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Influence of Muscle Strength on Mobility in Critically Ill Adult Patients on Mechanical Ventilation

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Influence of Muscle Strength on Mobility in Critically Ill Adult Patients on Mechanical Ventilation

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

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Abstract

INFLUENCE OF MUSCLE STRENGTH ON MOBILITY IN THE CRITICALLY ILL ADULT PATIENT ON MECHANICAL VENTILATION

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Patients in the intensive care unit (ICU) setting are prone to develop muscle weakness and the causes are multi-factorial. Muscle strength in adult, critically ill patients on mechanical ventilation decreases with immobility. The influence of muscle strength on different muscle groups and its influence on progressive mobility in the adult, critically ill patient on mechanical ventilation has not been examined. Identifying muscle strength in this patient population can benefit overall muscle health and minimize muscle deconditioning through a progressive mobility plan. The objective of this dissertation was to describe muscle strength in different muscle groups and to describe the influence of muscle strength on mobility in critically ill adult patients on mechanical ventilation (MV). Fifty ICU patients were enrolled in this descriptive, cross sectional study**.** Abdominal core, bilateral hand grip and extremity strength was measured using three measurement tools. Mobility was measured using the following scale: 0=lying in bed; 1=sitting on edge of bed; 2=sitting on edge of bed to standing; 3=walking to bedside chair and 4=walking >7 feet from the standing position. Predictors of mobility were examined using stepwise regression. Abdominal core, bilateral hand grip and extremity strength demonstrated statistically significant relationships with all variables. Extremity strength accounted for 82% of the variance in mobility and was the sole predictor (β=0.903; F=212.9; p=0.000). Future research addressing the outcomes of implementing a mobility protocol in this patient population and prioritizing when such a protocol should be implemented would be beneficial to ongoing plans to decrease MV, ICU and hospital days. Muscle strength tests implemented at the bedside are crucial to implementing a progressive mobility plan for critically ill adults while they are on MV therapy.

Manuscript 1

Influence of Muscle Strength on Early Mobility in Critically Ill Adult Patients: Systematic Literature Review

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Abstract

Muscle strength may be one indicator of readiness to mobilize that can be used to guide decisions regarding early mobility efforts and to progressively advance mobilization. The objective of this literature review was to provide a synthesis of current measures of muscle strength in the assessment of early mobilization in critically ill adult patients who are receiving MV therapy. Research studies conducted between 2000-2015 were identified using PubMed, CINHAL, MEDLINE, and the Cochrane Database of Systematic Reviews databases using the search terms "muscle strength", "intensive care", "mechanical ventilation" and "muscle weakness". Nine articles used manual muscle testing, the Medical Research Council scale and/or hand-held dynamometer to provide objective measures for assessing muscle strength in the critically ill adult patient population. Further research is needed to examine the application

of standardized measures of muscle strength for guiding decisions regarding early and progressive advancement of mobility goals in adult ICU patients on MV.

Immobility in the Critically Ill Adult Patient

Muscle weakness, prevalent in the critically ill patient, is multi-factorial in its causes and may be compounded by neuromuscular, cardiovascular, pulmonary, psychological, pharmacological and equipment barriers (De Jonghe et al., 2007; Schweickert & Hall, 2007; Winkelman, 2007). Intensive care unit (ICU) patients may experience deficits in their attention, arousal and cognitive abilities (Waak, Zaremba, & Eikermann, 2013), especially if neuromuscular blocking agents and sedatives have been administered as part of their plan of care. Neuromuscular dysfunction has been identified as an etiology of muscle weakness due to disease processes found in the ICU patient population, such as sepsis, multiple organ dysfunction syndromes, and acute respiratory distress syndrome (De Jonghe et al., 2002; Herridge et al., 2003). Further complicating muscle weakness in critically ill patients are possible neurosensory impairments (e.g., tactile, auditory, visual) and localized barriers/injuries (e.g., invasive lines/tubes, pressure ulcers) frequently experienced during critical illness (Waak et al., 2013). Reduced venous return resulting in deep vein thrombosis (Convertino, Bloomfield, & Greenleaf, 1997; Timmerman, 2007) and pulmonary complications, such as atelectasis and pneumonia, are unfortunate sequelae of muscle weakness and immobility (Convertino et al., 1997; Timmerman, 2007).

Persistent muscle weakness and immobility due to muscle deconditioning can be unfortunate consequences of mechanical ventilation (MV) therapy. Mechanical ventilation, the process of exchanging oxygen and carbon dioxide using a device, may impact early mobilization and lengthen the ICU stay. It is well established that the implementation of an early mobilization program improves patient outcomes, to include functional status, patients getting out of the bed sooner in the ICU setting, and decreased hospital and ICU days In critically ill adult patients, MV therapy is an intervention used to support one's exchange of oxygen and carbon dioxide in the lungs. It requires an artificial airway to be placed in the patient's trachea to support this gas exchange. It is well established that the implementation of an early mobilization program improves patient outcomes, to include functional status, patients getting out of the bed sooner in the ICU setting, and decreased hospital and ICU days (Bailey et al., 2007; Burtin et al., 2009; Morris et al., 2008; Winkelman et al., 2012). However, health care team members are often hesitant to initiate early mobility interventions for patients who require MV because of perceptions that they may put the patient at increased risk of accidental extubation or injury. In recent years, several research studies have concluded that mobilizing patients on MV therapy is safe, feasible and minimizes the long-term effects of immobilization (Bailey et al., 2007; Burtin et al., 2009; Morris et al., 2008; Winkelman et al., 2012). Muscle strength is often assessed in other patient populations to guide the delivery of activity interventions and determine rehabilitation needs. Less attention, however, has been focused on identifying the influence of muscle strength on early mobilization in the critically ill adult patient on MV therapy. Equally important is determining how muscle strength can be measured in this patient population at the bedside. Understanding and recognizing the influence of muscle strength on decreasing muscle deconditioning has the potential to increase early mobilization in this patient population. Muscle strength is an important measure for predicting and evaluating early mobilization in the critically ill adult patient on MV therapy. Therefore, a literature review was performed to provide a synthesis of current measurements of muscle strength used in the assessment of readiness to mobilize in critically ill adult patients who are receiving MV therapy. The questions guiding the systematic literature review were:

(a) What measurements have been used to assess muscle strength in adult critically ill patients receiving mechanical ventilation therapy?

