THE ASSESSMENT OF INTENSIVE CARE UNIT-ACQUIRED WEAKNESS IN ADULT PATIENTS AT RISK OF POST INTENSIVE CARE SYNDROME

Submitted in fulfilment of the requirements for the degree of Master of Health Sciences in Clinical Technology in the department of Biomedical and Clinical Technology, Faculty of Health Sciences at the Durban University of Technology

Noline van Vuuren

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Dr D R Prakaschandra: Date: 15 August 2024
(Supervisor-DUT)

Mr M E Memela: _____ Date: _____
(Co-supervisor-DUT)

Dr E van der Merwe: Date: 15/08/2024
(Co-supervisor-Livingstone Hospital)

AUTHOR'S DECLARATION

This study represents original work by the author. It has not been submitted to any other tertiary institution. Where the work by others is made use of, this has been duly acknowledged.

SIGNED: __ _____

Mrs Noline van Vuuren
(B. Tech: Clinical Technology)

I hereby certify that the above statement is correct.

SIGNED: _____

Dr D R Prakaschandra
(PhD)

SIGNED: _____

Mr M E Memela
(M. Tech; Clinical Technology)

SIGNED: _____

Dr E van der Merwe
(MBChB, FRCP, MMed)

DEDICATION

I dedicate this work to my two sons, Matthys and Nico van Vuuren. Hope this will inspire you two to reach for your dreams, embrace every opportunity and cherish each moment. I have no doubt that both of you will achieve greatness.

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ABSTRACT

INTRODUCTION: Intensive care unit-acquired weakness (ICUAW) is a syndrome of generalised neuromuscular weakness that develops in critically ill patients for which there is no alternative explanation other than the critical illness itself, and which has a prevalence of 25% to 80% in ICU survivors. The diagnosis and grading of ICUAW is made by excluding other causes of neuromuscular weakness and by repetitive clinical examination of muscle strength using the Medical Research Council Sum-Score (MRC-SS). The aim of the study was to evaluate ICUAW, and diagnostic methods available for this condition, in ICU survivors at risk of post intensive care syndrome (PICS) in a South African tertiary public sector hospital.

METHODOLOGY: A prospective, single-centre observational study was conducted in a multi-disciplinary tertiary ICU in Eastern Cape. Patients at risk for post intensive care syndrome were included in the study. Patients were evaluated for ICUAW at six weeks and six months post-hospitalisation with the MRC-SS and handheld dynamometry (HDD). Full criteria ICUAW is defined as an MRC-SS of less than 48 out of 60.

RESULTS: We enrolled 150 patients in the study, of which 103 patients completed the six month follow-up. At six weeks and six months, respectively, 3 and 2 patients' MRC-SS were less than 48/60. The median MRC-SS was 58/60 (IQR: 52-60) at six weeks and 60/60 (IQR: 58-60) at six months. There was an average change of 32,75% in the mean force from six weeks to six months for all muscle actions on both sides, with $p < 0.001$ indicating a significant difference. Fair correlations ($r = 03-0.5$) were observed between the MRC scale and HHD measurements for each muscle action from six weeks to six months. The correlation between the MRC scale and HHD proved to be significant ($p < 0.001$).

CONCLUSION: There is a low incidence of the full criteria of ICUAW in relatively young and previously healthy ICU survivors at risk for PICS. Both the MRC-sum scores and HHD measurements showed a significant improvement over six months and there was an acceptable correlation between them. The findings of this study indicate that the strength assessed by both methods is related and tends to change in a similar direction over time.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ABBREVIATIONS

ADFlex	Ankle Dorsiflexion
AKI	Acute kidney injury
ARDS	Acute respiratory distress syndrome
CFS	Clinical Frailty Scale
CIM	Critical illness myopathy
CIMP	Critical illness neuromyopathy
CIP	Critical illness polyneuropathy
EFlex	Elbow Flexion
FDA	Food and Drug Administration
HFlex	Hip Flexion
HGD	Handgrip dynamometry
HHD	Handheld dynamometry
HIV	Human Immunodeficiency Virus
ICU	Intensive care unit
ICUAW	Intensive care unit-acquired weakness
IQCODE	Informant Questionnaire on Cognitive Decline in Elderly
IQR	Interquartile Range
KExt	Knee Extension
LTH	Livingstone tertiary hospital
MMT	Manual muscle testing
MRC	Medical Research Council
MRC-SS	Medical Research Council Sum Score
N	Newton
NDMR	Nondepolarizing muscle relaxant
NMBA	Neuromuscular blocking agent
PI	Principal investigator
PICS	Post intensive care syndrome
SAbd	Shoulder Abduction
SAPS 3	Simplified Acute Physiology Score III
SD	Standard Deviation
SOFA	Sequential Organ Failure Assessment
WExt	Wrist Extension

CHAPTER 1: INTRODUCTION

1.1 Background and rationale

Intensive care unit-acquired weakness (ICUAW) is a syndrome of generalised neuromuscular weakness that develops in critically ill patients for which there is no alternative explanation other than the critical illness itself (Chlan *et al.* 2015). Physical impairment can have a profound impact on ICU survivors and their families because it decreases the patient's ability to perform daily tasks and may even prevent them from returning to work (Colbenson, Johnson and Wilson 2019; Qin *et al.* 2022). Diagnosing and grading ICUAW is important for counselling patients about the anticipated duration of physical recovery and appropriate rehabilitative care (Fan *et al.* 2014a).

ICUAW has a prevalence of 25% to 80% in ICU survivors and is a component of post intensive care syndrome (PICS) (Colbenson, Johnson and Wilson 2019). PICS is defined as a constellation of symptoms that include new or worsened impairment of physical, cognitive and/or mental health, which can have a negative impact on the lives of ICU survivors (Needham *et al.* 2012; Chlan *et al.* 2015; Colbenson, Johnson and Wilson 2019).

During critical illness, inflammatory and microcirculatory processes can lead to the development of myopathy and neuropathy, and as such, ICUAW is a neuromuscular manifestation of a multi-organ dysfunction syndrome (Batt *et al.* 2013). Another contributing factor is prolonged immobility (with its known association with loss of muscle mass) (Asfour 2016). Risk factors for ICUAW include longer length of ICU stay higher age, sepsis, sedation, longer duration of mechanical ventilation and multi-organ failure (Batt *et al.* 2013; van Aartsen and van Aswegen 2018; Othman *et al.* 2024).

Clinical examination shows diffuse, symmetric weakness involving all extremities, decreased tone, and deep tendon reflexes which may be normal, decreased, or absent (Stevens *et al.* 2009). International sources agree that the diagnosis and grading of ICUAW is made by excluding other causes of neuromuscular weakness and by

repetitive clinical examination using the Medical Research Council sum-score (MRC-SS) (Fan *et al.* 2014a; Kress and Hall 2014; Appleton, Kinsella and Quasim 2015).

The MRC-SS is an inexpensive tool that uses grading scales to assess muscle strength in the upper and lower extremities, and it was utilized in 84% of the studies reviewed by Fan et al. (2014a) to diagnose ICUAW. The MRC scale evaluates the strength of each muscle action and is scored a value of zero (no contraction) to five (normal power). These scores are added up to calculate an MRC-SS that range from 0 to 60, with a score of less than 48 indicating ICUAW (Connolly *et al.* 2013; Hermans *et al.* 2014; Asfour 2016). Although the MRC-SS is the most common diagnostic tool used to identify ICUAW, inter-observer agreement studies have found it lacking in sensitivity, particularly in distinguishing between grades four and five (Vanpee *et al.* 2011). Handheld dynamometry (HHD) may detect these minimal changes in a more objective manner (Bohannon 2001). A study conducted by Bohannon (2001) showed a 78.7% correlation between manual muscle testing (MMT) and handheld dynamometer measurements of knee extensor muscle strength in 128 acute rehabilitation patients. Dynamometry has been used to investigate the change in muscle strength in a South African study of 12 patients with penetrating trunk trauma which showed an overall improvement over six months, but a slower rate of recovery of the lower limb muscles (van Aswegen *et al.* 2008). In another South African study dynamometry showed an overall improvement in muscle strength of ICU survivors over six months (van Aartsen and van Aswegen 2018).

Further research to evaluate and compare performance-based measures of physical function in ICU survivors has been suggested in peer-reviewed publications (Fan *et al.* 2014a; Needham *et al.* 2017). Given the impact of neuromuscular weakness on the quality of life of ICU survivors, the lack of clear post-hospital discharge guidelines for evaluating ICUAW and a paucity of studies on the correlation of existing diagnostic tools (Stevens *et al.* 2009; van Aartsen and van Aswegen 2018), further research in this field is imperative. Evaluating the correlation between MRC scale and HHD will add to the existing body of research which ultimately informs clinical practice related to the diagnosis and follow-up of ICUAW.

1.2 Aims and objectives

1.2.1 Aims of the study

The aim of the study was to evaluate ICUAW and diagnostic methods available for this condition in ICU survivors in a South African tertiary public sector hospital, who are at risk of PICS.

1.2.2 Study objectives

1. To assess the incidence of ICUAW among ICU survivors at risk of PICS at six weeks and six months after hospital discharge as measured by the MRC-SS.
2. To compare the changes observed in muscle power, as measured by the MRC scale and HHD, at six weeks and six months following hospital discharge.
3. To investigate the correlation between the MRC scale and HHD measurements.

1.3 Flow of dissertation

Chapter 1 – Introduction: This chapter serves as an introduction to ICUAW, outlines the aims and objectives, and provides the rational for the study.

Chapter 2 – Literature Review: This chapter provides an overview of the current research in the field of ICUAW comprising pathophysiology, risk factors, diagnosis, and treatment.

Chapter 3 – Materials and Methods: This chapter presents and explains the design, materials and methods used to collect information and conduct the statistical analysis of the study, while upholding the ethical considerations of the participants.

Chapter 4 – Results: In this chapter, the results and findings of the study are presented in accordance with the study objectives.

Chapter 5 – Discussion: This chapter is a discussion of the results in the context of the study objectives, and existing literature.

Chapter 6 – Conclusion: This chapter summarises and synthesises the key findings, insights, and implications of the study.

CHAPTER 2: LITERATURE REVIEW

With the advances in critical care medicine there has been an increase in the number of ICU survivors. However, 30% to 80% of these survivors suffer from long-term complications (Colbenson, Johnson and Wilson 2019). Needham *et al.* (2012) describe PICS as a constellation of new or worsened impairments of physical, cognitive, and/or mental health which are not related to the ICU admission diagnosis and are therefore unexpected and may last years after ICU discharge.

ICUAW is the best known physical impairment associated with PICS and is defined as the development of severe limb weakness due to critical illness (Chlan *et al.* 2015). Twenty-five to eighty per cent of ICU survivors are at risk of developing physical impairment while in ICU (Colbenson, Johnson and Wilson 2019). Prolonged mechanical ventilation, immobility, malnutrition, oversedation and systemic inflammation are just some of the risk factors that are associated with the development of ICUAW (Chlan *et al.* 2015; Asfour 2016).

Physical impairment can have a profound impact on ICU survivors and their families because it decreases the patients' ability to perform daily tasks and may even prevent them from returning to work (Colbenson, Johnson and Wilson 2019; Qin *et al.* 2022). Previous research has shown that ICU survivors can have muscle weakness and impaired functional status for years after hospital discharge (Asfour 2016).

2.1 Pathophysiology and risk factors for ICUAW

Fan *et al.* (2014a) describe ICUAW as a syndrome of generalised weakness that develops while the patient is critically ill, and for which there is no alternative explanation other than the critical illness itself. Muscle biopsies from the early 1990s have already shown that critically ill patients experience muscle wasting due to muscle protein loses and/or a reduction in the muscle fibres (Griffiths and Jones 2007). Muscle weakness can be attributed to different pathologies such as critical illness myopathy (CIM), characterised by symmetrical limb and respiratory muscle weakness; critical illness polyneuropathy (CIP), defined as symmetric, distal sensory-motor axonal polyneuropathy affecting the limbs, respiratory, sensory, and autonomic nerves; or a

combination of both, referred to as critical illness neuromyopathy (CIMP) (Jolley, Bunnell and Hough 2016; Intiso *et al.* 2022; Qin *et al.* 2022). It is often impossible to identify the predominant pathology causing the weakness, and therefore Appleton, Kinsella and Quasim (2015) proposed the term 'intensive care unit acquired weakness' be used for the clinical syndrome.

Although critical illness itself can be the reason for ICUAW, there are various other aspects that can contribute to the risk factors associated with ICUAW (Kress and Hall 2014). Several studies have reported that critically ill patients experience a decrease of 2% of muscle mass per day due to severity of illness, which may include organ dysfunction, sepsis as well as immobility and prolonged ventilation (Farhan *et al.* 2016; Fazzini *et al.* 2023). The muscles of critically ill patients undergo structural changes that can affect the mitochondrial function, which in turns plays a critical role in the pathogenesis of ICUAW (Jolley, Bunnell and Hough 2016; Wang *et al.* 2020; Voiriot *et al.* 2022). Herridge *et al.* (2003) observed a reduction of 18% body weight from baseline in their cohort of 109 patients with acute respiratory distress syndrome (ARDS) at hospital discharge. Although immobility and mechanical ventilation are not necessarily mutually exclusive, many patients in ICU are immobile and it has been observed that ventilation for more than seven days can contribute to the incidence of ICUAW (Fan *et al.* 2014a). Fan *et al.* (2014a) conducted a meta-analysis that identified 14 studies showing that the longer patients were exposed to mechanical ventilation, the higher the incidence of ICU-acquired weakness.

Muscle weakness is more common in patients with sepsis due to the fact that proinflammatory cytokines interfere with the signalling pathways that regulate muscle mass (Yang *et al.* 2018). Recent literature has found severity of illness, neuromuscular blockage, aminoglycosides, female, multiple organ failure, systemic inflammatory response syndrome, sepsis, electrolyte disturbances, hyperglycaemia, hyperosmolarity, high lactate level, duration of mechanical ventilation, parenteral nutrition and use of norepinephrine to be significantly associated with ICUAW (Kress and Hall 2014; Yang *et al.* 2018; Wang *et al.* 2020).

Brunello *et al.* (2010) reported that 30% of ICU patients are exposed to steroids. Steroids promote the breakdown of muscle protein and inhibit protein synthesis which leads to muscle wasting, inhibits muscle growth and repair (Farhan *et al.* 2016).

Currently the benefits of steroid use may outweigh the risk factors, but it is recommended that steroids be prescribed at the lowest appropriate dose and duration for recognised indications (Farhan *et al.* 2016; Qin *et al.* 2022). Steroid treatment has become a standard part of the treatment for patients with severe COVID-19 (Qin *et al.* 2022).

Neuromuscular blocking agents (NMBAs) induce muscle relaxation at the neuromuscular junction and are used in emergency situations in ICU (Wang *et al.* 2020). Although NMBAs are considered a risk factor for muscle weakness, they are recommended for use in ARDS patients to facilitate protective mechanical ventilation (Papazian *et al.* 2010).

Several other risk factors that are not directly related to ICU admission are also considered to be associated with ICUAW, such as age and gender (Boelens, Melchers and van Zanten 2022). According to Pfoh *et al.* (2016), old age and pre-ICU comorbidity were associated with physical decline post-ICU because muscle mass decreases and the contractility of the muscle declines (Chlan *et al.* 2015; Asfour 2016). While there is no definitive consensus on the association between gender and ICUAW, females physiologically have lower muscle strength than males, and females receiving hormonal therapy can also have reduced muscle strength (De Jonghe *et al.* 2002).

2.2 Diagnosis of ICUAW

According to Stevens et al. (2009), although several methods can be used to diagnose ICUAW in critically ill patients, including MRC-SS, HHD, and handgrip dynamometry, none of them are considered the gold standard. The authors recommended that a simple diagnostic criteria should be used in the diagnosis of ICUAW (Stevens *et al.* 2009). According to this criteria, the patient's weakness should follow the onset of critical illness and not be related to any other underlying causes, and the weakness should be symmetric involving both upper and lower extremities (Stevens *et al.* 2009; Fan *et al.* 2014a). MRC-SS is the most common test used to evaluate neuromuscular weakness, and ICU-AW is defined by an MRC-SS of less than 48 or a mean score of less than four across all testable muscle actions (Fan *et al.* 2014a; Asfour 2016; Bohannon 2019).

