints, and it was the most consistent correlate of the rectus femoris muscle thickness. The triceps brachii muscle, on the other hand, was not a potential alternative muscle for muscle thickness assessment under current measurement conditions in this study. Moreover, the validity argument for the biceps brachii muscle remained incomplete until the ultrasound measures of the biceps brachii muscle thickness is tested against a gold standard criterion such as MRI, CT scan, or DEXA, in the future. Therefore, the biceps brachii muscle should be treated as a complementary site for diagnostic ultrasound muscle thickness assessment/measurement in the hemodialysis population particularly when access to the rectus femoris muscle is restricted pending validation against a gold standard criterion. The qualitative findings suggested that healthcare professionals lack and need an objective tool for the assessment and measurement of muscle status in ESRD patients that could improve education and communication with patients and escalation of patients' cases, when needed. Also, patients reported that they were willing to accept the measurement of muscle status as part of their routine renal care from trained healthcare professionals and that the data obtained from diagnostic ultrasound measurement of

the muscle could be motivational to the patient for lifestyle changes. In summary, our findings suggested that diagnostic ultrasound is a reliable objective measure of muscle thickness in ESRD patients undergoing hemodialysis. The biceps brachii muscle is the most reliable and potential upper limb alternative to the rectus femoris muscle for muscle thickness assessment, and both healthcare professionals and patients are receptive to its integration into routine renal care. However, protocol standardization, adequate rater training, and criterion validation of the biceps brachii muscle are needed for routine clinical use.

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Appendix 1

Demographic Information Sheet

Demographic Information

Patient Code: _____

Age (years):

Height (cm)

Body mass (kg)

Limb dominance (L or R):

Pre-dialysis body mass (Kg):

Post-dialysis body mass (Kg):

Mid-upper arm circumference:

Disease etiology:

Dialysis start date:



Appendix 2

Healthcare Professionals' Recruitment Poster

Study Recruitment

*We want to know about
your experience with
ultrasound*

Recruiting:

- Nephrologists
- Dieticians
- Nurses

→

Join our study exploring
healthcare professionals'
experiences with ultrasound
use in Hemodialysis

30-minute interview



A photograph of a medical ultrasound machine with a monitor and a probe.

Contact

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Appendix 3

Patients' Recruitment Poster

Study Recruitment

*We want to know about
your experience with
ultrasound*

Recruiting:

- Hemodialysis Patients

→

Join our study exploring
patients' experiences with
ultrasound

30-minute interview



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Appendix 4

Healthcare Professionals' Interview Script

Interview Script for Health care Professionals

Questions

What is your understanding of the relationship between US and nutritional status?

- Do you think an understanding nutritional status important to your practice?

Do you think that muscle ultrasound can provide meaningful results about a patient's status?

- How confident are you that upper arm sites provide meaningful data for patient nutrition status?

How comfortable are you working within an emerging measurement technique?

- How comfortable are you working without direct standards for muscle ultrasound.
- Are you comfortable relying on repeated measures and clinical judgement to interpret findings?

Do you think that muscle ultrasound will change in patients over time?

- Do you think that multiple clinicians performing measurement will change the outcomes or quality?

Given the option, would you rather ultrasound the leg or the arm?

What are your thoughts about implementing muscle ultrasound routinely or as a standard of care?

- What barriers, if any, are there to implementing muscle ultrasound into practice?
- What do you consider the benefits to be? Could these benefits outweigh the potential impact it may have on workload?

Could understanding musculature help you better understand changes to a patient's clinical picture?

In your opinion, could understanding muscle changes guide or impact your interventions as a clinician?

Do you believe muscle ultrasound can be conducted by a variety of clinicians and still yield good results?

What is your current experience using ultrasound machine in your current practice?

- How comfortable confident are you using an ultrasound machine?
- With additional training, how comfortable/confident would you be using an ultrasound machine to measure patient's muscle mass during their dialysis treatment?

What kinds of challenges have you faced in applying a protocol across different patients?

What helps ensure the technique or protocol is applied the same way across team members?

Appendix 5

Patients' Interview Script

Interview Script for Patients

Questions

Can you describe your experience with ultrasound?

Would you trust results interpretation by nurses/dieticians/physiotherapists as much as nephrologists or radiologist?

- Which team member do you consider to be the most qualified to conduct ultrasound measurements?
 - Can you explain why?

What would make this ultrasound experience better for other patients with similar conditions to yours?

Do you think this ultrasound tool would be helpful for other conditions?

Do you think a better understanding of your muscles would result in you making any changes to your diet?

How about physical activity?

Do you think this type of measurement tells your health care professionals something useful about your body?

Do you feel confident that this ultrasound method gives good information to your health care professional about your health?

Do you think conducting serial ultrasound measurements of muscle mass would be a useful tool in assessing nutritional and functional status?

Do you think this information would be helpful to guide nutrition interventions and/or treatment decisions?

How would you feel about different health care professionals conducting and explaining US assessment in your routine care?

How do you feel about having routine measurements of your muscle mass using ultrasound during hemodialysis as part of your care?

Would you be willing to have routine measurements of your muscle if the results could help to improve delivery of care provided by your renal healthcare team?

- Have you had this ultrasound test done more than once by the same health care professional?
 - Did the test feel the same each time?
 - Did different providers do the ultrasound test on you?
 - Did it feel the same regardless of who did it?

Once comfortably on the dialysis machine, how willing are you to undergo additional ultrasound measurement of your muscles?

- Would you have a preference of where your muscles are measured? The upper arm or quadriceps?

How important is it to you to understand changes in your muscles over time? Why or why not are changes in your muscles important to you?

Did your medical care team ever explain to you this ultrasound test? Did their explanations match your experience or understanding?

If you're open to muscle ultrasound, which professional would you like to see conduct muscle ultrasound on you?

- Who do you consider to be the best person to conduct this measurement? Do you think an ultrasound result could bias your care?

Would you want health care professionals to continue using this ultrasound method on other patients or hospitals?

Appendix 6

Preamble for Participants

Preamble for Healthcare Professionals

Before we begin, here is some background on muscle ultrasound and its relevance to this study. End-stage renal disease (ESRD) requiring dialysis presents complex challenges, particularly in assessing and managing nutrition. Malnutrition is common in this population and is associated with muscle wasting, reduced physical function, lower quality of life, and increased health care utilization. Assessing nutritional status in dialysis patients is multifaceted and typically involves a combination of clinical, biochemical, and functional measures.

Emerging evidence suggests that muscle size and changes in muscle mass over time may serve as useful indicators of nutritional status. Muscle ultrasound is a non-invasive, bedside tool that can provide this information; however, it is not currently used in routine practice in Thunder Bay.

This qualitative study explores the perceptions and experiences of patients and health care providers regarding the use of muscle ultrasound in the dialysis setting. The goal is to better understand its potential role in assessing nutrition-related changes and guiding care.

Preamble for Patients

Before we begin, we'd like to tell you a bit about muscle ultrasound. People with kidney failure who need dialysis often have special nutrition needs. It can be hard to know exactly what their bodies need to stay strong and healthy. When nutrition isn't right, it can lead to problems like weight loss, weaker muscles, and feeling more tired. These issues can make life harder and increase the need for medical care.

Right now, health care teams use different tests to check nutrition. One idea is to use ultrasound to look at muscle size. This might help us see if someone is losing muscle and might need changes to their diet. Although this is not something we currently use in Thunder Bay, we want to learn more about it.

This study will ask patients and staff what they think about using ultrasound to check muscles during dialysis. We want to understand if this is something that feels helpful, comfortable, and useful to them.