(b) Which measurements demonstrate readiness for early mobilization in adult critically ill patients receiving mechanical ventilation therapy? Understanding and recognizing the influence of muscle strength on decreasing muscle deconditioning has the potential to increase early mobilization in this patient population.

Muscle Strength in the Critically Ill Adult Patient

Despite the dissemination of literature promoting the importance of early mobilization in the critically ill patient receiving MV therapy, there is a lack of research that has explored the influence of muscle strength on early mobilization in this patient population. Numerous patients admitted to an ICU setting acquire a syndrome described as a neuromuscular dysfunction, which is characterized as generalized limb and respiratory muscle weakness (Bolton, 2005). This syndrome, which has come to be known as critical illness neuromyopathy (CINM), occurs in critically ill patients without previous neuromuscular disease, indicating its simultaneous development with the critical illness and/or treatments (De Jonghe et al., 2002; Schweickert & Hall, 2007; Stevens et al., 2007). CINM has a respiratory neuromuscular weakness and peripheral neuromyopathy components (De Jonghe et al., 2007). The respiratory neuromuscular component of CINM has been shown to be a predictor of delayed weaning in patients receiving MV therapy as well as associated with peripheral myopathy weakness (De Jonghe et al., 2007). Although the respiratory component the respiratory component of CINM is not the focus of this literature review, it is a vital assessment area in the overall outcome of critically ill adults being able to perform activities during and following their ICU stay.

The peripheral neuromyopathy weakness component of CINM, which has come to be described as ICU-acquired weakness (ICU-AW) (de Jonghe, Lacherade, Sharshar, & Outin, 2009), has raised awareness of its clinical significance in the critically ill adult. The prevalence of muscle weakness in patients who regain normal consciousness after greater than 1one week of MV therapy is 25% - 60% (de Jonghe et al., 2009). These patients have demonstrated muscle waste peaking during the first three weeks of ICU stay, indicating early physical activity in this patient population can benefit overall muscle health and minimize muscle deconditioning (Gruther et al., 2008). Patients experiencing ICU-AW often have a diagnosis of sepsis leading to multiple organ and respiratory failure requiring prolonged MV therapy (Stevens et al., 2007). Patients exhibiting both limb and respiratory weakness are at risk of experiencing clinically significant decline in their muscle strength, requiring purposeful interventions to support early mobility. While there has been a significant focus on respiratory muscle weakness, less emphasis has been placed on measuring limb strength as a potential influence of mobility readiness.

Methods

Eligibility Criteria and Sources

Using the preferred reporting items for systematic reviews and meta-analyses (PRIMSA) guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009), the PubMed/MEDLINE, CINAHL, and the Cochrane Database of Systematic Reviews databases were searched to access research studies published between the years 2000 – 2015 to reflect current best practice. The articles were primary research conducted in an adult ICU setting on patients receiving MV therapy, assessing muscle strength and reported in the English language. This literature review was conducted from May 2014 – November 2015 using the search terms "muscle strength", "intensive care", "mechanical ventilation" and "muscle weakness". Although this literature search started in May 2014, it was not completed until November 2015. Although this literature search started in May 2014, it was not completed until November 2015 due to time constraints in completing the search.

Search and Study Selection

Using the PubMed database, the above-mentioned search terms were used with a search date range of "01/01/2000 through 11/14/2015", "humans", "English language", and "adults: 19+ years" as additional limiters. The results yielded a total of 97,848 articles. Each search term was added to the search builder section of the advanced search method using the "AND" operator, yielding (34) articles. This same process was used for each of the other database searches. Screening of the articles was independently performed by the primary author. Using the inclusion and exclusion criteria, initial screening included a review of each article's title, which eliminated (17) articles due to the title having a different patient or disease foci, such as red blood cells, neurologic disease, electrical stimulation and heart transplantation. An additional (11) articles were eliminated after reading the title, full abstract, introduction and methodology sections of the articles due to alternate focus of research, to include rehabilitation therapy, glycemic control and MV weaning. The remaining (6) articles were read in their entirety based on meeting the inclusion criteria and were included in this systematic review. Ancestry searches (review of references in selected articles) Using the inclusion and exclusion criteria, initial screening included a review of each article's title, which eliminated (17) articles due to the title having a different patient or disease foci, such as red blood cells, neurologic disease, electrical