The MRC-SS (Appendix 3) is an inexpensive tool that assess and grades the muscle strength based on the patient's effort to overcome resistance in the upper and lower extremities (Bohannon 2019). This tool has been extensively utilized in research for the diagnosis of ICUAW. (Fan *et al.* 2014a). Each muscle action is scored a value of zero (no contraction) to five (normal power); these scores are added up to calculate a total sum score of out of 60, and a score of less than 48 indicates ICUAW (Connolly *et al.* 2013; Hermans *et al.* 2014; Asfour 2016). For the assessment of muscle weakness using the MRC-SS to be accurate, the patient must be conscious and cooperative, and the examiner should give clear instructions and motivate the participant to try and achieve their maximum effort (Connolly *et al.* 2013).

Several studies have investigated the inter-observer variability of the MRC-SS and confirmed that there is a moderate to good agreement between investigators (Hermans *et al.* 2011; Connolly *et al.* 2013). But is has been reported that investigators own strength can be limited to provide an adequate counter force in very strong patients (Michalski *et al.* 2022). However, one study found that although there may be good inter-observer agreement, patient effort variability can be the cause of errors (Connolly *et al.* 2013). Hough, Lieu and Caldwell (2011) screened 135 critically ill patients for muscle weakness using the MRC-SS, but 62 patients were excluded from the final assessments because they could not be tested due to non-muscular factors such as delirium or the extent of their injuries. For this reason, they concluded that although MRC-SS is a useful tool for assessing weakness, it is insufficient for detection of ICUAW during early admission (Hough, Lieu and Caldwell 2011). Inter-observer agreement studies have also noticed that the MRC-SS is limited in its sensitivity to distinguish between grades four and five and authors recommend that additional measurement tools be used to determine the strength changes in these muscles (Bohannon 2001; Vanpee *et al.* 2011).

HDD uses a handheld device that measures the force generated over a particular time by a muscle group and may be a more objective tool to quantify muscle strength (Bohannon 2001). Measurements are performed with gravity eliminated and patients are instructed to exert an increasing effort against the HHD. It is important for the examiner to provide adequate stability and use the same point of reference for resistance (Bohannon 2019). A testing procedure (Appendix 4) that provides clear

guidelines on the positioning of the patient, dynamometer placement and subject stabilisation has been recommended by several studies that have used HHD to establish normal values (Andrews, Thomas and Bohannon 1996; Bohannon 1997; Douma *et al.* 2014). Several studies have reported in the reliability and validity of HHD and have concluded that both are dependent on the strength of the tester to counter the effort of the patient (Bohannon 2019). Vanpee *et al.* (2011) concluded in their study that HHD is a valid tool to measure peripheral muscle strength in patients that can overcome gravity, and as with MRC-SS patients, who are conscious and co-operative. HHD may detect the minimal changes in muscle strength in a more objective manner than the MRC-SS (Bohannon 2001). Using a standardized protocol alongside HHD increases its reliability (Kim *et al.* 2014). It is relatively expensive and therefore less accessible for many healthcare facilities especially in budget constraint and limited resource countries(van Aswegen *et al.* 2008; Bohannon 2019).

Although the MRC-SS and HHD scored high in a round-table consensus statement, experts do not agree on the ideal test for identifying ICUAW in the follow-up of ICU patients (Needham *et al.* 2017). Electromyography and nerve conduction studies are considered to be superior methods to diagnosis muscle weakness as these tests can detect muscle weakness within 24 to 48 hours and can identify the underling pathology causing the muscle weakness (Wang *et al.* 2020). Since electromyography and nerve conduction are invasive, expensive, require technical expertise and are not routinely available, these are infrequently used in clinical practice to diagnose ICUAW (Kramer 2017; Wang *et al.* 2020). The American Thoracic Society statement on ICUAW recognised that many institutions may not be adequately resourced to deliver a comprehensive approach using these methods (Fan et al., 2014a). Nerve and muscle biopsies are only recommended for scientific research as they are invasive and can cause many complications (Wang *et al.* 2020).

2.3 Prevention and treatment of ICUAW

A study that reviewed the pharmacological therapy for the prevention and treatment of weakness after critical illness concluded that there is no pharmaceutical therapy available to treat ICUAW (Shepherd *et al.* 2016). Despite the lack of pharmaceutical options available to treat ICUAW several studies have recommended early physical and occupational therapy (Jolley, Bunnell and Hough 2016). According to (Zang *et al.*

2020), early mobilisation in ICU can reduce the incidence of ICUAW weakness, thereby reducing the occurrence of lasting muscle weakness after discharge. Several studies have recommended rehabilitation programmes, but their availability depends on how well-resourced the particular clinical setting is (Morgan 2021).

2.4 Effect of ICUAW on the recovery of ICU patients

Although there is a lack of treatment options and limited access to rehabilitation therapies, 55% to 70% of ICU survivors do make a full recovery over time (Intiso *et al.* 2022). Several studies have reported on the incidence of ICUAW, but only a few of them reported on the recovery and functional outcomes of the survivors (Intiso *et al.* 2022). ICUAW can have both short- and long-term implications for ICU survivors, including lower quality of life, functionality and ability to return to work (Asfour 2016; Boelens, Melchers and van Zanten 2022; Qin *et al.* 2022). This change in quality of life can also lead to psychological dysfunction for both the patient and their families (Van Aerde *et al.* 2020). It has been reported that ICU survivors may have a physical weakness for up to five years after discharge (Herridge *et al.* 2011),

2.5 Studies emanating from the South Africa

The literature review has identified a substantial knowledge gap pertaining to the evaluation of physical impairment in ICU survivors worldwide, and even more so in the South African public health sector. A recent scoping review that aimed to quantify the burden of PICS in the South African public health sector identified only two publications that studied neuromuscular weakness (Van der Merwe and Paruk 2022). These included a small pilot study (three patients after attrition), and a subsequent follow-up study of 23 patients (after attrition), both of which explored the physical limitations in young predominantly male ICU survivors after penetrating trunk trauma (van Aswegen *et al.* 2008; Van Aswegen *et al.* 2010). Lastly, there was a research dissertation conducted in the private health care sector in SA, which reported on the neuromuscular performance of 11 patients six months after discharge (Van Aartsen 2016). These three small studies used HHD to evaluate muscle strength and generally found that patients improved significantly over six months, and that there was no difference in strength between the study group and the control group, except if ventilated for five or more days.

From reviewing the literature, it is clear that neuromuscular weakness is common after critical illness and that it may have a profound impact on patients' lives after hospital discharge. There is no consensus on the optimal method of diagnosis of ICUAW, and it is unclear if HHD may add value over clinical examination. Further research to evaluate and compare performance-based measures of physical function in ICU survivors have been suggested in peer-reviewed publications (Fan *et al.* 2014a; Needham *et al.* 2017). Furthermore, there is a paucity of South African studies in this field, and they have small numbers of participants. This study aimed to add to this field of research by investigating the incidence and trajectory of neuromuscular weakness in ICU survivors from an Eastern Cape tertiary hospital, and by correlating two diagnostic methods.

CHAPTER 3: MATERIALS AND METHODS

The primary aim of the research was to evaluate ICUAW and diagnostic methods available for this condition in ICU survivors at risk of PICS in a South African tertiary public sector hospital. The first objective of the study was to assess the incidence of ICUAW among ICU survivors at risk of PICS at six weeks and six months after hospital discharge as measured by the MRC-SS. The second objective was to compare the changes observed in muscle power, as determined by the MRC scale and HHD, from six weeks and six months following hospital discharge. Lastly, the third objective focused on establishing if there was a correlation between the MRC scale and HHD measurements.

3.1 Study design

This was a single-centre prospective observational cohort study. This study was nested in a PhD study regarding the general occurrence and co-occurrence of symptoms of PICS and health-related quality of life in ICU survivors at risk of PICS. The current study focuses on one aspect of PICS, namely intensive care unit-acquired weakness (ICUAW). The incidence of ICUAW after hospital discharge and the diagnostic methods available to diagnose this condition are explored.

3.2 Study population

The Livingstone Tertiary Hospital (LTH) is a provincial government-funded hospital in Gqeberha, Eastern Cape (South Africa) and serves 1.6 million people of which 1.15 million live in urban settings and informal dwellings (Africa 2014). The adult ICU is a closed, multi-disciplinary 16-bed unit, incorporating four step-down/high care beds. Previously, the ICU admitted an average 800 patients per year. However, since COVID-19, the admission numbers have declined due to staff shortages. Due to resource constraints in the public sector, patients referred to ICU are triaged based on national and local guidelines. Therefore, patients are less likely to be admitted to the ICU if they have a higher frailty, advanced chronic disease, and irreversible organ damage.

3.3 Sample strategies

3.3.1 Participants

Consecutive patient sampling was conducted in the LTH ICU to identify critically ill patients who stayed for more than 48 hours with a shocked state, organ failure, or received respiratory support during that time, and did not have a physician-diagnosed neurological condition on admission that manifests with neuromuscular weakness. Subsequently, we commenced with recruitment and enrolled consented patients into the study until we had reached our estimated sampling size.

3.3.2 Sample size

The sample size, estimated using the Yamane calculation, was determined in consultation with a biostatistician.

$$n = \frac{N}{1 + Ne^2}$$

Where n is the sample size, N is the population size, and e is the error limit (Israel 1992; Singh and Masuku 2014).

To calculate the sample size (n) using Yamane's formula with a population size (N) of 849 and a desired precision level (e) of 10% (which is 0.10 as a proportion):

Substitute the given values:

$$n = \frac{846}{1 + 846(0.10^2)}$$

$$n \approx 89.41$$

Rounded to the nearest whole number, the sample size (n) is approximately 89.

Therefore, according to Yamane's formula, with a population size (N) of 849 and a desired precision level (e) of 10%, the recommended sample size is approximately 89 individuals.

In addition, the observed attrition rate in studies of ICU survivors (due to death, non-attendance, and other reasons) is unpredictable but may be as high as 25% to 56% (Cuthbertson *et al.* 2005; Marra *et al.* 2018). The attrition was more than 40% in one South African study (van Aswegen *et al.* 2011). Considering the reported attrition rates,

we enrolled 150 patients to analyse at least 75 patients. Seventy five patients, after “worst case scenario” attrition, with a conservatively estimated PICS incidence of 25%, was considered adequate to test for association (VanVoorhis and Morgan 2007).

3.3.3 Inclusion criteria

The following criteria were used to select and enrol patients into this study:

1. Patients who received respiratory support (defined as invasive, non-invasive, or high flow nasal oxygen) for 48 hours or more
2. Patients who stayed in ICU > 48 hours with shocked states and /or organ failure

3.3.4 Exclusion criteria

The following criteria were used to exclude patients from the study:

1. Patients younger than 18 years
2. Prisoners
3. Moribund or life expectancy less than six months at the time of screening
4. Residing more than 300 km from enrolling centre
5. Patients who cannot be interviewed in English or Xhosa
6. Active psychosis at the time of admission
7. Patients who are suspected to have pre-existing cognitive impairment as measure by the Short Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE) (Quinn *et al.* 2014)
8. Patients with central neurological admission diagnosis
9. Cardiac arrest with physician-diagnosed anoxic brain damage
10. Homeless patients
11. Patients who are admitted with neuromuscular weakness and spinal cord injury
12. Significant recent ICU time (receipt of mechanical ventilation in the 2 months before the current admission)
13. ICU admission > 5 ICU days in the month before the current ICU admission
14. Long-stay patients admitted after the final enrolment date will be excluded due to practical timeline constraints.

3.4 Data collection methods and procedures

Patient demographics and clinical data was collected upon enrolment in the study and were captured on a data collection sheet (Appendix 1). A full medical history from the patient or their family confirmed that the admission symptoms and previous history did not include any neuromuscular weakness. Patients were invited to attend an ICU follow-up clinic at six to eight weeks and six months post-hospital discharge.

At both the six week and six month follow-up, demographic and clinical information was verified for each patient. Patients were assessed for ICUAW using the MRC-SS (MRC score < 48/60). HHD (measured in Newtons) was used to measure peripheral muscle strength in the same muscle groups that were assessed during the MRC-SS. All data collected was recorded on data collection sheet (Appendix 1). All data collected was captured in a deidentified Excel spreadsheet that was used for the data analysis.

3.5 Outcome measures and instrumentation

3.5.1 Clinical Frailty Scale

The Clinical Frailty Scale (CFS) is a nine-point scale that serves as a valuable tool in evaluating the level of frailty (Appendix 2). The higher the level of frailty, the more likely it is that the patient will experience complications or poorer recovery in the ICU (Rockwood and Theou 2020; Qin *et al.* 2022). This scale can be used to determine the appropriate care and interventions for each patient based on their functional status (Church *et al.* 2020). The CFS is used as a triage tool in resource limited settings. During the COVID-19 pandemic waves, when hospitals were overwhelmed, CFS was an even more important triaging tool than under normal circumstances (Labenz *et al.* 2020).

3.5.2 Medical Research Council scale

The MRC-SS assesses the muscle strength of three muscle groups in the upper and lower limbs (Appendix 3) for all patients at both time intervals. Each muscle is graded a score on scale of zero (no muscle contraction) to five (normal muscle contraction). A maximum score out of 60 is calculated, with a score of less than 48 indicating ICUAW (Hermans *et al.* 2014; Asfour 2016). The patient was sitting on the edge of the bed with their feet dangling for the following assessment: shoulder abduction, elbow flexion,

wrist extension and knee extension. They were in a supine position for the hip flexion and ankle dorsiflexion. The test was repeated if the patient did not understand the instructions or did not apply the maximum effort (Ciesla *et al.* 2011).

3.5.3 Handheld dynamometer

HHD is a portable isometric handheld device that measures the force of a muscle action in Newtons. We used the MicroFET2 HHD (Hogan Health Industries, Inc. 8020 South 1300 West, West Jordan, USA) to measure peripheral muscle strength for each muscle group assessed by the MRC-SS in all patients at both follow-up time intervals. The PI followed a testing procedure that provided guidance on patient and dynamometer positioning and used the 'make' technique to apply adequate resistance as a counterforce for the patients' effort (Appendix 4). The PI gave clear instructions to the patient about what was expected of them and conducted a practice run on the first muscle action tested to familiarise them with the procedure, without applying any force during the practice run. The patient was instructed to apply maximal force against the device for a minimum of four to a maximum of ten seconds, while the PI applied a stable counterforce. Testing was aborted immediately if the patient experienced any discomfort or pain. A patient's HHD measurements were compared to the predicted values (Appendix 5) of healthy subjects relative to age, gender, and dominant/non-dominant side (Bohannon 1997).

The MicroFET2 was stored in a hard-sided protective carrying case and comes with a calibration certificate to confirm proper calibration at the time of shipment (Appendix 6). The device is FDA approved and has previously been used for studies conducted internationally and in South Africa.

3.5.4 Interobserver reliability

To ensure reliability and validity, the MRC-SS were conducted by one doctor (PI of the PhD Study), while the HHD measurements were performed by the PI. In certain cases where the PI could not counter the strength of the participant a male doctor had to perform the HHD measurement. Both the PI and male doctor used the protocol outlined in Appendix 4 for assessing muscle strength test using the HHD and the PI observed the technique of the male doctor with each participant to ensure that he followed the protocol correctly. The MRC-SS scale measurements were kept blinded until after the

completion of the HHD measurements. This enhances the reliability and validity of the muscle strength measurements obtained with the HHD.

3.6 Data analysis

Data was captured and entered in a deidentified Excel spreadsheet. Deidentified data was send to the biostatistician and analysed with RStudio, 2015. Descriptive statistics (demographics, clinical admission, and follow-up data) were used to summarise categorical and continuous variables in a format suitable for illustrating the results. Continuous data was tested for normality using the Kolmogorov-Smirnov test. Distributed data was reported as means (standard deviation) and skewed data as medians (interquartile ranges). Discrete data was presented as numbers (percentages). Demographic and clinical data were analysed using the Student's t-test for parametric continuous variables, the Mann-Whitney U test for non-parametric continuous variables, and the chi-square test for categorical variables, except where cells in a 2x2 table had fewer than five counts. The change in ICUAW was measured by the MRC-SS and HHD (Newtons) as per defined muscle actions, at six weeks and six months after hospital discharge. Pearson’s correlation coefficients were calculated for the MRC scale and HHD measurements for each muscle action to establish whether the relationships between these variables were significant. In this type of analysis, a Pearson correlation coefficient (r) is considered statistically significant at a p-value of smaller than 0,05 for a sample size of 103. Furthermore, for practical significance, irrespective of the sample size, a correlation coefficient (r) of 0,30 or greater, is deemed significant, both statistically and practically (Gravetter and Wallnau 2009). A Pearson’s coefficient of > 0.8 is considered very strong, 0.6-08 moderately strong, 0.3-0.5 fair and less than 0.3 poor (Chan 2003).

3.7 COVID-19 guidelines

The study was influenced by the COVID-19 pandemic, and we had to implement and uphold COVID-19 protocols to ensure staff and patient health.

3.7.1 Enrolment

Some of the participants were enrolled in the study while they were still admitted in the COVID ICU unit. Personal protective equipment was worn by the investigator during

the interview and all equipment was cleaned afterwards. The informed consent document was placed in a plastic sleeve and stored in a locked cupboard in the investigator's office. This was filed with the data collection sheet at a later stage.

3.7.2 Follow-up visits

Patients were phoned a week before their visit to remind them about the appointment and to find out from them if they were experiencing any COVID-19 symptoms. They were advised to reschedule their appointments if they were experiencing any symptoms. Security was informed daily of the participants that would attend the clinic to ensure that they were granted direct access to a non-COVID section of the ICU. Upon arrival at the hospital all patients were screened for COVID-19, and temperatures were taken. During the visit hands were sanitised regularly, and everyone was wearing masks. All equipment was cleaned thoroughly after each visit.

3.8 Ethical considerations

Full ethical approval (IREC 135/21) was granted by the Durban University of Technology Institutional Research Ethics Committee for this research proposal (Appendix 7). Permission to conduct the study in Livingstone Tertiary Hospital was obtained from the Eastern Cape Health Research Committee (Appendix 8) and Livingstone Tertiary Hospital Senior Management (Appendix 10). Ethical clearance (H20-HEA-PSY-001) had already been obtained for the PhD study from the Nelson Mandela University REC-H (Appendix 11).

3.8.1 Informed consent and anonymity

The study aimed to uphold the four principals of ethics namely autonomy (respect for patient rights), beneficence (the research should benefit the patients and contribute to their welfare), non-maleficence (to cause no harm to the patients and the benefits should outweigh the risks), and justice (all patients should be treated fairly and equally) (Varkey 2021). Furthermore, it adhered to the principles of the Helsinki declaration in the execution of this study ("World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects," 2013)

The following measures were followed to adhere to above principles:

- All potential candidates were interviewed, and a patient information sheet was supplied (Appendix 12) prior to enrolment.
- Written informed consent (Appendix 13) was obtained from all the patients when they agreed to participate in the study. They were given the opportunity to ask any questions in case the information sheet was unclear. They were also reminded that they can withdraw from the study at any time without prejudice or penalty. They would not be asked to explain their reason for withdrawal.
- Patients were asked if they are fluent and comfortable to be interviewed in English. If not, they were given a Xhosa patient information sheet (Appendix 14) and a Xhosa speaking medical doctor was asked to conduct the study interview in Xhosa and obtain the informed consent (Appendix 15).
- Patients who defaulted on follow-up dates were phoned to remind them of the follow-up date and to ensure that symptomatic avoidance was not a reason for non-attendance. Voluntary withdrawal from the study, however, was respected by the study leader.
- Adhered to the recommended exclusion criteria.
- Data sheets were kept in a locked cupboard in a locked office in the hospital. Only de-identified data was shared with the statistician.
- To minimise exposure to COVID-19 for the study subjects, they were seen individually at a consultation room at a specific time. Their files were prepared beforehand, therefore avoided sitting in queues and problems associated with accessing their files.

The patients could access their study results upon request to the PI or co-investigators. The statistician was presented with deidentified data for the analysis of the results to uphold anonymity.

CHAPTER 4: RESULTS

The primary aim of the research was to evaluate ICUAW and diagnostic methods available for this condition in ICU survivors at risk of PICS in a South African tertiary public sector hospital.

The first objective of the study was to assess the incidence of ICUAW among ICU survivors at risk of PICS at six weeks and six months after hospital discharge as measured by the MRC-SS. The second objective compared the changes observed in muscle power, as determined by the MRC scale and HHD, from six weeks and six months following hospital discharge. Lastly, the third objective focused on establishing a correlation between the MRC scale and HHD measurements.

4.1 Introduction

This was a single-centre prospective observational cohort study that was performed at LTH in Gqeberha, South Africa between 1st August 2020 and 20th May 2022. Enrolment commenced shortly after the peak of the first local COVID-19 wave, and the study period included the second and third waves of the pandemic. To provide context, Figure 4.1 offers a concise overview of the weekly laboratory-confirmed COVID-19 cases in the Eastern Cape Province, classified by district, from 3rd March 2020 to 21st May 2022 (Diseases 2022).

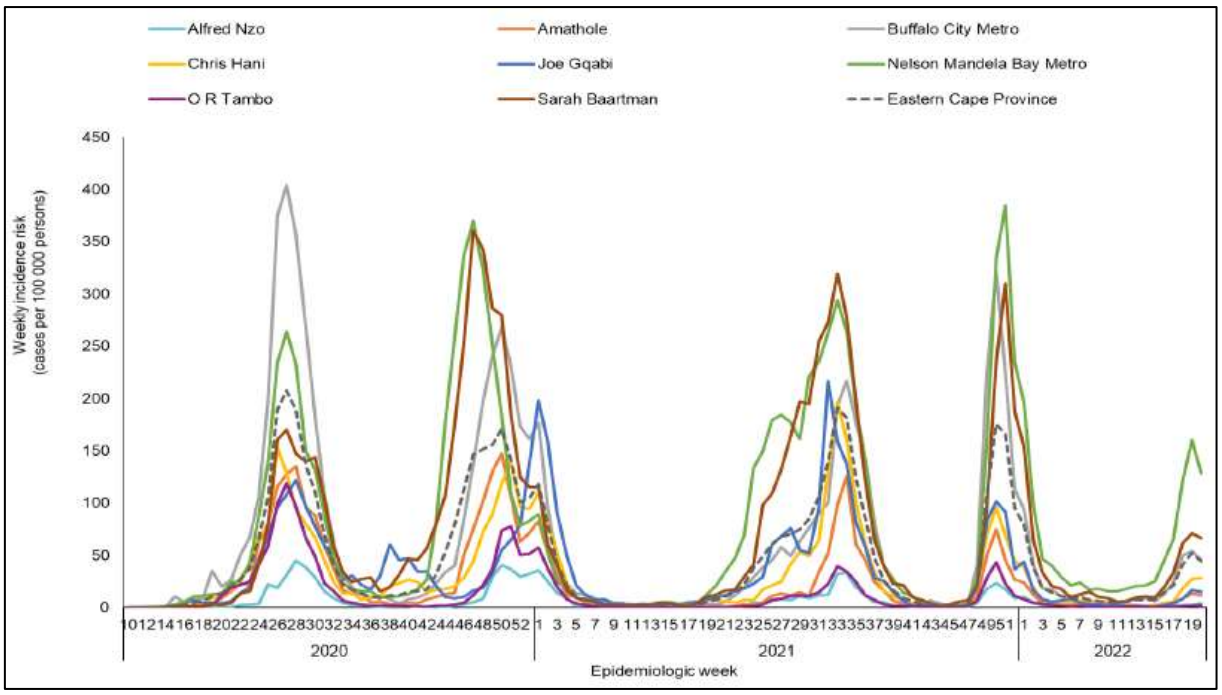


Figure 4.1: Weekly incidence risk of laboratory-confirmed cases of COVID-19 in the district of Eastern Cape Province
Source: (Diseases 2022)

Throughout the study period, a total of 679 critically ill patients were screened as potential participants, with 201 individuals meeting the inclusion criteria. Consent was obtained from 150 participants, who were subsequently enrolled in the study. However, due to various factors such as mortality after enrolment and other reasons for attrition during the follow-up visits, 103 participants completed their six months visit and their results was included in the final data analysis (Figure 4.2). A comprehensive overview of the contributing factors for excluding 478 patients from enrolment are summarised in the pie chart (Figure 4.3).

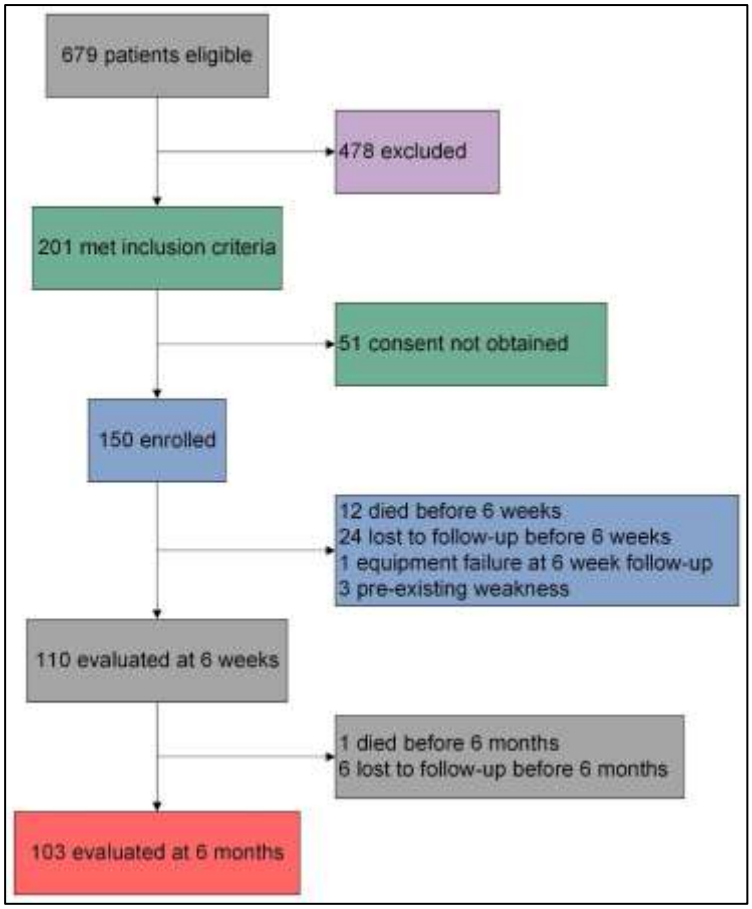
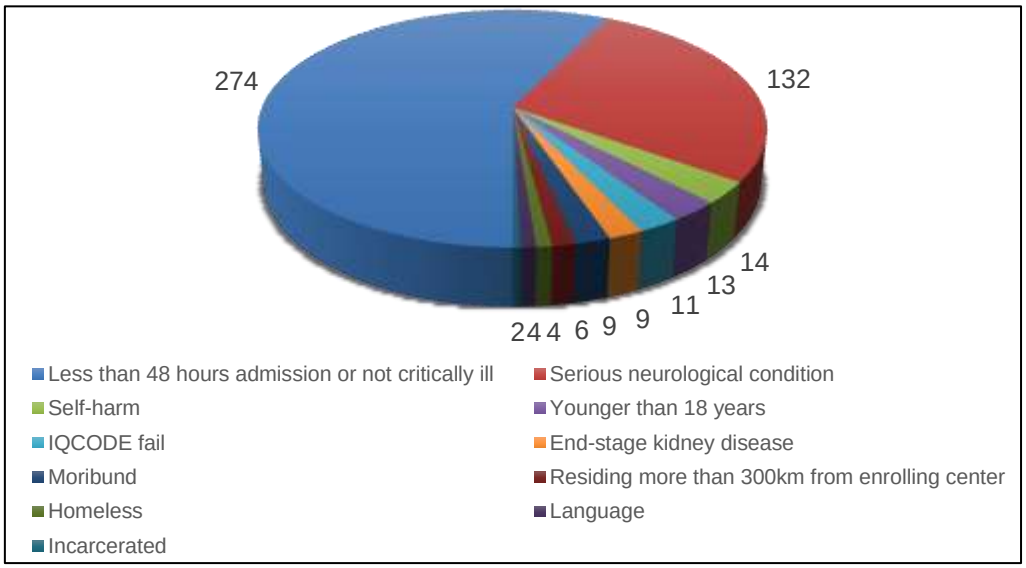


Figure 4.2: Flow diagram presenting patient enrolment and evaluation throughout the study



Data expressed as numbers. IQCODE = Informant Questionnaire on Cognitive Decline in Elderly

Figure 4.3: Pie chart summarising the contributing factors for exclusion from the study

4.2 Baseline demographics and comorbidities

One hundred and three patients completed the six month follow-up and were included in the final analysis of the data. Table 4.1 shows the baseline demographics and comorbidities for the study group.

Table 4.1: Baseline demographics and comorbidities of the study group

Demographics	**All patients *n* = 103**
Baseline	
Age, mean years (SD)	42 (12)
Female, n (%)	56 (54)
Right handed, n (%)	90 (87)
Unemployed pre-ICU, n (%)	21 (21)
Pre-Admission	
Hypertension, n (%)	36 (35)
Diabetes mellitus, n (%)	21 (20)
HIV positive, n (%)	9 (9)
Clinical Frailty Scale, median score (IQR)	2 (2-2)

SD = Standard Deviation, ICU = Intensive Care Unit, HIV = Human Immunodeficiency Virus, IQR = Interquartile Range

The study group had a mean (SD) age of 42 (± 12) years, and 54% were females. The Kolmogorov-Smirnov test of normality confirmed a normal distribution for age distribution (K-S test statistics (D) is 0.090, p = 0,357). The age distribution of the study patients is presented on the histogram and the curve indicates the frequency distributions (Figure 4.4). The cohort included 21 (20%) patients with preexisting diabetes, 36 (35%) with hypertension, and 9 (9%) were HIV positive. The CFS is a comprehensive 9-point scale that quantifies frailty by assessing function in individual patients and is used as a triage tool in resource limited settings (Appendix 2). The median (IQR) CFS score for our patient cohort was 2 (2-2).

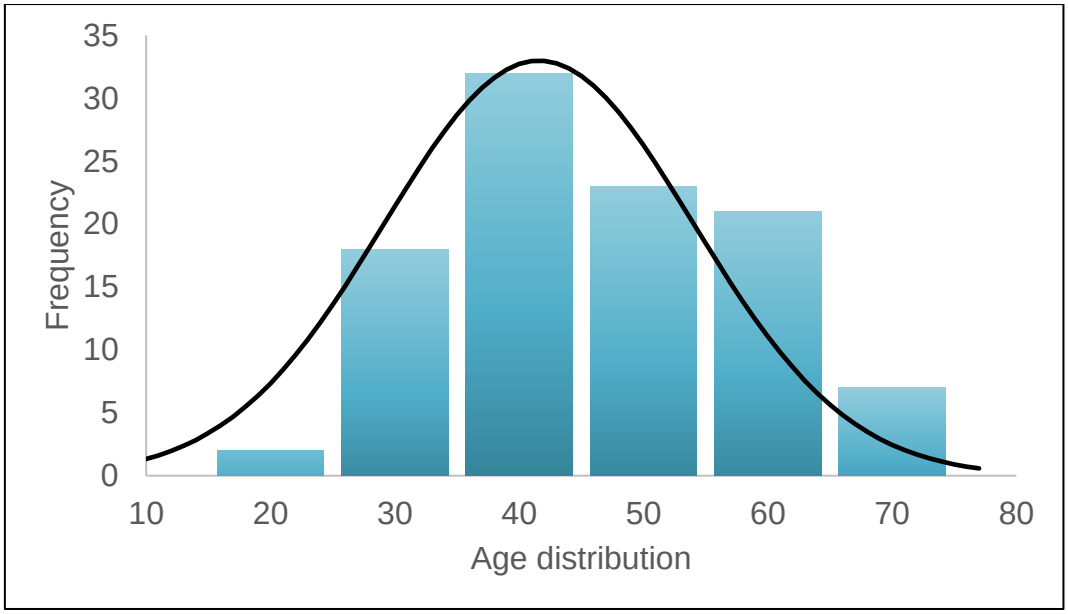


Figure 4.4: Histogram of the cohort age distribution

4.3 Admission and in-hospital data

The admission and in-hospital data of the patients are presented in Table 4.2. Most patients were admitted for medical emergencies (61%), while trauma (21%) and surgery (18%) were other reasons for admission. Of the study participants, 49 (48%) were admitted for COVID-19 pneumonia. The mean (SD) simplified acute physiology score III (SAPS 3) was 50.28 (± 11), and the median (IQR) maximum sequential organ failure assessment (SOFA) was 4 (4-9).