stimulation and heart transplantation. An additional (11) articles were eliminated after reading the title, full abstract, introduction and methodology sections of the articles due to alternate focus of research, to include rehabilitation therapy, glycemic control and MV weaning. The remaining (6) articles were read in their entirety based on meeting the inclusion criteria and were included in this systematic review. Ancestry searches (review of references in selected articles) were performed on the six publications acquired and two additional publications were identified that fit the inclusion and exclusion criteria and were added to this systematic review. One additional article was included in this review upon receiving this article in a journal subscription as it, too, also met the inclusion and exclusion criteria. A total of nine articles were included in this literature review. Risk of bias was determined by evaluating the methodological quality of all articles that met the inclusion criteria to the extent to which these studies could be replicated. Publication bias was minimized by using a variety of databases to search for relevant research articles. All articles included in the analysis were evaluated as low bias. Criteria for inclusion are listed in Table 1 and were identified based on desired patient population (adults greater than 18-years old), location of the patient (ICU setting), patients receiving MV therapy during the study, study was focused on assessing muscle strength, patients comprehended the English language and the study was an original study. Exclusion criteria, also listed in Table 1, included patients not in the ICU setting during the study and patients with pre-existing neuromuscular disorders, any missing limbs, unable to ambulate upon ICU admission with or without an assistive device, any nerve stimulation needs and patients not awake, sedated or paralyzed at the time of the study. Criteria for inclusion are listed in Table 1 and were identified based on desired patient population (adults greater than 18-years old), location of the patient (ICU setting), patients receiving MV therapy during the study, study was focused on assessing muscle strength, patients comprehended the English language and the study was an original study. Exclusion criteria, also listed in Table 1, included patients not in the ICU setting during the study and patients with pre-existing neuromuscular disorders, any missing limbs, unable to ambulate upon ICU admission with or without an assistive device, any nerve stimulation needs and patients not awake, sedated or paralyzed at the time of the study. Refer to Figure 1 for a descriptive flowchart of the literature search in the PubMed database.

Data Collection Process and Data Items

Using Garrard's Matrix Method (2011), a table was developed to systematically summarize the eight articles. Topics for abstraction from each article included: (a) the authors' name and year of publication; (b) the research design, which included the timeframe of the study; (c) sample and setting; (d) method(s)/devices used to measure strength; (e) statistical analysis, and; (f) the main outcomes of the study. The principal summary measures reported in each manuscript were identified and include descriptive analysis and tests of significance. A summary of this process can be found in Table 2.

Results

Nine publications between the years 2008-2015 were included in this systematic review. Eight were prospective design studies and one was a randomized controlled trial (RCT) design. The age range of the subjects was 23- to 93-years and 56% of the studies had more male than female subjects. In four of the studies (44%) and 56% of the studies had more male than female subjects. In four of the studies (44%), there were more female patients enrolled than male patients (Ali et al., 2008; Chlan, Tracy, Guttormson, & Savik, 2015; Nordon-Craft, Schenkman, Ridgeway, Benson, & Moss, 2011; Yosef-Brauner, Adi, Shahar, Yehezkel, & Carmeli, 2015). The settings for the studies varied between Medical ICUs (MICU), Surgical ICUs (SICU), and a

Medical-Surgical ICU. Three articles did not specify the type of ICU setting their study was conducted (Baldwin, Paratz, & Bersten, 2013; Chlan et al., 2015; Yosef-Brauner et al., 2015) and one study identified using only surgical ICU patients (Lee et al., 2012). Seven articles reported MV measurements using median and interquartile ranges (IQR) for the days spent on MV (Ali et al., 2008; Baldwin & Bersten, 2014; Baldwin et al., 2013; Chlan et al., 2015; De Jonghe et al., 2007; Lee et al., 2012; Nordon-Craft et al., 2011). With the exception of one publication (Burtin et al., 2009), articles included subjects with sepsis or infection and respiratory disease as a diagnosis. One study included subjects with a diagnosis of sepsis but not respiratory disease (Baldwin & Bersten, 2014) and another study identified a history of cardiac and respiratory disease (Burtin et al., 2009) in its subjects.

All the studies assessed the patients' ability to focus their attention to perform simple commands following enrollment. Three studies (Ali et al., 2008; Baldwin & Bersten, 2014; Baldwin et al., 2013) used the Attention Screening Exam (Ely et al., 2001), a valid method for ICU patients and two studies used a screening method for assessing awakening and comprehension (De Jonghe et al., 2007; Lee et al., 2012). One study used both methods to assess attention to commands (Nordon-Craft et al., 2011). Another study enrolled patients who received intravenous sedation and/or neuromuscular blocking agents in the ICU, however, did not assess the participants' ability to follow commands (Burtin et al., 2009). Two studies did not identify a specific method for determining comprehension or ability to follow simple commands (Chlan et al., 2015; Yosef-Brauner et al., 2015).

There were two measures predominately used in the nine studies to determine muscle strength. The Manual Muscle Test (MMT), as measured by the compares the patient's muscle strength in six different muscles groups in the upper and lower extremities bilaterally and is measured to determine the Medical Research Council (MRC) 0-5 summated score, which has been deemed a reliable and valid test to assess muscle strength and was used in seven studies (Ali et al., 2008; Baldwin & Bersten, 2014; Baldwin et al., 2013; De Jonghe et al., 2007; Lee et al., 2012; Nordon-Craft et al., 2011; Yosef-Brauner et al., 2015). The MMT compares the patient's muscle strength in six different muscles groups in the upper and lower extremities bilaterally and is measured to determine the Medical Research Council (MRC) 0-5 summated score, which has been deemed a reliable and valid test to assess muscle strength (De Jonghe et al., 2002). The lower MRC scores, grades 0-3, provide reliability in the assessment of strength in patients experiencing weakness (Baldwin et al., 2013). However, grades 4-5 has been noted to not demonstrate a similar reliability, especially in the critically ill patient population, requiring another assessment tool to validate findings regarding strength (Baldwin et al., 2013). Hand-held dynamometry (HHD), a standard method used to quantify the force or strength of hand grip muscle strength, was used in seven studies in this review (Ali et al., 2008; Baldwin & Bersten, 2014; Baldwin et al., 2013; Burtin et al., 2009; Chlan et al., 2015; Lee et al., 2012; Yosef-Brauner et al., 2015). This device measures handgrip strength and quadriceps force and has been used in studies involving the critically ill patient population (Burtin et al., 2009; Vanpee, Hermans, Segers, & Gosselink, 2014; Vanpee et al., 2011) and it has demonstrated high interrater reliability (Mathiowetz, Weber, Volland and Kashman, 1984). Due to the difficulty in differentiating between the MRC 4-5 scores in the critically ill patient, HHD measurement was used in conjunction with the MRC scores in five out of the seven studies (Ali et al., 2008; Baldwin & Bersten, 2014; Baldwin et al., 2013; Lee et al., 2012; Yosef-Brauner et al., 2015). The MRC score was not used in two studies, however, the HHD measure was used in these studies (Burtin et al., 2009; Chlan et al., 2015). Three studies used the MRC score along with maximum inspiratory pressure (MIP) measurements (Baldwin & Bersten, 2014; De Jonghe et al., 2007; Yosef-Brauner et al., 2015). Measurement of MIPs, in addition to using the MRC scale to measure muscle strength, revealed severe respiratory muscle weakness associated with limb weakness (De Jonghe et al., 2007).

The only randomized controlled trial (RCT) article included in this review focused on safety and efficacy using a prescriptive cycle ergometer (MOTOmed Letto 2, Germany) intervention to prevent the decrease in functional exercise capacity, functional status (using the Berg Balance Scale), and quadriceps force in critically ill subjects, measured at ICU and/or hospital discharge (Burtin et al., 2009). Isometric quadriceps force was quantified using a HHD (Microfet 2, Netherlands) and it was determined that quadriceps force improved more between ICU discharge and hospital discharge in the treatment group (1.83 ± 0.91 $N \cdot kg^{-1}$ vs. 2.37 ± 0.62 $N \cdot kg^{-1}$, $p<.01$) than in the control group (1.86 ± 0.78 $N \cdot kg^{-1}$ vs. 2.03 ± 0.75 $N \cdot kg^{-1}$, $p=.11$) (Burtin et al., 2009).

There was one study that used three measurements, MMT, MRC and HHD, to determine muscle strength in the SICU setting (Lee et al., 2012). Recognizing data from the SICU varied from findings in the MICU in other studies, this study suggested that the HHD was a viable tool for predicting mortality in the ICU setting (Lee et al., 2012). Another study used four measures, MRC, HHD, maximum inspiratory pressure (MIP) and sitting balance (SB), mainly in the SICU setting, over three time intervals (Yosef-Brauner et al., 2015). In this study, the authors described no significant difference of these measures at baseline, however, Time 1 (T1, baseline) and Time 2 (T2, after 48-72 hours) demonstrated a statistically significant improvement ($P < 0.05$) for MIP and MRC in the treatment group, while only the MIP parameter for T1 and Time 3 (T3, time of discharge from the ICU) tests showed a statistically significant difference for T1 and

T3 (Yosef-Brauner et al., 2015). This study was also able to demonstrate a statistically significant decrease in the number of ICU hospitalization days and a trend towards decrease ventilation time (Yosef-Brauner et al., 2015).

There was only one study in which a measurement of physical activity (i.e., bed mobility, transfers and gait) and muscle strength was summarized, noting that patients who were discharged home showed higher initial MMT and functional independence measure (FIM) scores (Nordon-Craft et al., 2011). In addition, this study used the MMT-summary score instead of the MRC sum score because the MMT had a greater incidence of detecting small and significant changes in patients with ICU-AW (Nordon-Craft et al., 2011). This was also the only article in this review that identified criteria for progression of activity that included neuromuscular and cognitive status assessment, as well as the patient's subjective report of their fatigue (Nordon-Craft et al., 2011).

The studies identified for the systematic review focused on measurements of muscle strength in critically ill adults receiving MV therapy, however, only one study examined the relationship between muscle strength and the development of criteria for progression of activity (Nordon-Craft et al., 2011). The outcome measures of the studies did not include active mobilization initiation, frequency or duration out of the bed.

Discussion

In the critically ill adult patient, several factors can be measured that may identify the degree at which one will be able to determine muscle strength. First, assessing patients' ability to focus their attention on simple commands appears to be a principle factor to determine prior to the initiation of any muscle strength measurement. Each of the measurements used in the above studies requires that the patient comprehend how to perform the measurements to provide an accurate return demonstration. Determining a patient's comprehension abilities to accurately follow directions is imperative in scoring the measurements precisely. Whether using the Attention Screening Exam (Ely et al., 2001) or a set of questions (De Jonghe et al., 2002), identifying the patient's ability to accurately respond to commands is relevant in determining their ability to follow such commands related to muscle activities. It is also worth considering using the CAM-ICU (Confusion Assessment Method for the ICU) in its entirety to assess the overall mentation status (Ely et al., 2001). The CAM-ICU tool, a step-wise process that assesses multiple facets of a patient's mentation, including determining if there are any acute mental status changes, the patient's attention to details/instruction, their level of consciousness, and if any disorganized thinking exists (Ely et al., 2001). This tool will provide objective data to assess the patient's readiness to comprehend instructions given on how to perform the various muscle strength measures and it has demonstrated high interrater reliability (Ely et al., 2001).

Second, based on this literature review, muscle strength in the patient located in the medical and/or surgical ICU receiving MV therapy can be measured using the MRC, MMT, HHD and MIP measures. Although the MRC has limitations in the ICU patient population, using the MRC in conjunction with a HHD and/or the MIP techniques provides the objective measurements needed to address these limitations. The HHD and MIP measurements can also vary based on the patient's strength during their acute phase of critical illness. However, these measures may better indicate the level of strength an acutely ill adult patient may be experiencing and how this strength is improving over time during this phase of their illness, further indicating the patient's readiness to perform early mobilization. While the MMT, MRC and HHD measures have been used in various settings, such as in rehabilitation and outpatient settings, the use of these measures in the ICU settings remains unclear. In addition, there is diminished use of muscle strength measures in the ICU setting to demonstrate early and progressive mobility in this patient population.