Among the 42 patients who required mechanical ventilation, 18 patients (43%) required ventilation for a period exceeding seven days. The median (IQR) length of stay in the intensive care unit (ICU) was 7 (5-13) days. Furthermore, the median (IQR) hospital stay for these patients was 23 (13-36) days. During their admission, patients developed various complications including acute respiratory distress syndrome (ARDS) 73 (71%) and sepsis 84 (82%), and 23 (22%) of the patients with sepsis developed septic shock. Acute kidney injury (AKI) was present in 56 (54%) of the patients. A total of 35 patients (34%) had ICU infections that required antibiotic treatment, 30 patients (29%) received vasopressor treatment to manage low blood pressure, and 28 patients (27%) required treatment for hyperglycaemia. ICUAW was diagnosed in 30 (29%) patients in ICU.

Table 4.2: Admission and in-hospital data of the study group

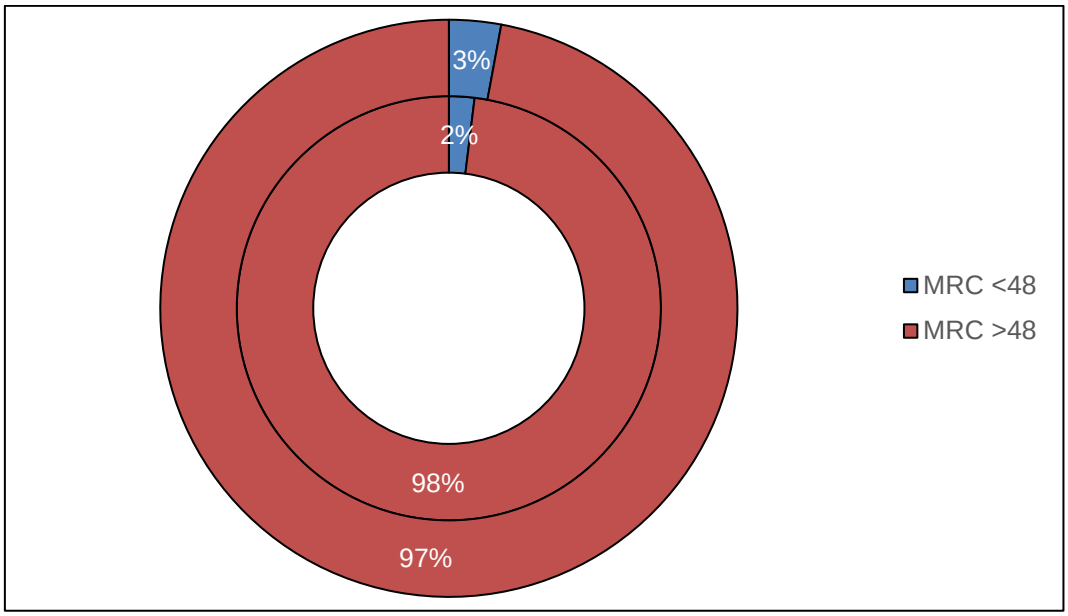
Characteristic	All patients *n* = 103
Referring discipline and diagnosis	
Medicine, n (%)	63 (61)
COVID-19, n (%)	49 (48)
Surgical, n (%)	19 (18)
Trauma, n (%)	21 (20)
Severity of illness	
SAPS 3 score, mean (SD)	50 (11)
Admission SOFA score, median (IQR)	4 (4-8)
Maximum SOFA score, median (IQR)	4 (4-9)
Respiratory support	
Ventilated, n (%)	42 (46)
Ventilated days, mean (SD)	5 (12)
Ventilated > 7 days (n = 42), n (%)	18 (43)
Non-invasive respiratory support, n (%)	56 (54)
Non-invasive respiratory support days, mean (SD)	4 (4)
Length of stay	
ICU days, median (IQR)	7 (5-13)
Hospital days, median (IQR)	23 (14-36)
Other complications	
ARDS, n (%)	73 (71)
AKI, n (%)	56 (54)
Hyperglycaemia, n (%)	28 (27)
Sepsis (community acquired / nosocomial), n (%)	84 (82)
Septic shock, n (%)	23 (22)
ICU acquired infection, n (%)	35 (34)
ICU acquired weakness, n (%)	30 (29)
ICU drugs	
Vasopressor, n (%)	30 (29)
Vasopressor days, mean (SD)	4 (4)
NDMR, n (%)	5 (5)
Steroid treatment, n (%)	76 (74)
Steroid treatment days, mean (SD)	5 (4)

SAPS 3 = Simplified Acute Physiology Score III, SD = Standard Deviation, SOFA = Sequential Organ Failure Assessment, IQR = Interquartile Range, ICU = Intensive Care Unit, ARDS = Acute Respiratory Distress Syndrome, AKI = Acute Kidney Injury, NDMR = Nondepolarizing muscle relaxant

4.4 Measurement of muscle strength using the MRC-SS

Muscle strength of the study group was assessed with the MRC-SS at six weeks and six months after hospital discharge. ICUAW weakness is defined as an MRC-SS of < 48/60 (Hermans *et al.* 2014). The pie chart (Figure 4.5) illustrates the incidence of full criteria ICUAW at six weeks (3%) and at six months (2%) for the study group. In cases where patients had missing data regarding either their left or right side, we utilised information from the opposite corresponding limb to substitute the missing data.

Despite the patient sample showing a low incidence for full criteria ICUAW, post hoc analysis showed that 64 patients (62%) at six weeks and 34 patients (33%) at six months had lower than normal muscle strength (MRC-SS < 60). Also 35 patients (34%) and 6 patients (6%) had an MRC-SS of less than 55/60 at six weeks and six months, respectively.



MRC = Medical Research Council

Figure 4.5: The pie chart presents the incidence of ICUAW at six weeks and six months

In Table 4.3, the changes in muscle strength, as measured by the MRC scale, are presented for both time points. At six weeks, the median (IQR) MRC scale for each muscle action tested ranged from 4 (4-5) to 5 (4-5), indicating good, if not always normal, muscle strength. Over the six-month period, the results showed a significant increase in muscle strength, with the median (IQR) MRC scale reaching the maximum scale of 5 (5-5) for all muscle actions on both sides. The total MRC-SS (combined strength of all the muscles tested) also showed a notable increase from a median (IQR) of 58 (52-60) at six weeks to a median (IQR) of 60 (58-60) at six months. This difference was statistically significant ($p < 0.001$).

Table 4.3: MRC score at six weeks and six months for study group

Muscle Action Tested	Side	MRC score 6 weeks Median (IQR)	MRC score 6 months Median (IQR)
Shoulder Abduction	**Right**	5 (4-5)	5 (5-5)
	Left	4 (4-5)	5 (5-5)
Elbow Flexion	**Right**	5 (4-5)	5 (5-5)
	Left	5 (4-5)	5 (5-5)
Wrist Extension	**Right**	5 (5-5)	5 (5-5)
	Left	5 (4-5)	5 (5-5)
Hip Flexion	**Right**	4 (4-5)	5 (5-5)
	Left	4 (4-5)	5 (5-5)
Knee Extension	**Right**	5 (4-5)	5 (5-5)
	Left	5 (4-5)	5 (5-5)
Ankle Dorsiflexion	**Right**	5 (5-5)	5 (5-5)
	Left	5 (5-5)	5 (5-5)
Total **MRC-SS**		58 (52-60)	60 (58-60)

MRC = Medical Research Council, MRC-SS = Medical Research Council-Sum Score, IQR = Interquartile Range

4.5 Measurement of peripheral muscle strength using HHD

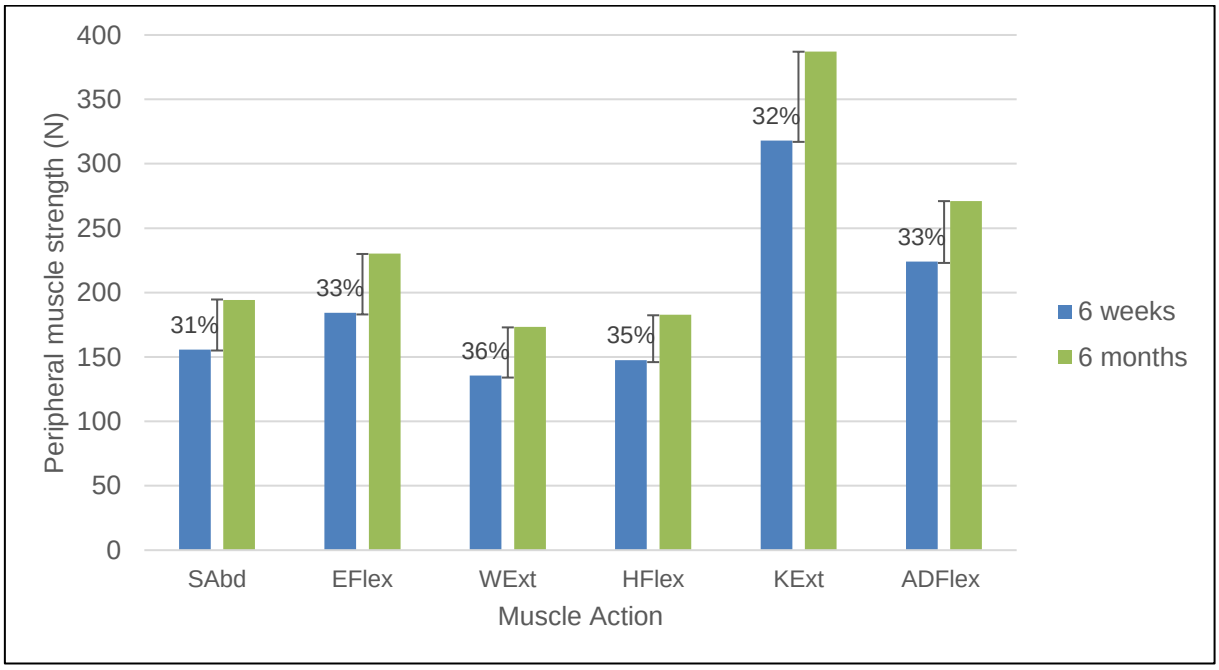
The study group's peripheral muscle strength was assessed at six weeks and six months by measuring the isometric forces of the patients with an HHD. The following muscle actions (corresponding to the MRC-SS) were tested: shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion (Appendix 4). The data presented in Table 4.4 shows the mean (SD) force (Newton) measurements of the various muscle actions for both the right and left sides of the body at six weeks and six months follow-up. There was a mean (SD) change of 32,75% (2.30) in the mean force from six weeks to six months for all muscle actions on both sides, with $p < 0.001$ indicating a significant difference. Where patients lacked data pertaining to their left or right side, we used data from the corresponding opposite side to complete the missing information. The rationale for this was that ICUAW is a largely symmetrical condition.

Table 4.4: HHD measurements at six weeks and six months for the study group

Muscle action tested	Side	Mean (SD) force (N) at 6 weeks	Mean (SD) force (N) at 6 months	% Change from 6 weeks to 6 months	p-value
Shoulder Abduction	**Right**	154 (64)	192 (71)	31	<0.001
	Left	158 (60)	199 (68)	34	<0.001
Elbow Flexion	**Right**	184 (74)	230 (82)	32	<0.001
	Left	184 (77)	228 (81)	32	<0.001
Wrist Extension	**Right**	136 (59)	173 (62)	36	<0.001
	Left	137 (65)	166 (59)	33	<0.001
Hip Flexion	**Right**	148 (72)	185 (74)	37	<0.001
	Left	147 (72)	179 (72)	34	<0.001
Knee Extension	**Right**	317 (125)	387 (125)	32	<0.001
	Left	317 (126)	386 (131)	30	<0.001
Ankle Dorsiflexion	**Right**	226 (86)	272 (85)	33	<0.001
	Left	219 (84)	265 (89)	29	<0.001

SD = Standard Deviation, N = Newton

A notable increase in the force generated during the muscle actions tested on participants' dominant side from six weeks to six months are illustrated in the clustered column chart (Figure 4.6).



SAbd = Shoulder Abduction, EFlex = Elbow Flexion, WExt = Wrist Extension, HFlex = Hip Flexion, KExt = Knee Extension, ADFlex = Ankle Dorsiflexion, N = Newton

Figure 4.6: The clustered column chart illustrates the change in muscle strength from six weeks to six months

4.6 Correlation between MRC scale and HHD measurements

The correlation between the MRC scale and handheld dynamometer (HHD) measurements for each muscle action were evaluated with the Pearson's product moment correlation. A Pearson correlation coefficient (r) is deemed statistically significant at the 0.05 level when (r) is greater than or equal to 0.19 for a sample size of 103, and any correlation coefficient (r) of 0.30 or greater is considered significant, both statistically and practically, irrespective of the sample size. As shown in Table 4.5, there was fair correlation between the MRC scale and HHD measurements for most of the muscle actions at both six weeks and six months except for ankle dorsiflexion that showed a poor correlation at six months. Although the correlations at six months were generally fair, they tended to be on the lower end of the fair range.