Another implication for future research and clinical practice is the collaborative outcomes that can occur with the involvement of interprofessional team members. Nursing, physical therapy, occupational therapy, respiratory therapy and provider disciplines are familiar with the impact they individually contribute to the care of acutely ill adult patients. Patients in the ICU setting and those on MV therapy may have limited interventions by certain disciplines, based on the patient's progression towards identified goals. Further studies, however, should examine the impact the interprofessional team could have on these patients' outcomes regarding early and progressive mobilization, length of MV therapy days, number of days in the ICU and hospital setting and their return to their pre-hospital baseline functional status. Collectively, the interprofessional team can impact these outcomes and potential provide more evidence to hospital leadership to endorse more routine and standardized support from these services in the ICU settings.

Last, the studies in this literature review measured muscle strength using a variety of methods. However, none of the studies could demonstrate how these tools influenced mobility in the adult critically ill patient population. The MMT, MRC, HHD and MIP, along with critical thinking skills and support of an interprofessional team may provide safe and feasible early and progressive mobility for the ICU patient, as demonstrated by the patient's activity out of the bed while on MV therapy. There is a need to develop a standardized method for quantifying muscle strength and applying these results to determine the patient's activity level (e.g., sitting on the edge of the bed, out of bed to chair or out of room ambulating a specific distance). Evaluation of the relationship between muscle strength and mobility could provide translational tools to improve early and progressive mobilization in this patient population.

Of note, there were a range of different diagnoses and comorbidities across the studies that are common across different ICU settings. This supports the use of a standardized method to measure muscle strength and exploration of strength thresholds that may be related to, and possibly predict, mobilization readiness. Standardizing the method to measure muscle strength in this patient population also provides an opportunity for health care team members to more clearly communicate the patients' plan of care as it relates to early and progressive mobility.

Conclusions

While the purpose of this literature review was to identify factors that influence muscle strength in the adult, critically ill patient receiving MV therapy, it is quite clear that this is an area of science that requires additional research. There are very few articles addressing muscle strength in the critically ill adult patient receiving MV therapy with the purpose of guiding their early and progressive mobility activities. MMT, MRC and HHD appear to have positive benefits in quantifying these patients' muscle strength with predictive value on their functional abilities. Additional studies measuring muscle strength and its impact on early mobilization are needed in the adult intensive care settings with patients requiring MV therapy.

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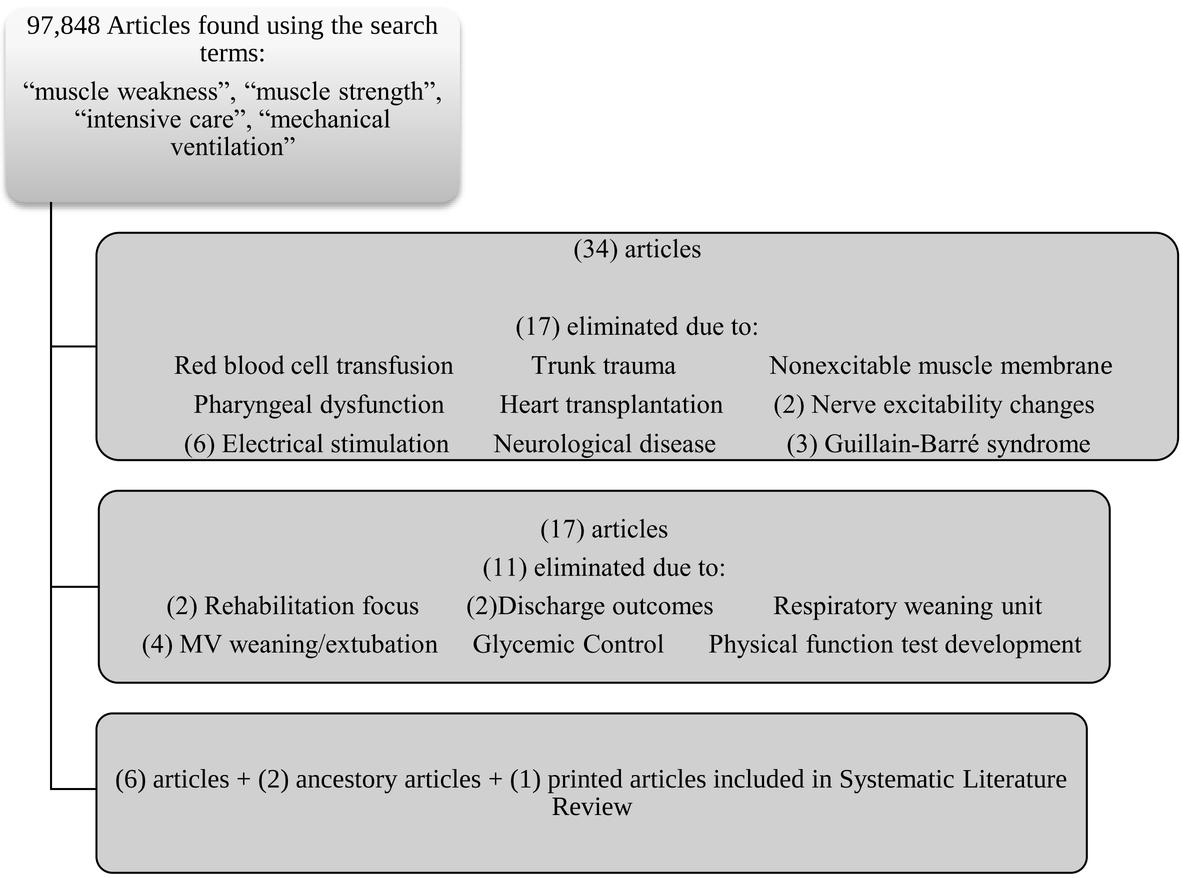