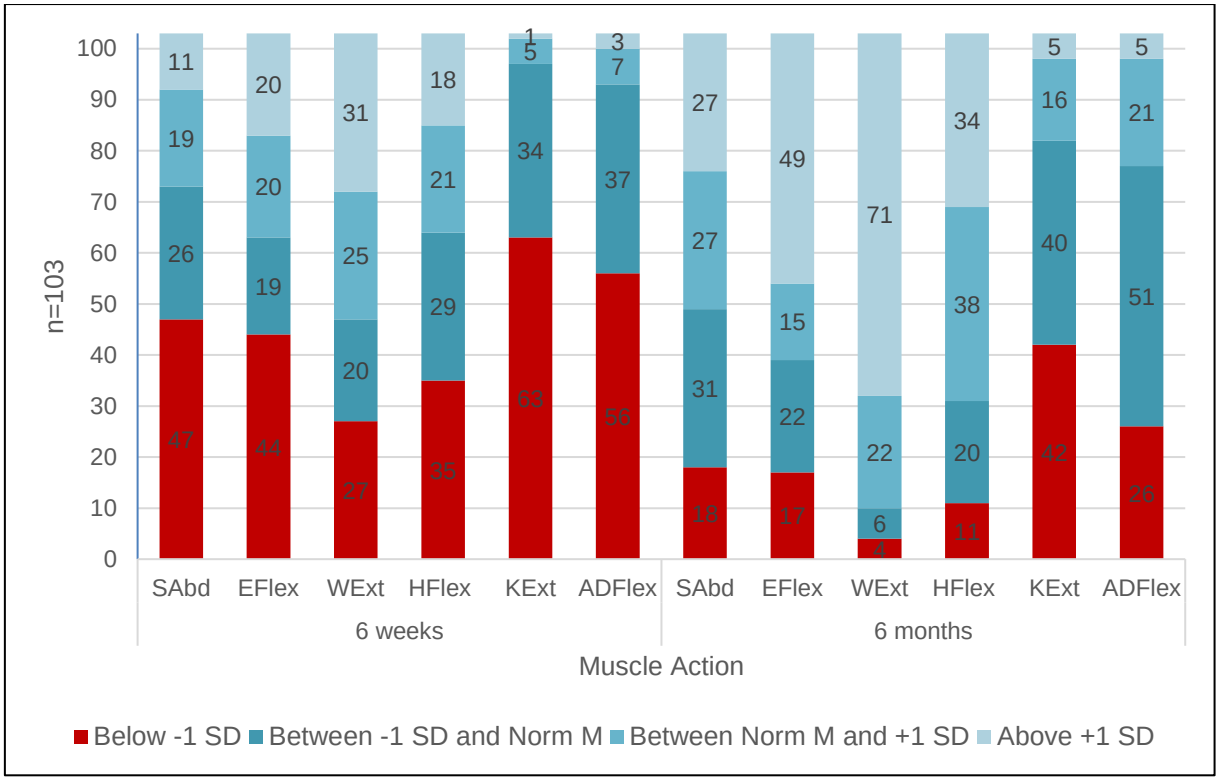
Table 4.5: Pearson Product Moment Correlations – MRC vs HHD

	Left				Right			
	6 weeks		6 months		6 weeks		6 months	
	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value
SAbd	0.57	<0.001	0.45	<0.001	0.55	<0.001	0.43	<0.001
EFlex	0.48	<0.001	0.34	<0.001	0.50	<0.001	0.31	<0.001
WExt	0.39	<0.001	0.32	<0.001	0.44	<0.001	0.31	<0.001
HFlex	0.51	<0.001	0.36	<0.001	0.55	<0.001	0.34	<0.001
KExt	0.50	<0.001	0.33	<0.001	0.50	<0.001	0.36	<0.001
ADFlex	0.48	<0.001	0.23	<0.01	0.55	<0.001	0.28	<0.01

SAbd = Shoulder Abduction, EFlex = Elbow Flexion, WExt = Wrist Extension, HFlex = Hip Flexion, KExt = Knee Extension, ADFlex = Ankle Dorsiflexion
r>0.8 = Very strong. 0.6-08 = Moderately strong, 0.3-0.5= Fair, r<0.3 = Poor,

4.7 Frequency distribution of HHD values against predicted values

Additional analysis was performed to compare the study group's average muscle force to predicted values for their age, gender, and dominant/non-dominant side (Appendix 5). The stacked column chart (Figure 4.7) shows how the patients' forces were categorised against the predicted values. During the initial assessment at six weeks, an average of 44% of the participants had a muscle strength below one standard deviation (SD) in the assessed muscle actions. However, at the six months assessment, this figure decreased, with an average of 19% of the participants with a muscle strength below one standard deviation (SD) in all the muscle actions assessed.



SAbd = Shoulder Abduction, EFlex = Elbow Flexion, WExt = Wrist Extension, HFlex = Hip Flexion, KExt = Knee Extension, ADFlex = Ankle Dorsiflexion, n = number of participants, SD = Standard Deviation, M = Mean

Figure 4.7: The stacked column chart illustrates frequency distributions of HHD categorical data

Table 4.6 presents data on the number of participants with muscle strength below one SD and an MRC-SS < 60, along with the corresponding p-values, at both the six week and six-month follow-up. At six weeks and six months, respectively, an average of 36% and 12% of participants had an MRC-SS < 60 and HHD measurements less than one SD of the predictive values. The differences between six weeks and six months are statistically significant for all muscle actions, as indicated by the p-values being less than 0.001. This shows a significant improvement in muscle strength measured by HHD for our cohort over six months.

Table 4.6: Participants with muscle strength below 1 SD and MRC-SS<60

	< 1 SD at 6 Weeks n (%)	< 1 SD at 6 Months n (%)	p-value
Shoulder Abduction	40 (39)	15 (15)	<0.001
Elbow Flexion	38 (37)	11 (11)	<0.001
Wrist Extension	24 (23)	4 (4)	<0.001
Hip Flexion	31 (30)	10 (10)	<0.001
Knee Extension	47 (46)	19 (18)	<0.001
Ankle Dorsiflexion	44 (43)	16(16)	<0.001

SD = Standard Deviation, n = number

CHAPTER 5: DISCUSSION

This research aimed to contribute to closing the substantial knowledge gap, as evidenced from the literature review, that exists in the field of evaluation of physical impairment in ICU survivors post hospital discharge. The paucity of research in this field is even more evident in South Africa. A recent international systematic review identified only 15 studies that described physical weakness associated with PICS (Ohtake *et al.* 2018), and a South African scoping review identified only two studies with 3 and 19 patients, respectively, who completed six months follow-up (Van der Merwe and Paruk 2022). Further research to evaluate and compare performance-based measures of physical function in ICU survivors has been suggested in peer-reviewed publications (Fan *et al.* 2014a; Needham *et al.* 2017). Our study, a single-centre observational study of patients at risk of PICS, evaluated neuromuscular weakness at six weeks and six months post-hospitalisation with the MRC-SS and HHD measurements. With 103 participants completing the evaluation at six months, it is the largest study to date to objectively evaluate neuromuscular function in South African ICU survivors and the first to compare and correlate different methods.

The first objective of the study was to assess the incidence of ICUAW, as measured by the MRC-SS, among ICU survivors at risk of PICS at six weeks and six months after hospital discharge. The second objective was to compare the changes observed in muscle power, as determined by the MRC scale and HHD, at six weeks and six months following hospital discharge. The third objective was to investigate correlation between the MRC scale and HHD measurements.

5.1 Incidence of intensive care unit-acquired weakness

Among relatively young and previously healthy ICU survivors at risk for PICS there was a low incidence of full-criteria ICUAW weakness after hospital discharge. The MRC-SS improved from six weeks to six months, which is consistent with the findings of other studies. Needham *et al.* (2013) conducted a follow-up trial involving the participants from the EDEN study (National Heart *et al.* 2012) which investigated the physical and psychological functioning of ICU survivors after one year. They reported

a low incidence of ICUAW weakness at six months after hospital discharge, with only 7% of their patients having an MRC-SS below 48, despite having an older mean (SD) age of 47 (± 14) years. The patients in the EDEN trial were all intubated and ventilated for a mean (SD) of 11 (± 9) days and spent a median (IQR) of 14 (± 11) days in ICU. Fan *et al.* (2014b) reported an incidence ICUAW of 15% at six months in survivors of acute lung injury who had a median (IQR) ICU stay of 14 (10-23) days and who required mechanical ventilation for a median (IQR) of 9 (15-17) days. In contrast, less than half of the patients in our study were intubated, and those who were, spent a mean (SD) of 5 (± 12) days on the ventilator. Also, our study participants had a median ICU (IQR) stay of 7 (5-13) days, which is less in both cases than the patients in these studies. Invasive mechanical ventilation is associated with immobilisation and inflammatory states, and considered a risk factor for ICUAW (Asfour 2016). These differences between the study cohorts from higher income countries and our study may explain the somewhat lower incidence of full criteria ICUAW weakness in our study group.

While the full-criteria ICUAW cut-off is 48/60, Van Aerde *et al.* (2020) concluded, after a five-year ICU follow-up trial study, that any MRC-SS below normal can have a lasting impact on a patient's mortality, strength, functional capacity, and physical function. In the acute setting a MRC-SS < 48/60 is a well-validated cut-off, but the van Aerde study provided exploratory data that indicates that an MRC-SS of 55 at ICU discharge best described the relationship between strength and five-year mortality (Van Aerde *et al.* 2020). This also implies that any submaximal MRC-SS on follow-up may be associated with poorer clinical outcomes, and this should be explored in future research. Post hoc analysis showed that many patients had subnormal MRC scores despite not qualifying for the full criteria of ICUAW. In a country where the public transport system is poorly developed and many patients are dependent on manual labour for income, it is likely that any degree of neuromuscular weakness is bound to impact on their quality of life, activities of daily living, return to work, psychological state, and rehabilitation needs. There is considerable scope for further studies in this field in South Africa.

5.2 Peripheral muscle strength as measured with HHD

All muscle actions exhibited a significant improvement in mean force from six weeks to six months, with percentage changes ranging between 29% to 37% ($p < 0.001$). For

instance, in shoulder abduction, both the right and left sides demonstrated an average force increase of around 30%, while elbow flexion and wrist extension showed improvements of approximately 32% to 36%. Similarly, hip flexion, knee extension, and ankle dorsiflexion also displayed substantial increases in mean force, ranging from 29% to 37%. The comparable percentage change across various muscle groups indicates a substantial and consistent improvement in muscle strength, suggesting recovery among the participants.

Limited information is available on muscle strength assessment in ICU survivors after hospital discharge using HHD. In the systemic review mentioned earlier only five of the 15 studies included used HHD to determine neuromuscular weakness (Ohtake *et al.* 2018). Of these, there was only one study that reported on HHD measurements in Newton six months after discharge, and which could therefore be used for comparison. In the one South African study included, HHD was used to determine changes in muscles strength over six months in young male patients who survived penetrating trunk trauma (van Aswegen *et al.* 2008). A greater overall improvement in upper limb muscle strength was observed compared to the lower limbs (van Aswegen *et al.* 2008). The left bicep muscles showed an increase of 47.9%, and a 28.5% increase in the left triceps muscles, while the hamstring showed a minimal increase of 14% for both sides. Although the values of the 12 patients in this small pilot study were still somewhat lower than the control group at six weeks and six months, they did not reach statistical significance at either visit, implying recovery. Van Aswegen *et al.* (2010) subsequently performed a similar but larger study where 23 of the 42 patients completed the six-month follow-up. The exact values were not reported in this publication but there was no difference between the short ventilation group (< 5 days) and the control group HHD measurements. In contrast, the long ventilation group (greater than or equal 5 days) had a significantly lower strength than the control group at six months (Van Aswegen *et al.* 2010).

5.3 Correlation between MRC scale and HHD measurements

We evaluated the correlation between the MRC scale and HHD measurements for each muscle action at six weeks and six months. There was fair correlation between the MRC scale and HHD measurements for most of the muscle actions at both six weeks and six months. Statistically significant correlations, as indicated by p-values

less than 0.001, were observed indicating that the strength assessed by both methods is related and tends to change in a similar direction over time. Although the correlations at six months were generally fair, they tended to be on the lower end of the range. The reason for this could be attributed to the minimal to no change in participants' MRC scores from six weeks to six months due to the subjective distinction between an MRC score of 4 and 5, despite ± 30% improvement in participants' HHD measurements. It was noted that ankle dorsiflexion had a poor correlation at six months. This may reflect on how well the investigators managed to preserve isometric ankle dorsiflexion contractions during the test and/or the variability in the participants performance of the test. According to Baschung Pfister *et al.* (2018) it is difficult for examiners to grade mild muscle weakness with manual muscle testing and it should not be used to evaluate changes (either improvement or deterioration), and concluded that HHD could be used to evaluate isometric muscle strength. This is in keeping with our findings, where the improvements were better characterised by the percentage change in the HHD measurements as compared to the MRC-SS. A caveat when recommending the HHD is that it must be performed technically correctly following a standardised protocol and the examiners must be experienced and trained in muscle testing (Baschung Pfister *et al.* 2018).

5.4 Frequency distribution of HHD values against predictive values

Additional analysis of the data was performed. The average muscle force of the study participants was compared to the predicted values from Bohannon (1997). These predictive are based on age, sex, and dominant/non-dominant side. While this was not a specific focus of the study's outcomes, reference values are commonly used to compare HHD measurements. The results showed that a significant percentage of our participants (44% and 19%, respectively, at 6 weeks and 6 months) exhibited lower strength (< 1 SD) in the respective muscle actions as compared to predictive values. The data indicates that participants underwent improvement in their muscle strength, with most individuals transitioning out of the lower-than-one SD category, especially in the areas of shoulder abduction, elbow flexion, wrist extension, and hip flexion.

The average percentages of participants with muscle strength below one SD and an MRC-SS < 60 at six weeks and six months (36% and 12%) were likely to be patients who were truly affected by muscle weakness at these visits. An international study by

Solverson, Grant and Doig (2016) also used HHD to assess the persistence of muscle weakness among ICU survivors after hospital discharge. The authors found that weakness extended across all muscle groups, with the quadriceps displaying the greatest level of weakness. They observed that, depending on the muscle group tested, between 52% and 69% of patients achieved lower than 80% of predicted muscle power at three months (Solverson, Grant and Doig 2016). Direct comparison between the two studies is limited by the differences in study visit timelines and the fact that they used a cut-off of 80% of predicted, while we used a cut-off of -1 standard deviation.

While our patients did improve when compared to the Bohanna predictive values, they may not be accurate for the South African population. Notable differences in mean muscle strength were observed when normative values were compared between a Dutch and American populations and that study concluded that reference force values may vary among different countries and populations (Douma *et al.* 2014). No information is available on the reference values for muscle power in lower income countries (Benfica *et al.* 2018). In view of this we recommend the establishment for HHD predictive values, based on age, gender, and dominant/non-dominants side, for South Africa to be able to compare HHD measurements in clinical practice and research.

5.5 Strengths of this study

- This is one of the few studies to report the use of HHD assessment of multiple muscle groups in ICU survivors in the setting of a follow-up clinic, and the first in South Africa, to the knowledge of the researcher.

5.6 Limitations of the study

- We did not assess patients' MRC score weakness during or upon discharge from the hospital.
- We did not record the specific investigator responsible for performing the HHD for each patient. This lack of documentation can affect the consistency of the data collected. Different investigators might apply varying amounts of counterforce during the measurements, potentially leading to inconsistencies or

outliers in the data. By not recording the specific investigator, it becomes challenging to assess whether variations in the data are due to differences in technique or other factors.

- There were no normative HHD values for the SA population to utilise. However, it is important to correct for age and sex, and therefore predictive values from other countries were used.

5.7 Recommendations for future research

- Future research could explore how HHD can be utilized in diagnosing ICUAW. They can investigate the potential of HHD as a diagnostic tool for identifying ICUAW in patients. Researchers might focus on how effective HHD is in measuring muscle strength and detecting weakness in ICU patients, possibly leading to improved diagnosis and treatment of this condition.
- Researchers intending to use HHD as a diagnostic tool for muscle assessment should consider utilising normative values specific to their country. In cases where such values are not available, researchers are encouraged to generate normative values specific to their country.

CHAPTER 6: CONCLUSION

This chapter summarises and synthesises the key findings, insights, and implications of the study.

The aim of the study was to evaluate ICUAW and its diagnostic methods in ICU survivors at risk of PICS in a South African tertiary public sector hospital. The results showed a low incidence for full-criteria ICUAW at six weeks and six months after hospital discharge among relatively young and previously healthy ICU survivors. There was a significant improvement in the median MRC sum score over the study period, but 33% still had a subnormal score at six months. The HHD measurements in this study cohort also showed a significant increase in mean force with an average percentage change of 33% across the different muscle actions from six weeks to six months. Consistent percentage changes across various muscle strengths suggests a degree of recovery over the follow-up period.

Fair correlations were observed between the MRC scale and HHD measurements for each muscle action from six weeks to six months, indicating that the strength assessed by both methods is related and tends to change in a similar direction over time. The six-months correlations were weaker than at six weeks. This could be explained by the minimal change in participants' MRC-SS from six weeks to six months and the difficulty to differentiate between 4 or 5 on the MRC scale. In view of this, HHD measurement, which is objective in all its measurements, may therefore be the preferred test in research, disability assessments and clinical settings. A caveat when recommending the HHD is that it must be performed technically correctly and that the clinician doing the test must be able to counter the patient's power. Combining HHD with tests like the six-minute walk, SF-36 physical component, and Instrumental Activities of Daily Living score allows healthcare providers to assess both muscle strength and broader aspects of physical function and quality of life, providing a holistic view of a patient's health status and functional abilities. This comprehensive approach can aid in better diagnosis, treatment planning, and monitoring of progress in patients with conditions like ICU-Acquired Weakness (ICUAW).