Figure 1: Systematic Literature Review Flowchart

Inclusion Criteria	Exclusion Criteria
✓ Adults >18 years old ✓ Admitted to an ICU setting ✓ Receiving mechanical ventilation for duration of their participation in study ✓ Assessing muscle strength ✓ English language, spoken and comprehended by the patient ✓ Original Study (not a review, editorial)	✓ Patients not in the ICU setting during study ✓ Patients with pre-existing neuromuscular disorders, trauma, missing limbs, orthopedic disorders, unable to ambulate independently or with an assist device during their admission and patients with cardiac dysfunctions ✓ Patients using nerve stimulation ✓ Patients not awake, currently on sedation, paralyzed or that require stimulated muscle force

Table 1: Literature Search Inclusion and Exclusion Criteria

Table 2: Matrix Table of Systematic Literature Review

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Ali, N.A., O'Brien, J.M., Hoffman, S.P., Phillips, G., Garland, A., Finley, J.C., Almoosa, K., … Midwest Critical Care Consortium, 2008 Objective: (a) ICUAP is in-dependently associated with increased mortality; (b) determine if HHD is a concise measure of global strength and is independently associated with mortality	Prospective, multicenter, cohort study May 2005-April 2007	(5) medical ICUs in academic medical centers (AMC) affiliated with the Midwest Critical Care Consortium 174 subjects enrolled and 136 completed study Adults $\geq$ 18 years old, on MV for $\geq$ 5 days	Muscle strength measured with Medical Research Council (MRC) scale Dominant hand-held device (HHD) using the JAMAR device Assessments repeated next day Maximum total MRC score and handgrip from either day = subject's strength	Spearman's r = 0.90, *p*-value<0.001 between ICU-acquired paresis (ICU-AP) and MRC Using sex-specific thresholds for handgrip, handgrip strength had good test performance when compared with an ICU-AP diagnosis by MRC (sensitivity 80.6%, specificity 83.2%) Odds of hospital mortality higher in subjects with ICU-AP Odds Ratio (OR) = 7.8, 95% confidence interval (CI), 2.4-25.3, *p* = 0.001	Hospital mortality higher in patients with ICU-AP than without weakness, per MRC exam and HHD HHD may provide rapid, simple alternative to MRC exam for ICU-AP diagnosis Number of ICU- and hospital-free days were significantly reduced in ICU-AP subjects per MRC exam, with strong correlation with handgrip strength No reference to mobility; perfect agreement of interobservers for 12 pts but didn't state timing or location of Evaluations (all in ICUs??)

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Baldwin, C.E. and Bersten, A.D., 2014 Objective: concurrently investigate relative differences in both thickness and strength or respiratory and peripheral muscles during routine care	Prospective, cross-sectional with a case-controlled element November 2010 – December 2011	16 subjects for both critically ill and healthy group Consecutive patients $\geq$ 18 years old, requiring $\geq$ 12 hours MV, with sepsis, in a single tertiary ICU	HHD used to determine isometric hand-grip, elbow flexion, and knee extension forces (Jamar, Illinois; Lafayette manual muscle test system, Indiana) MRC sum score graded 3 upper limb and 3 lower limb groups bilaterally to ascertain meeting ICU-AW criteria score of <48 out of 60 Measurements done when subjects able to perform all measures	Mean (SD) or median (IQR), Independent – samples *t* test, Pearson *r*, *z*-scores for muscle thickness and strength with reference values obtained from the control group for within-group analysis by repeated measures analysis of variance MRC sum score median = 48 (42-54 IQR); MRC sum score < 48 (indicating ICU-AW) n=8 (50%) Mean difference (95% CI) between critically ill and healthy subjects force: elbow flexion 14.4 (10.2 to 18.5, $p \leq 0.001$); handgrip 23.5 (16.0 to 30.5, $p \leq 0.001$); knee extension 19.0 (14.0 to 23.9, $p \leq 0.001$)	(13) subjects limited to limb exercises in bed with “some” stable for fully assisted transfer to chair; (3) subjects able to perform standing transfer to chair from up to 2-person physical assistance Subjects weaker than control group ($p \leq 0.001$) in respiratory and limb muscle strength measures Future studies should investigate unexplained variances in muscle strength, (e.g., severity of illness) other than size and mass Only 20% of subjects able to return to their pre-admission residence on discharge

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Baldwin, C.E., Paratz, J.D., and Bersten, A.D., 2013 Objective: (a) investigate test-retest and interrater reliability of a muscle strength assessment with portable dynamometry in survivors of critical illness; (b) examine the minimal detectable difference force required to mitigate measurement error; (c) depict peak forces per MRC scale	Repeated measures November 2009 – December 2010	(17) critically ill patients and (12) healthy volunteers Single tertiary ICU Patients $\geq$ 18 years old with an ICU length of stay of $\geq$ 5days and anticipated hospital admission of a further 3 days Protocol initiated at 13-days (IQR, 10-16) of ICU admission MV 240-hours (IQR, 107-355)	Interrater reliability assessed using (2) physiotherapists; Test-retest assessed by one examiner 2-days later Peak isometric hand grip, elbow flexion, and knee extension force measured in modified recumbent positions (3) times bi-laterally, over 6-sec intervals Grip strength measured with JAMAR hydraulic hand dynamometer in the 2nd handle position to the nearest 0.5 kg Elbow flexion and knee extension strength measured with Lafayette manual muscle test system in high range to the nearest 0.1 kg MRC score given for each muscle action after HHD testing for each muscle group	Descriptive statistics Triplicate force readings for each muscle group were averaged and logarithmically transformed for reliability analysis, reported as the geometric mean (95% CI) Interrater and test-retest reliability analyzed with a 2-way mixed model intraclass correlation coefficient (ICC, [95% CI]) Scatter plots used to represent range of forces contained within corresponding MRC scale grades for each muscle action, measured by examiner A on the initial test day	High interrater agreement of hand grip and knee extension forces but wide-ranging 95% CIs for bilateral elbow flexion in critically ill patients High test-retest agreement of hand grip and knee extension forces in the critically ill patients and greater reliability right elbow flexion than left There was overlap of force values between MRC grades of all muscle groups in critically ill sample and considerable range of forces represented within MRC grades 4 and 5.

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Burtin, C., Clerckz, B., Robbeets, C., Ferdinande, P., Langer, D., Troosters, T, Hermans, G…Gosselink, R., 2009 Objectives: (a) investigate whether daily training, using bedside cycle ergometer, is safe/effective intervention in preventing or attenuating the decrease in functional exercise capacity, functional status, and quadriceps force associated with longer ICU stay	Randomized Controlled Trial December 2005 – February 2007	(90) critically ill patients in the medical and surgical ICU at University Hospital Gasthuisberg, Belgium (45 = treatment group, 45 = control group)	Allocation to treatment or control group using sealed opaque envelopes in random block sizes Assessments taken at both day of ICU discharge and day of hospital discharge Treatment group received control group interventions plus cycling exercise session (5) days/week, using bedside cycle Isometric quadriceps force quantified using HHD in supine position with 30° knee flexion; instructions given to extend knees maximally over 3-secs with three repetitions Berg Balance Scale ("from sit to stand") Physical Functioning item of the Short Form-36 (SF-36) Health Survey questionnaire	Descriptive statistics, 95% CI Differences between groups evaluated using unpaired Student's *t* tests, Wilcoxon, Mann-Whitney U test (variables not normally distributed) or Fisher's exact tests (comparing proportions) Spearman's correlation coefficients (95% CI)	(37/71) patients (52%) in surgical ICU; (8/19) patients (42%) in medical ICU; 84% patients were intubated Quadricep force improved more between ICU discharge and hospital discharge in treatment group than control group Handgrip force not different between treatment and control group at ICU discharge and hospital discharge Handgrip force was not correlated with other outcome measures At hospital discharge, quadricep force and SF-36 correlated ($r = .46$, $p < .001$) and the 6-Minute Walking Distance test correlated with quadriceps force ($r = .55$, $p < .001$)

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Chlan, L.L, Tracy, M.F., Guttormson, J. and Savik, K, 2015 Objective: (a) describe daily peripheral muscle strength measurements in subjects receiving MV therapy; and, (b) describe the relationships among factors that influence ICU-AW	Prospective, descriptive, correlational study September 2006 – March 2011 (participants were a subset from a randomized clinical trial on self-management of anxiety using preferred, relaxing music, in patients receiving MV therapy)	120 subjects in (12) ICUs at (5) hospitals in the Minneapolis-St Paul, Minnesota, area	JAMAR Hydraulic Hand Dynamometer (Patterson Medical) – serial measurements over time Used Mathiowetz et al.'s standardized protocol to assess hand grip, using the mean of (3) grip trials Occupational Therapist consulted to modify protocol for this study's subjects	Descriptive statistics, graphing and mixed effects modeling	Median baseline grip strength diminished, ranging from 1-102 pounds-force Pattern of grip strength indicated subjects either started at a higher grip strength and their strength declined or they started at a low level of strength and either stayed low or further declined Females grip strength was lower than males The older the patient, the grip strength diminished The longer on MV therapy, grip strength was decreased Did not have data on subjects' activity level prior to ICU admission nor on respiratory muscle strength

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
De Jonghe, B., Bastuji-Garin, S., Durand, M-C., Malissin, I., Rodrigues, P., Cerf, C., Outin, H.…Group de Réflexion et d'Etude des Neuromyopathies En Réanimation, 2007 Objective: (a) Assess severity of respiratory neuromuscular function; (b) correlation between respiratory and limb muscle strength.	Prospective, observational study June 2003 – June 2005	2-medical ICUs, 1-surgical ICU, 1-medico-surgical ICU in two university hospitals and one university-affiliated hospital 116 consecutive patients after ≥ 7-days of MV	Maximal inspiratory/ expiratory pressures and vital capacity Muscle strength measured in the four limbs with MRC scale	Categorical variables = n (%) and compared using chi-square or Fisher's exact test Median (IQR) used and compared using the Mann-Whitney test Associations between MRC score's and other inspiratory/expiratory pressures and vital capacity outcome measures analyzed using Spearman's correlations and analysis of variance	Bedside measurement of muscle strength at awakening revealed severed respiratory muscle weakness associated with limb weakness (median MRC score = 41 for 115 patients [99.1%]; IQR = 21-52). Significant correlations between MRC score inspiratory pressures (rho = 0.35, *p* = .001), expiratory pressures (rho = 0.49, *p* < .0001), and vital capacity (rho = 0.31, *p* = .007) Low MRC score was an independent predictor of delayed successful extubation (odds ratio, 3.03; 95% CI, 1.23-7.43; *p* = .02)