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APPENDICES

Appendix 1: Data Collection Sheet

Patient Sticker	**Livingstone ICU Study Data Collection Sheet ☺** Study Number_____

1	Date of admission to ICU *DD MM YY*			Date of ICU discharge			ICU Days completed on discharge			
2	Discharged to: (Ward/Hospital)			Date of hospital discharge			Hospital Length of stay			
3	Contacts and minimum 3 tel. numbers and who they are									
4	Address									
5	Gender	Male		Female			Age			
6	Race	Black		Indian			Coloured		White	Asian/ Other
7	Pre-morbid employment	Salaried/Formal		Informal sector			Pension		None	Student

8	Admission Diagnosis							ICD-10		
9	Referring discipline	Medicine	ANY Trauma	Gen Surg	Cardio thorax	Ortho	Spinal	Vascular	O&G	Urology
	Emergency									
	Elective									

10	Co-morbidities													
	Active TB		Cardiovascular			HIV				Previous Psychopathology				
	Yes	No	IHD	Yes	No	Known	Unknown	Diagnosed now		Yes	No			
	COPD		PVD	Yes	No	Positive		Negative		DX if Yes:				
	Yes	No	HPT	Yes	No	On HAART?		Yes	No					
	Diabetes		CVA	Yes	No	Premorbid		CD4	%	Frailty Score				
	Yes		CCF	Yes	No									
	CKD					Date				CCI Score				
	Yes	No				Viral Load Log								
	Chronic Dialysis									IQCODE score				
	Yes	No				Date								

11	Spinal Injury	Yes	No	If Yes, Motor level on discharge from ICU									
12	Admission SAPS 3 score			%	13	Admission SOFA score			14	Highest SOFA score			

15	Invasive Ventilation	Yes	No			Non-invasive Ventilation			Bipap	HFNO	No		
	Invasive Ventilation Days					Non-invasive Ventilation Days							
	ARDS	Yes	No			Use of Restraint			Yes	No			
	Septic Shock	Yes	No			Delirium			Yes	No			
	Sepsis (on admission or ICU acquired) *Definition: life-threatening organ dysfunction with ≥ 2 ↑ in SOFA score*					ICU weakness	Yes	No	MRC score				
	Yes	No				AKI			Yes	No			
	ICU Acquired Infection Requiring Antibiotics	Yes	No			Acute Dialysis			Yes	No			
						Hypo/Hyperglycemia requiring treatment			Yes	No			

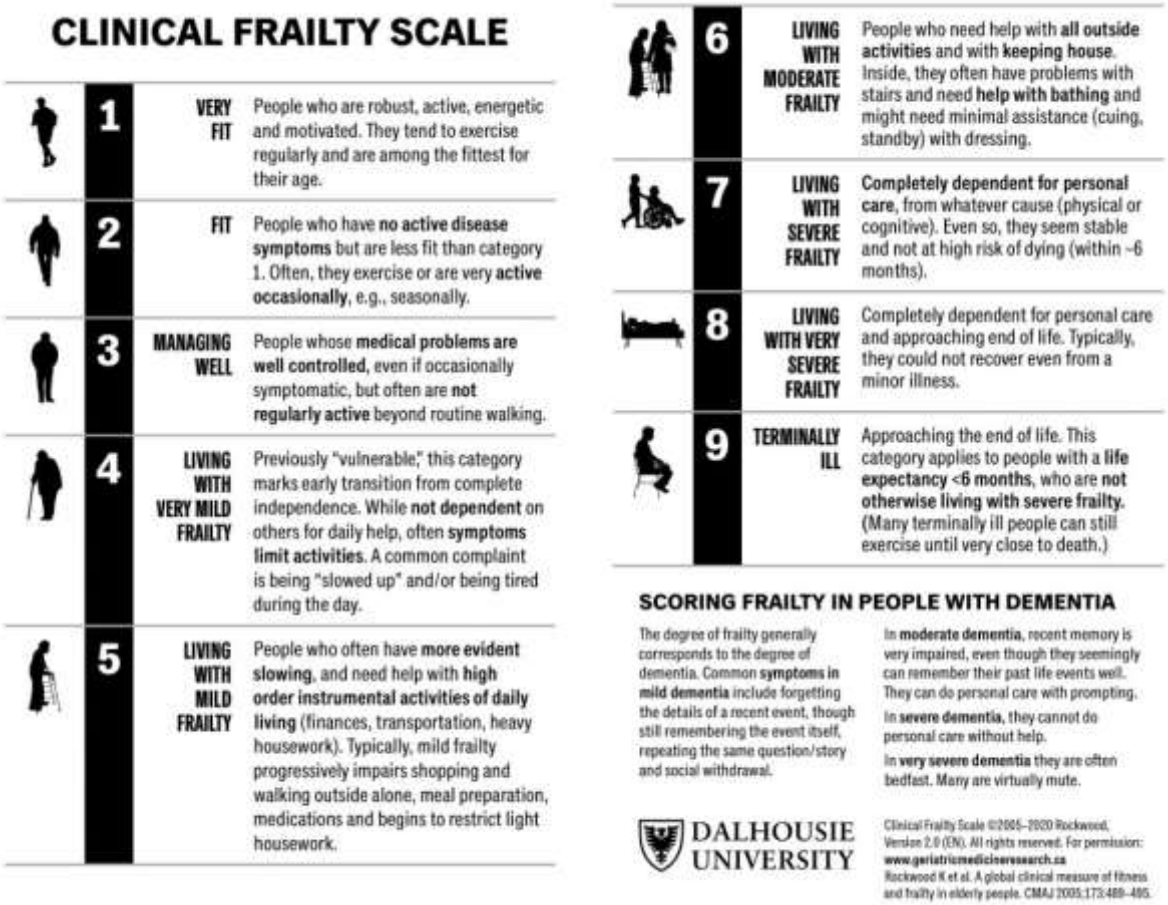
16	Drugs			Days	Drugs			Days
	Required Vasopressors	Yes	No		Anti-psychotics	Yes	No	
	Benzodiazepines	Yes	No		Alpha agonists	Yes	No	
	Non-Benzo Sedatives	Yes	No		NDMR infusion	Yes	No	
	Opiates	Yes	No		Corticosteroids	Yes	No	

17	Baseline SF-36 PCS		Baseline SF-36 MCS	

18	6 Weeks Follow-up											
	Employment/Study	Yes	No			Physio	Yes	No				
	If No reason					OT	Yes	No				
	Redundant	Resigned Other	Resigned Health Reason			Speech Therapy	Yes	No				
						Memories of Restraints	Yes	No				
	Temporary Incapacitated	Permanently Incapacitated				Other Frightening ICU Memories						
	Receiving disability grant	Yes	No									
	SF-36 Questionnaire					HADS-A		IES-R				
	Total score:	MCS:	PCS:			HADS-D		IADL				
						NeuroScreen						
	6MWT	Yes	No	N/A	Distance:		Height:		Weight:			
	RIGHT	MRC Score	HHD			LEFT	MRC Score	HHD				
	Shoulder Abduction					Shoulder Abduction						
	Elbow Flexion					Elbow Flexion						
	Wrist Extension					Wrist Extension						
	Hip Flexion					Hip Flexion						
	Dorsiflexion of Ankle					Dorsiflexion of Ankle						
	Knee Extension					Knee Extension						

19	6 Months Follow-up											
	Employment/Study	Yes	No			Physio	Yes	No				
	If No reason					OT	Yes	No				
	Redundant	Resigned Other	Resigned Health Reason			Speech Therapy	Yes	No				
						Memories of Restraints	Yes	No				
	Temporary Incapacitated	Permanently Incapacitated				Other Frightening ICU Memories						
	Receiving disability grant	Yes	No									
	SF-36 Questionnaire					HADS-A		IES-R				
	Total score:	MCS:	PCS:			HADS-D		IADL				
						NeuroScreen						
	6MWT	Yes	No	N/A	Distance:		Height:		Weight:			
	RIGHT	MRC Score	HHD			LEFT	MRC Score	HHD				
	Shoulder Abduction					Shoulder Abduction						
	Elbow Flexion					Elbow Flexion						
	Wrist Extension					Wrist Extension						
	Hip Flexion					Hip Flexion						
	Dorsiflexion of Ankle					Dorsiflexion of Ankle						
	Knee Extension					Knee Extension						

Appendix 2: Clinical Frailty Scale



Source: (Rockwood 2005)

Appendix 3: Medical Research Council Sum Score

Table 1
Diagnosis of ICU-acquired weakness

Medical Research Council (MRC) Scale:			
0 = no contraction			
1 = flicker or trace of contraction			
2 = active movement, with gravity eliminated			
3 = active movement against gravity			
4 = active movement against gravity and resistance			
5 = normal power			
Upper Extremity Strength			
Right		*Left*	
Shoulder abduction	___/5	Shoulder abduction	___/5
Elbow flexion	___/5	Elbow flexion	___/5
Wrist extension	___/5	Wrist extension	___/5
Lower Extremity Strength			
Right		*Left*	
Hip flexion	___/5	Hip flexion	___/5
Knee extension	___/5	Knee extension	___/5
Foot dorsiflexion	___/5	Foot dorsiflexion	___/5
Total Score = ____\60			

Total score <48 or average score of 4 consistent with the diagnosis of ICU-Acquired Weakness.

Used with the permission of the Medical Research Council without formal changes. Available at https://www.mrc.ac.uk/research/facilities-and-resources-for-researchers/mrc-scales/mrc-muscle-scale/.

Appendix 4: Handheld Dynamometer Assessment Protocol

Muscle Action	Patient Position	Limb/Joint position	HHD Position	Stabilisation Region
Shoulder Abduction (deltoid muscle)	Supine	Shoulder abducted 45°; elbow extended.	Just proximal to lateral epicondyle of humerus just above the elbow	Superior aspect of shoulder
Elbow Flexion (biceps brachii)	Supine	Shoulder at neutral; elbow flexed 90°; forearm supinated	Slightly proximal to styloid process of the radius just below the wrist	Superior surface of the arm or shoulder
Wrist Extension	Supine	Shoulder at neutral; elbow flexed 90"; wrist at neutral; fingers relaxed	Just proximal to metacarpophalangeal joints of the hand	Distal Forearm
Hip Flexion (iliopsoas muscle)	Supine	Hip flexed 90°; knee relaxed; contralateral limb in neutral	Anterior surface of the upper leg at femoral condyles just above the knee	Pelvis
Knee Extension (quadriceps femoris)	Sitting at the edge of the bed	Knees and hips flexed to 90°; participant's hands resting on his or her lap	Slightly proximal to the malleoli on the anterior aspect of the lower leg just above the ankle	An assistant stabilises at the shoulders
Dorsiflexion of Ankle (tibialis anterior)	Supine	The hip, knee and ankle at 0°	Slightly proximal to the metatarsophalangeal joints of the foot	Knee maintained in full extension; leg supported with foot off table

Appendix 5: HHD Predictive values

Women 20-29						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	153,2	28,8		Shoulder Abduction	135,9	21,2
Elbow Flexion	154,9	20,7		Elbow Flexion	152,6	21,8
Wrist Extension	99,6	16,8		Wrist Extension	94,4	19
Hip Flexion	139,9	27		Hip Flexion	132,9	29,6
Dorsiflexion of Ankle	294,9	51,5		Dorsiflexion of Ankle	273,3	45,5
Knee Extension	467,3	88,8		Knee Extension	465,7	97,7

Women 30-39						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	138,5	25,2		Shoulder Abduction	135,5	21,2
Elbow Flexion	163,8	28,1		Elbow Flexion	160,8	31,8
Wrist Extension	104,6	17,6		Wrist Extension	98	19,8
Hip Flexion	119	38,3		Hip Flexion	115,5	36,5
Dorsiflexion of Ankle	248,7	75,5		Dorsiflexion of Ankle	252,9	55,8
Knee Extension	408,3	128,8		Knee Extension	410,8	122,6

Women 40-49						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	139	33,1		Shoulder Abduction	129,1	26,2
Elbow Flexion	151,3	21,7		Elbow Flexion	156,9	25,3
Wrist Extension	102,1	17,5		Wrist Extension	99,4	21,2
Hip Flexion	124,8	43,2		Hip Flexion	122,4	46,9
Dorsiflexion of Ankle	251	54,4		Dorsiflexion of Ankle	247,1	51,3
Knee Extension	380,6	86,5		Knee Extension	362,7	60

Women 50-59						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	137,2	24,7		Shoulder Abduction	134,9	29,9
Elbow Flexion	155,3	25,3		Elbow Flexion	156,3	22,4
Wrist Extension	99,7	18,4		Wrist Extension	98,5	17,2
Hip Flexion	116,2	30,5		Hip Flexion	115,1	21,6
Dorsiflexion of Ankle	252,9	53,3		Dorsiflexion of Ankle	240,1	48,7
Knee Extension	334,7	75,8		Knee Extension	318,7	72,6

Women 60-69						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	112,1	25,1		Shoulder Abduction	103,7	16,1
Elbow Flexion	130,6	21,4		Elbow Flexion	134,2	19
Wrist Extension	83,2	17,7		Wrist Extension	85,2	19,8
Hip Flexion	103,3	26,7		Hip Flexion	98,7	24,6
Dorsiflexion of Ankle	235,7	74,9		Dorsiflexion of Ankle	230,5	57,3
Knee Extension	273,6	80,8		Knee Extension	265,9	83,2

Women 70-79						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	95,9	21,9		Shoulder Abduction	101,6	21,3
Elbow Flexion	129,9	27		Elbow Flexion	130,3	28,7
Wrist Extension	69,8	17,6		Wrist Extension	61,4	17,8
Hip Flexion	92,1	27,2		Hip Flexion	91,8	28,9
Dorsiflexion of Ankle	166,2	48,7		Dorsiflexion of Ankle	153,3	36,1
Knee Extension	210,1	45,6		Knee Extension	204,7	43,9

Men 20-29						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	258,4	61		Shoulder Abduction	246,3	43,9
Elbow Flexion	285	38,2		Elbow Flexion	278,5	47,8
Wrist Extension	184,3	27,6		Wrist Extension	171,1	23,6
Hip Flexion	211,7	39,7		Hip Flexion	206,7	41,4
Dorsiflexion of Ankle	385,9	64,4		Dorsiflexion of Ankle	368,7	44,2
Knee Extension	575,2	73,7		Knee Extension	578,6	94,7

Men 30-39						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	249,2	60,2		Shoulder Abduction	237,2	69,6
Elbow Flexion	268,5	47,1		Elbow Flexion	281,2	54,3
Wrist Extension	169,5	41,5		Wrist Extension	172,5	39,9
Hip Flexion	223,6	47,4		Hip Flexion	225,9	58,1
Dorsiflexion of Ankle	372,6	89,6		Dorsiflexion of Ankle	388,4	81,5
Knee Extension	572,9	76,5		Knee Extension	572,5	82,8

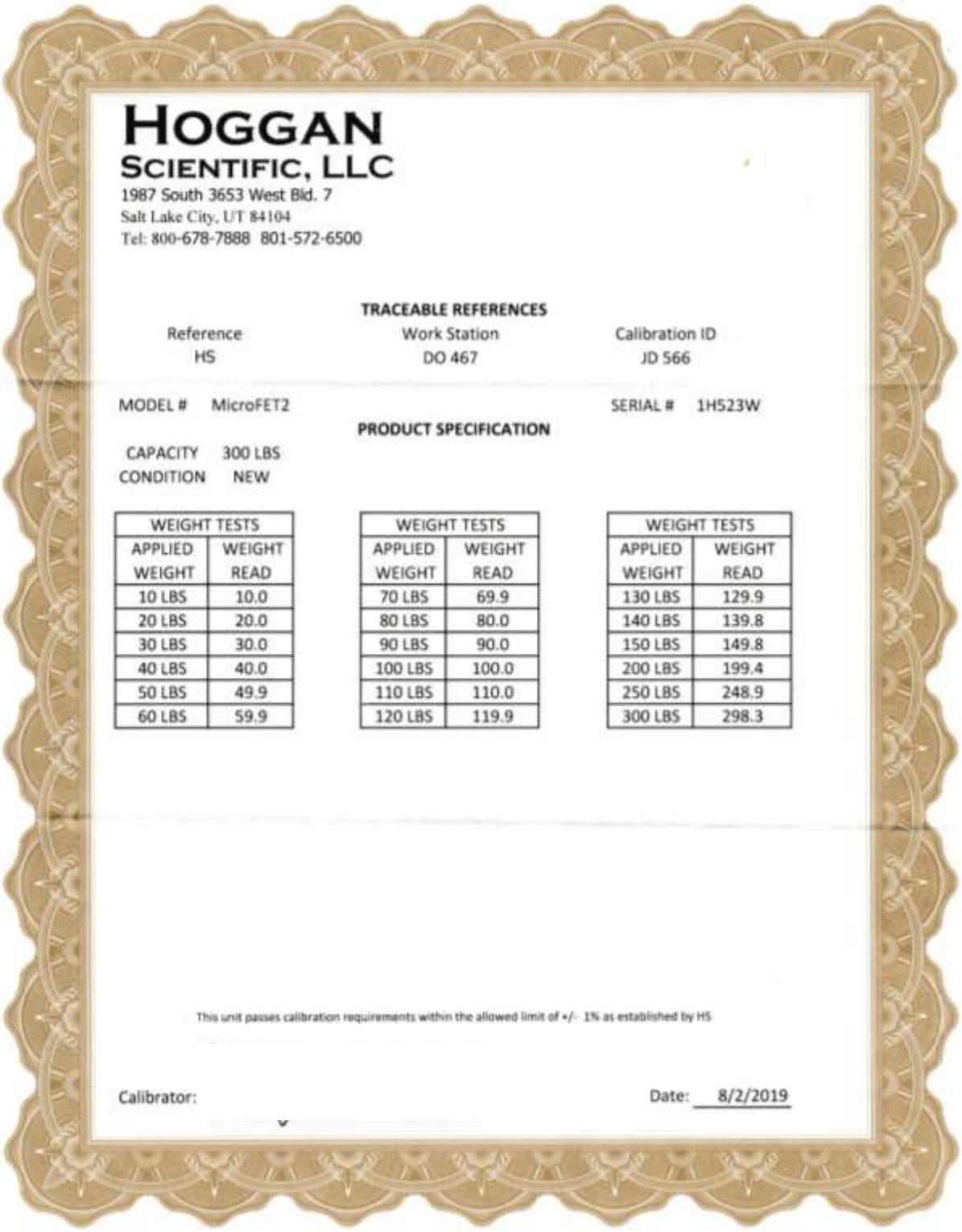
Men 40-49						
Dominant	Force	SD		Non- Dominantinant	Force	SD
Shoulder Abduction	245,5	37,5		Shoulder Abduction	244,9	43,1
Elbow Flexion	268,5	33,6		Elbow Flexion	269,8	29,7
Wrist Extension	185,1	38,1		Wrist Extension	178,6	32,2
Hip Flexion	190,7	43,3		Hip Flexion	184,2	37,3
Dorsiflexion of Ankle	376,1	63,7		Dorsiflexion of Ankle	362,7	58,5
Knee Extension	583	73,7		Knee Extension	588,9	72,5

Men 50-59						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	240,4	57,6		Shoulder Abduction	222,5	47,5
Elbow Flexion	286,9	38,5		Elbow Flexion	268,2	49,6
Wrist Extension	148,9	35		Wrist Extension	144,7	35,9
Hip Flexion	195,2	61,9		Hip Flexion	203,1	58,6
Dorsiflexion of Ankle	323,2	90,8		Dorsiflexion of Ankle	311	63,3
Knee Extension	470,9	92,3		Knee Extension	467,7	103,1

Men 60-69						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	203	45,1		Shoulder Abduction	195,8	44,7
Elbow Flexion	259,4	48,9		Elbow Flexion	243,6	42,7
Wrist Extension	138,3	29,9		Wrist Extension	125,8	24,4
Hip Flexion	169,1	49		Hip Flexion	167,6	47,6
Dorsiflexion of Ankle	269	76,9		Dorsiflexion of Ankle	272,7	61,2
Knee Extension	386,9	94,3		Knee Extension	376,5	67,3

Men 70-79						
Dominant	Force	SD		Non- Dominant	Force	SD
Shoulder Abduction	191,8	31,5		Shoulder Abduction	187,9	33,7
Elbow Flexion	237,3	39,9		Elbow Flexion	237,5	38,1
Wrist Extension	130,1	22,3		Wrist Extension	126,5	22,1
Hip Flexion	167,4	38,7		Hip Flexion	162,1	39,2
Dorsiflexion of Ankle	240	47,3		Dorsiflexion of Ankle	246	47,6
Knee Extension	360,3	72,6		Knee Extension	365,9	76,9

Appendix 6: MicroFet2 Calibration Certificate



HOGGAN SCIENTIFIC, LLC

1987 South 3653 West Bld. 7
Salt Lake City, UT 84104
Tel: 800-678-7888 801-572-6500

TRACEABLE REFERENCES

Reference	Work Station	Calibration ID
HS	DO 467	JD 566

MODEL # MicroFET2 SERIAL # 1H523W

PRODUCT SPECIFICATION

CAPACITY 300 LBS
CONDITION NEW

WEIGHT TESTS	
APPLIED WEIGHT	WEIGHT READ
10 LBS	10.0
20 LBS	20.0
30 LBS	30.0
40 LBS	40.0
50 LBS	49.9
60 LBS	59.9

WEIGHT TESTS	
APPLIED WEIGHT	WEIGHT READ
70 LBS	69.9
80 LBS	80.0
90 LBS	90.0
100 LBS	100.0
110 LBS	110.0
120 LBS	119.9

WEIGHT TESTS	
APPLIED WEIGHT	WEIGHT READ
130 LBS	129.9
140 LBS	139.8
150 LBS	149.8
200 LBS	199.4
250 LBS	248.9
300 LBS	298.3

This unit passes calibration requirements within the allowed limit of +/- 1% as established by HS

Calibrator:

Date: 8/2/2019

Appendix 7: Durban University of Technology Institutional Research Ethics Committee Ethics Approval Letter

Institutional Research Ethics Committee
Research and Postgraduate Support Directorate
2nd Floor, Berwyn Court
Gate 1, Steve Biko Campus
Durban University of Technology

P O Box 1334, Durban, South Africa, 4001

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

www.dut.ac.za

13 December 2021

Ms N Van Vuuren
1 Merlot Estate
56 Longwy Avenue
Lorraine
Port Elizabeth
6070

Dear Ms Van Vuuren

The assessment of intensive care unit-acquired weakness in Adult patients at risk of post intensive care syndrome
Ethical Clearance number IREC 135/21

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

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

Any adverse events [serious or minor] which occur in connection with this study and/or which may alter its ethical consideration must be reported to the IREC according to the IREC Standard Operating Procedures (SOP's).

Please note that any deviations from the approved proposal require the approval of the IREC as outlined in the IREC SOP's.

Yours Sincerely

Prof J K Adam
Chairperson: IREC

Appendix 8: Eastern Cape Health Research Committee Approval Letter

Province of the
EASTERN CAPE
HEALTH

Room 000 • 0th Floor • Grosvenor Lodge • 31 Taylor Street • King Williams Town Eastern Cape
Private Bag X0038 • Bhisho • 5605 • REPUBLIC OF SOUTH AFRICA
Tel.: +27 79 074 0859 • Email: Yvonne.Gxeka@echealth.gov.za/ygxeka@gmail.com

Date: 08 September 2021

Title: The Assessment of intensive care unit-acquired weakness in Adult patients at risk of post intensive care syndrome

Dear Ms N. van Vuuren

The Department of Health would like to inform you that your application for conducting a research on the above-mentioned topic has been **PROVISIONALLY** approved pending your submission of the following documents:

1. Final research proposal and
2. Ethical approval *(Research Ethics Committee registered with the National Health Research Ethics Council)*

NB: Final approval will only be granted after submission of the above required documents. Submissions are done online using the address nhrd.hst.org.za

Your compliance in this regard will be highly appreciated.

Secretariat: Eastern Cape Health Research Committee
EASTERN CAPE DEPARTMENT OF HEALTH

Appendix 9: Permission Letter to Perform the Study at Livingstone Tertiary Hospital

19 August 2021

Noline van Vuuren

Student nr: 22064204

Cell: 082 733 5091

22064204@dut4life.ac.za

Dr A Knock

Acting Senior Medical Manager

Livingstone Tertiary Hospital

REQUEST FOR PERMISSION TO CONDUCT A RESEARCH STUDY

This letter serves as a request for permission to conduct a research study at Livingstone Tertiary Hospital to obtain my Master of Health Sciences Degree in Clinical Technology at Durban University of Technology. The study will be conducted in the adult intensive care department under the supervision of Dr E. van der Merwe (Clinical Supervisor), Mr M.E. Memela (Institutional supervisor) and Dr D.R. Prakaschandra (Institutional co-supervisor).

The provisional title of the research study is the assessment of intensive care unit-acquired weakness in adult patients at risk of post intensive care syndrome. The muscle strength of patients will be assessed using the Medical Research Council scale and with a handheld dynamometer to determine the patient's weakness. This study in nested in a larger PhD study that look at the objectives of which are the general occurrence and co-occurrence of post intensive care symptoms (PICS) and health related quality of life in patients at risk of PICS.

Attached is the copy of the research proposal for the study. Your consideration and permission to conduct the study will be highly appreciated.

Kind Regards

Principal Investigator

Noline van Vuuren

Appendix 10: Livingstone Tertiary Hospital Letter of Permission

Province of the
EASTERN CAPE
HEALTH

21 October 2021

To: The Chairperson Durban University of Technology IREC

Dear Sir/Madam

Research proposal: The assessment of intensive care unit-acquired weakness in Adult patients at risk of post intensive critical care syndrome.

As acting Senior Medical Manager of Livingstone Tertiary Hospital I give permission to the above prospective observational study to be performed in the Department of Adult Critical Care (ICU), Livingstone Tertiary Hospital, provided that there is ethics approval and written permission is granted from the Department of Health via the NHRD.

Yours sincerely,

Dr A. Knock
Acting Senior Medical Manager
Livingstone Tertiary Hospital
Abner.knock@echealth.gov.za

Department of Health
Livingstone Tertiary Hospital
2021 -10- 21
Office of the
Senior Manager Medical Services

NELSON MANDELA
UNIVERSITY

PO Box 77000, Nelson Mandela University, Port Elizabeth, 6031, South Africa. mandela.ac.za

Chairperson: Research Ethics Committee (Human)
Tel: +27 (0)41 504 2347
sharlene.govender@mandela.ac.za

NHREC registration nr: REC-042508-026

Ref: [H20-HEA-PSY-001] / Approval]

1 May 2020 *(subject to national and institutional response to COVID-19 pandemic)*

Prof L Stroud
Faculty: Health Sciences

Dear Prof Stroud

EARLY SCREENING FOR SYMPTOMS OF THE POST INTENSIVE CARE SYNDROME (PICS) IN A TERTIARY ICU FOLLOW-UP CLINIC IN THE EASTERN CAPE

PRP: Prof L Stroud
PI: Dr E van der Merwe

Your above entitled application served at the Research Ethics Committee (Human) (meeting of *26 February 2020*) for approval. The study is classified as a high risk study. The ethics clearance reference number is **H20-HEA-PSY-001** and approval is subject to the following conditions:

1. The immediate completion and return of the attached acknowledgement to Imtaz.Khan@mandela.ac.za, the date of receipt of such returned acknowledgement determining the final date of approval for the study where after data collection may commence.
2. Approval for data collection is for 1 calendar year from date of receipt of above mentioned acknowledgement.
3. The submission of an annual progress report by the PRP on the data collection activities of the study (form RECH-004 available on Research Ethics Committee (Human) portal) by 15 November this year for studies approved/extended in the period October of the previous year up to and including September of this year, or 15 November next year for studies approved/extended after September this year.
4. In the event of a requirement to extend the period of data collection (i.e. for a period in excess of 1 calendar year from date of approval), completion of an extension request is required (form RECH-005 available on Research Ethics Committee (Human) portal)
5. In the event of any changes made to the study (excluding extension of the study), completion of an amendments form is required (form RECH-006 available on Research Ethics Committee (Human) portal).
6. Immediate submission (and possible discontinuation of the study in the case of serious events) of the relevant report to RECH (form RECH-007 available on Research Ethics Committee (Human) portal) in the event of any unanticipated problems, serious incidents or adverse events observed during the course of the study.
7. Immediate submission of a Study Termination Report to RECH (form RECH-008 available on Research Ethics Committee (Human) portal) upon expected or unexpected closure/termination of study.
8. Immediate submission of a Study Exception Report of RECH (form RECH-009 available on Research Ethics Committee (Human) portal) in the event of any study deviations, violations and/or exceptions.
9. Acknowledgement that the study could be subjected to passive and/or active monitoring without prior notice at the discretion of Research Ethics Committee (Human).

Please quote the ethics clearance reference number in all correspondence and enquiries related to the study. For speedy processing of email queries (to be directed to Imtaz.Khan@mandela.ac.za), it is recommended that the ethics clearance reference number together with an indication of the query appear in the subject line of the email.

We wish you well with the study.

Yours sincerely

Dr S Govender
Chairperson: Research Ethics Committee (Human)

Cc Department of Research Development
Faculty Administrator: Health Sciences

Appendix 12: Patient Information Sheet – English

LETTER OF INFORMATION

Title of the Research Study: The assessment of Intensive care unit-acquired weakness in adult patients at risk of post intensive care syndrome.

Principal Investigator/s/researcher: Noline van Vuuren, BTech Clinical Technology

Co-Investigator/s/supervisor/s: Dr D R Prakaschandra, PhD, Mr M E Memela, MTech; and Dr E van der Merwe, MBChB, FRCP, MMed

Brief Introduction and Purpose of the Study:

Greeting Good Day, how are you doing today?

Introduce yourself to the participant I am a post graduate student at DUT doing research for my Master of Health Sciences degree in Clinical Technology.

Invitation to the potential participant: You meet the inclusion criteria to take part in my study, and I would like to know if I could please have a few minutes of your time to explain my study and ask for consent to include you in the study?

What is Research: Research is the collection and analysis of data to increase our understanding of a topic and to acquire new knowledge.

Outline of the Procedures: We are assessing the incidence of ICUAW (intensive care unit-acquired weakness) of some of the patients admitted to the ICU (intensive care or critical care unit) at Livingstone Hospital. For this study, we will need to use information about your illness from your medical records. You are considered for this study because you stayed in ICU for more than 48 hours receiving support for respiratory and/or organ failure. We ask that you attend two ICU follow-up clinic dates after hospital discharge at Livingstone Hospital. The first one will be 6 to 8 weeks after discharge from hospital and the other 6 months after discharge. During the clinic visit, we will examine you, and evaluate your muscle strength using a scoring system and a small handheld device that can measure your muscle strength. The visit takes up to an hour and a half to complete.

The aim of the study is to evaluate ICUAW and diagnostic methods available for this condition in critical care survivors at risk of post intensive care syndrome. We will aim to enrol 150 patients in this study. Our objectives are to determine how many of our patients still experience muscle weakness after hospital discharge, to correlate two methods that can be used to measure muscle weakness and to compare the changes in muscle strength from 6 weeks to 6 months. We know from overseas studies that some critical care survivors are at risk to develop muscle weakness during their stay in ICU which can last till after discharge. Luckily not all ICU patients experience muscle weakness, but if you do and it is diagnosed after ICU discharge, we can support you better and refer you for therapy. This information could also help us make better decisions regarding your and other patients' care. There is not much information on how many South

African ICU patients still experience ICU weakness after hospital discharge. For this reason, we would like to find out through this study how many of our patients still experience muscle weakness after they are discharged.

Risks or Discomforts to the Participant: We do not foresee that you will experience any risks or discomforts, but there is a possibility of very mild muscle stiffness the next day.

Explain to the participant the reasons he/she may be withdraw from the Study: You have the right to decide that you do not want to be part of this study at any time. In that case, we will not contact you again, there will be no disadvantages for you and your information will not be kept by us or used for any studies. You must still attend the other appointment dates that are given to you on discharge from the hospital by your ward doctors. If you forget to come, we would like to phone you to remind you and to understand why you could not attend the visit.

Benefits: If we find any problems that need further treatment, we will arrange for you to see the best suited healthcare professional e.g., another doctor, physiotherapist.

Remuneration: Because this is a research study, we will pay you a transport fee per visit to make sure you can attend.

Costs of the Study: You will not be expected to cover any costs towards the study.

Confidentiality: You will be assigned a study number. De-identified data will be sent to statisticians. No one except the medical doctors and clinical technologist involved will know your personal details.

Results: We will put the results from all the patients together and then write up a report that discusses the incidence of ICUAW after ICU discharge and the methods used. Your name will not appear anywhere is this report.

Research-related Injury: It is unlikely that there will be any research-related injury.

Storage of all electronic and hard copies including tape recordings: Data collection sheets will be in locked cupboard and locked office of investigator. Two password protected computers will store deidentified data in spread sheets. Date collected will be kept for 5 years for reference if queries. Hard copies will be shredded after 5 years, and soft copies deleted from the computers.

Persons to contact in the Event of Any Problems or Queries: Please contact me, Mrs N van Vuuren (0827335091/nolinevanv@gmail.com), my supervisor, Dr D R Prakaschandra (0313736885/rosaleypra@dut.ac.za) or the Institutional Research Ethics Administrator (0313732375). Complaints can be reported to the Director: Research and Postgraduate Support Dr L Linganiso (0313732577/ researchdirector@dut.ac.za).

We would like to thank you if you do decide to help us in this study and we hope that we will be able to gather some useful information that will help both yourself and other patients at Livingstone Hospital ICU and in South Africa. Please feel free to ask us any questions you may have about the study.

Appendix 13: Patient Informed Consent – English

CONSENT

The assessment of Intensive care unit-acquired weakness in adult patients at risk of post intensive care syndrome.

Names of Researcher: Noline van Vuuren

Statement of Agreement to Participate in the Research Study:

- I hereby confirm that I have been informed by the researcher, Noline van Vuuren, about the nature, conduct, benefits, and risks of this study - Research Ethics Clearance Number: IREC 135/21.
- I have also received, read, and understood the above written information (Participant Letter of Information) regarding the study.
- I am aware that the results of the study, including personal details regarding my sex, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of research, I agree that the data collected during this study can be processed in a computerised system by the researcher.
- I may, at any stage, without prejudice, withdraw my consent and participation in the study.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research which may relate to my participation will be made available to me.

Full name of Participant	Date	Signature/Right Thumbprint

I, Noline van Vuuren, herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

Full name of Researcher	Date	Signature/Right Thumbprint
Full name of Witness	Date	Signature/Right Thumbprint

Appendix 14: Patient Information Sheet – Xhosa

ISihloko seSifundo soPhando: Uvavanyo lobuthathaka, nobulwelwe obufunyanwa ngabaguli abadala emveni konyango olumandla kwiyunithi yabagula kakhulu (Intensive Care Unit) abasemngciphekweni wobuthathaka nobulwelwe obulandela unyanyo kulondolozo olumandla.

UMphandi oyiNtloko/uMenzi-phando oyiNtloko: nguNoline van Vuuren, BTech Clinical Technology

Abadibaneli kuPhando/abaLawuli: Gqr D R Prakaschandra, PhD; Mnu M E Memela, MTech no Gqr E van der Merwe, MBChB, FRCP, MMed

Intshayelelo eMfutshane neNjongo yolu Phando:

Sibulisile, molweni, ninjani kodwa namhlanje?

Zazise kumthathinxaxheba: Ndingumfundi owenza isidanga esilandela esokuqala e-DUT, ndisenza uphando lwezifundo zam zesidanga seMaster of Health Sciences

kwiClinical Technology, itheknoloji yezonyango.

Isimemo kulowo unokuba ngumthathinxaxheba: Ufanelekile ukuba ungathatha inxaxheba kwesi Sifundo sam sophando, ngoko ndinqwenela ukwazi ukuba ungandinika na imizuzu embalwa yexesha lakho ndikucacisele ngolu phando lwam, futhi ndicele nemvume yokuba ndikubandakanye na wena kulo?

Yintoni uPhando: UPhando luqokelelo nohlalutyo lweenkcukacha ngenjongo yokwandisa ukuqonda kwethu umba othile, size ke njalo sifumane ulwazi olutsha.

INkcazo yeeNkqubo: Sivavanya ukwenzeka kwe-ICUAW (intensive care unit-acquired weakness -ubuthathaka obufunyanwa kwiyunithi yabagula kakhulu) kwabanye babaguli abalaliswe kwiyunithi yabagula kakhulu, i-ICU yaseLivingstone Hospital. Kolu phando sizakufuna ukuba sisebenzise iinkcukacha ezimalunga nokugula kwakho kumarekhodi onyango lwakho. Ubonwa ufanelekile kolu phando ngenxa yokuba uye walala e-ICU iiyure ezingaphezulu kuma-48 unikwa inkxaso kwingxaki yokuphelelwa ngumoya okanye/kunye neyokungasebenzi kakuhle kwelungu elithile lakho. Sicela ukuba uye kwiiklinikhi ezimbini zase-ICU ngaloo mihla uthe wayinikwa emva kokukhululwa kwakho eLivingstone Hospital. Utyelelo lokuqala luya kuba kwisithuba seeveki ezintandathu (6) ukuya kwezisibhozo (8) emva kokuba ukhululwe esibhedlele, kuze olunye lube kwisithuba seenyanga ezintandathu (6) emva kokuba ukhululwe. Kutyelelo lokuqala eklinikhi siya kuthi sikuxilonge, sivavanye amandla ezihlunu zakho sisebenzisa inkqubo yokunika amanqaku, sisebenzisa isixhotyana esincinane esibanjwa ngesandla esikwaziyo ukumeta amandla ezihlunu zakho. Utyelelo olu luthatha ixesha elingangeyure enesiqingatha ukugqitywa.

Injongo yolu phando kukuvavanya i-ICUAW neenkqubo ezikhoyo zokukhawulelana nale meko kwabo bathe baphila kunyango olumandla basemngciphekweni wokufunyanwa bubulwelwe obulandela olu nyango lumandla. Sinqwenela ukufumana abaguli abali khulu elinamashumi amahlanu (150). Iinjongo zethu kukufumanisa ukuba bangaphi na abaguli abasathi bafunyanwe bubuthathaka bezihlunu emva kokuba bekhululwe esibhedlele, sinxulumanise iinkqubo ezimbini ezinokuthi zisetyenziswe ekumeteni ubuthathaka bezihlunu nokuthelekisa utshintsho kumandla ezihlunu ukusukela kwiiveki ezintandathu (6) ukuya kwiinyanga ezintandathu (6). Siyazi ukuba ngokwakwiziphumo zophando lwaphesheya kolwandle, abantu abathe basinda ngonyango olumandundu basemngciphekweni wokuvelelwa bubuthathaka bezihlunu ngelixa balele e-ICU, ubuthathaka obo obunokubaphatha kude kuye kutsho nasemva kokukhululwa kwabo. Ngethamsanqa ke kodwa, asingabo bonke abaguli abaye balaliswa e-ICU abaye

bafunyanwe bobu buthathaka bezihlunu, kodwa ke ukuba kunokuthi kwenzeke kuwe oku emva kokuba ukhululwe e-ICU, singakubonelela ngokukuxhasa bhetele sikuthumele apho unokufumana unyango khona. Le nkcazelo futhi ingasinceda nasekubeni sithathe izigqibo ezifanelekileyo malunga nonyango lwakho nolwabanye abaguli. Azikho ngako iinkcukacha malunga nokuba bangaphi na abaguli base-ICU eMzantsi Afrika abasafunyanwa bobu buthathaka bezihlunu base-ICU emva kokuba bekhululwe esibhedlele. Ngeso sizathu ke, sinqwenela ukuba ngokwenza olu phando, sifumanise ukuba bangaphi na abaguli bethu abasathi bafunyanwe bubuthathaka bezihlunu emva kokuba bekhululwe esibhedlele.

Imingcipheko okanye Ubunzima kuMthathinxaxheba: Asiboni ukuba kungabakho imingcipheko onokubekeka kuyo okanye ubunzima onokubufumana, kodwa ke kambe kungabakhona kona ukuqina kancinane kwezihlunu ngosuku olulandelayo.

Mcacisele umthathinxaxheba izizathu ezinokumenza afune ukurhoxa kolu Phando: Unelungelo lokuba ungagqiba, nanini na, ekubeni akufuni ukuba yinxenye yolu phando. Xa kuthe kwenzeka njalo, asisayi kuphinda siqhagamshelane nawe, futhi ke akukho nanto iya kukuchaphazela kakubi, neenkcukacha ngawe azisayi kugcinwa sithi, kunjalo nje zingasoze zisetyenziswe nakuluphi na uphando. Kambe ke kusafuneka ukuba uye kutyelelo ngezo ntsuku uye wazinikwa ngelixa ukukhululwa esibhedlele ngoogqirha bewadi yakho. Ukuba uye walibala ukuza, singathanda ukuba sikufowunele ngenjongo yokuba sikukhumbuze neyokuqonda ukuba kungasizathu sini na ungakwazanga nje ukuza kolu tyelelo.

Okuluncedo: Ukuba sithe safumanisa kukho naziphi na iingxaki ezifuna olunye unyango, siya kwenza amalungiselelo okuba mawuye kubonana nonompilo ofanelekileyo, umzekelo, omnye ugqirha, unompilo onyanga ngovonyavonyo lwamalungu omzimba (physiotherapist).

Intlawulo: Ngenxa yokuba olu phando lolokuqokelela iinkcukacha zokufunda, siya kukuhlawulela iindleko zakho zokuhamba ngotyelelo ngalunye, ngenjongo yokuqinisekisa ukuba uyakwazi ukuza.

Iindleko zolu Phando: Wena awusayi kulindeleka ukuba uthwale naziphi na iindleko zolu phando.

Ubuhlebo: Uya kuthi unikwe inombolo yophando. Iinkcukachacha ezingavezi mninizo, ziya kuthi zithunyelwe kubaphengululi bamanani-nkcukacha (statisticians). Akukho namnye umntu oya kuzazi iinkcukacha zakho ngaphandle koogqirha abaqhuba unyango neengcali zetheknoloji yonyango.

Iziphumo: Iziphumo zabo bonke abaguli siya kuthi sizidibanise, size ke sibhale ingxelo eyandlala ukwenzeka kwe-ICUAW emva kokukhululwa e-ICU neenkqubo ezithe zasetyenziswa. Igama lakho alisoze livele nandawoni na kule ngxelo.

Ingozi enxulumene nolu Phando: Akubonakali ngathi kungabakho nayiphi na ingozi enxulumene nolu phando.

Ukugcinwa kwazo zonke iikopi ezisemitshinini nezisemaphepheni, kubandakanya nezikushicilelolizwi: Iimpepha zoqokelelo nkcukacha ziya kutshixelwa ekhabhathini ekwiofisi yomenziphando etshixiweyo. Kwiikhompuyutha ezimbini ezivulwa ngepasiwedi kuya kugcinwa kuzo iinkcukacha ezingabonisi mnini nge-*spread sheets*. Iinkcukacha eziqokelelweyo ziya kugcinwa isithuba seminyaka emihlanu (5), ukuze kumana ukubhekiswa kuzo xa kukho imibuzo ngazo. Iikopi ezingamaphepha ziya kutsheqwa zinqunqeke emva kweminyaka emihlanu (5), zize zona ezikwiikhompuyutha zicinywe.

Abantu onokunxulumana nabo xa kubakho iingxaki okanye imibuzo: Nceda ndifonele, Mam' N van Vuuren (0827335091/nolinevanv@gmail.com), umqapheli wam, uDkt D R Prakaschandra (031 373 6885/rosaleypra@dut.ac.za) okanye uMphathi we-Ethics yeBhaliswa eRhafho le-Institution (031 373 2375). Izimvo zingathathwa kwiNdoda: Uqeqesho Nobungqina-Postgraduate uDkt L Linganiso (031 373 2577/ researchdirector@dut.ac.za)

Sinqwenela ukukubulela ngokuthi ugqibe ekubeni usincedise kolu phando, futhi sithemba nokuba siya kukwazi ukuqokelela iinkcukacha eziluncedo, eziya kuba luncedo kuwe nakwabanye abaguli kwi-ICU yaseLivingstone Hospital naseMzantsi Afrika. Nceda ukhululeke ke usibuze nayiphi na imibuzo onokuthi kanti unayo malunga nolu phando.

Appendix 15: Patient Informed Consent – Xhosa

IMVUME

Uvavanyo lobuthathaka, nobulwelwe obufunyanwa ngabaguli abadala emveni konyango olumandla kwiYunithi yabagula kakhulu (Intensive Care Unit) abasemngciphekweni wobuthathaka nobulwelwe obulandela unyanyo kulondolozo olumandla.

Igama loMphandi/Amagama abaPhandi: Noline van Vuuren

Isitatimenti seMvume Yokuthatha iNxaxheba kwisiFundo soPhando:

- Apha ndiyaqinisekisa ukuba ndazisiwe ngumphandi, u Noline van Vuuren, ngohlobo, ngenkqubo, ngoncedo nangemingcipheko yolu phando – (iNombolo yeResearch Ethics Clearance Number – yesiQinisekiso seNtsulungeko yoPhando): IREC 135/27.
- Kananjalo ndiyifumene, ndayifunda, ndayiqonda le nkcazelo ibhalwe ngentla apha (iLeta yeNkcazelo yoMthathinxaxheba – Participant Letter of Information) emalunga nolu phando.
- Ndiyakuqonda ukuba iziphumo zolu phando, kubandakanya neenkcukacha ezingam ngokuphathelele kwisini, kubudala, umhla wokuzalwa oonobumba bokuqala bamagama am nokufunyaniswe kuxilongo lwam, zizinto eziya kusetyenziswa kwingxelo yolu phando zingadizwanga ukuba zibhekisele kubani na.
- Ngokweemfuno zophando olu, ndiyavuma ukuba iinkcukacha ezithe zaqokelelwa xa belusenziwa zingafakwa zisetyenzwe ngumphandi ngenkqubo yekhompuyutha.
- Mna ke, nanini na, ndisenokuyirhoxisa imvume nenxaxheba yam kolu phando, phofu ndinganikezeli nangawaphi na amalungelo am.
- Ndiye ndaba nalo ngokwaneleyo nethuba lokubuza imibuzo ndaza ke (ngokuzithandela) ndaxela ukuba ndikulungele ukuthabatha inxaxheba kolu phando.
- Ndiyakuqonda nokuba ndiyakwaziswa ngezinto ezintsha ezibalulekileyo eziye zaveliswa lolu phando ezinokuthi zichaphazele inxaxheba yam.

Igama elipheleleyo loMthathinxaxheba	Umhla	Umsayino/Ubhontsi wasekunene

Mna,Noline van Vuuren, apha ndiqinisekisa ukuba lo mthathinxaxheba ungentla apha uye wachazelwa ngokupheleleyo ngolu phando lungentla nohlobo, nenkqubo, nemingcipheko yolu phando.

Igama elipheleleyo loMphandi	Umhla	Umsayino
Igama elipheleleyo lengqina	Umhla	Umsayino

Appendix 16: Ethics Training Certificate

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DR RICHARD STEELE
BA HDE MTech(Hom)
HOMEOPATH
Registration No. A07309 HM
Practice No. 0807524
Freelance academic editor
Associate member: Professional Editors' Guild, South Africa

154 Magenta Place
Gxarha [Morgan Bay]
5292
Eastern Cape

082-928-6208
rsteele@vodamail.co.za
rsteele201@outlook.com

EDITING CERTIFICATE

Re: **Noline van Vuuren**
DUT master's dissertation: **THE ASSESSMENT OF INTENSIVE CARE UNIT-ACQUIRED WEAKNESS IN ADULT PATIENTS AT RISK OF POST INTENSIVE CARE SYNDROME**

I confirm that I have edited this dissertation and the references for clarity, language and layout. I returned the document to the author with track changes so correct implementation of the changes and clarifications requested in the text and references is the responsibility of the author. The intellectual content of the document is the responsibility of the author. I am a freelance editor specialising in proofreading and editing academic documents. My original tertiary degree which I obtained at the University of Cape Town was a B.A. with English as a major and I went on to complete an H.D.E. (P.G.) Sec. with English as my teaching subject. I was a part-time lecturer in the Department of Homoeopathy at the Durban University of Technology for 13 years and supervised many master's degree dissertations during that period.

Dr Richard Steele
10 November 2023
per email