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Lee, J.L., Waak, K., Grosse-Sundrup, M., Xue, F., Lee, J., Chipman, D., Ryan, C…Eikerman n, 2012 Objective: (a) evaluate the predictive value of strength measured by MMT and HHD at ICU admission for in-hospital mortality, SICU LOS; (b) MMT and handgrip strength measurements would be associated with hospital LOS and MV days	Prospective, observational study July 2011 – October 2011	(95) patients in the 20-bed SICU in a large tertiary AMC, who had surgery and relatively low disease severity level MV days varied from median 1.5 (IQR, 0 to 4.5) to 3 (IQR, 1.5 to 8.4) ≥18 years old	Manual Muscle Testing (MMT), JAMAR handgrip dynamometry (Sammons, Illinois), sum score on the MRC scale to quantify MMT MMT completed in 95 patients (88.8%), 44 (46.3%) met cutoff for ICU-AP (MRC < 48) median = 48 (IQR, 39.8 to 56.6) 80/94 patients (85.1%) = ICU-AP (12) muscle groups measured	Multivariant logistic regression used to identify which independent variables (MMT and HHD) were associated with mortality Spearman's correlation used to identify indepen-dent variables associated with SICU LOS, hospital LOS and MV days Lower level of disease severity and lower grip strength than Ali study and Sedation paused for exams for how long? Median time until strength testing could be reliably performed = 3days (IQR, 2-5 days)	MMT reliably predicted in-hospital mortality, number of vent days, SICU length of stay (LOS) and hospital LOS. Logistic regression demonstrated as strength increased, mortality decreased Grip strength and MMT-derived strength measurements r = .55, *p*<0.0001, but grip strength didn't predict patient outcomes in SICU Handgrip strength was not independently associated with mortality, LOS, MV days Global muscle weakness predicts mortality and MV duration in the ICU SICU and MICU data differ, suggesting HHD strength is a viable tool for predicting mortality

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Nordon-Craft, A., Schenkman, M., Ridgeway, K., Benson, A., and Moss, M., 2011 Objective: (a) described safety and feasibility of participation in PT intervention for patients with ICU-AW with MV for at least 7-days; (b) characterize the exam and intervention procedures with sufficient detail that can be implement a similar strategy	Case Series study March 2008-February 2009	19 patients with ICU- AW who required MV for at least 7-days, $\geq$ 18 years; 12 (63%) in MICU and 6 (32%) SICU	PT was provided by a therapist 5 days/week for 30mins/session MRC scoring system, MMT, FTSST, FIM, TUG, 2MWT, FIM (Functional Independence Measure) components measured bed mobility, transfers, and gait). Reliability of individual items of the FIM has not been established FTSST, TUG and 2MWT tests used to measure activity and balance 2MWT correlates with the 6MWT (r = 0.94) PT exam and interventions done with PT, RN, RT and MD team members	Median (IQR), frequencies	Lines/tubes temporarily disconnected for mobility Criteria for progression of activity based on the clinician's judgment of the patients' physiological response and cognitive status, and patients' subjective report of fatigue PT driven for initiating and early termination PT intervention is safe and feasible for patients with ICU-AW requiring MV for at least 7-days Team approach is necessary and critically ill patients can tolerate earlier mobilization than what typically occurs Most participants limited to perform functional activities w/baseline median FIM 2

RESEARCH STUDY	RESEARCH DESIGN	SAMPLE and SETTING	METHODS/DEVICES for MEASUREMENT	STATISTICAL ANALYSIS	MAIN OUTCOMES
Yosef-Brauner O, Adi N, Ben Shahar T, Yehezkel E and Carmeli E., 2015 Objectives: evaluate the effect of an intensive physical therapy protocol in subjects who contract ICU-AW, in terms of muscle strength, breathing and functional indices.	Prospective, single-blinded study June 2011 – February 2012	(18) ICU subjects with MV > 48-hours and expected to remain ventilated ≥ 48 additional hours (most were surgical subjects), randomly divided into (2) groups: control and treatment >18-years old, independent before admission, able to perform simple commands, and had a MRC physical strength examination score < 48 points.	Subject's family members were questioned regarding subject's pre-hospital functional parameters, using the Barthel Index(Mahoney & Barthel, 1965) Subjects were tested at (3) time periods: baseline (T1) for right and left hand grip strength using a Jamar dynamometer (Lafayette, IN), passive range of motion in the upright position, manual lung hyperinflation and bronchial suctioning; (T2), performed after 48–72 hours, included subjects who were ≥1 on the manual muscle test, active joint exercises, breathing exercises, manual lung hyperinflation, bronchial suctioning, sitting balance (SB) and trunk exercises; (T3) done at discharge from the ICU measuring the same parameters as done in T2.	Descriptive statistics, change in parameters between both groups and between T1 and T2 and T1 and T3. Chi-square for nominal variables; Mann-Whitney for ordinal variables and between groups; t-test for ratio variables and between groups; Wilcoxon and t-test to describe average differences between T1 and T2 and T1 and T3 Correlations described using Spearman's rho for ratio variables and Pearson's rho for ordinal variables	No statistical difference found between the two groups at baseline for MRC, dynamometry, maximum inspiratory pressure and SB T1 and T2 demonstrated a statistically significant improvement ($P < 0.05$) for MIP and MRC in the treatment group; only MIP parameter for T1 and T3 tests Statistically significant decrease in the number of ICU hospitalization days Trend towards decrease ventilation time Strong positive relationship between MRC and SB and MRC and right hand dynamometry Strong negative correlation between MRC and MIP in T1 and T2

Abbreviations:

SD = Standard Deviation	SICU = Surgical Intensive Care Unit
IQR = Interquartile Range	MICU = Medical Intensive Care Unit
CI = Confidence Interval	PT = Physical Therapy
ICC = Intraclass Correlation Coefficient	FTSST = Five Times Sit to Stand Test
AMC = Academic Medical Center	TUG = Time Up to Go
2MWT = 2-Minute Walk Test	RN = Registered Nurse
RT = Respiratory Therapist	MD = Medical Doctor
SB = Sitting Balance	

Manuscript 2

Influence of muscle strength on mobility in the critically ill adult patient on mechanical ventilation

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Abstract

Background: Patients in the intensive care unit (ICU) setting are prone to develop muscle weakness and the causes are multi-factorial. Muscle strength in adult, critically ill patients on mechanical ventilation (MV) decreases with immobility. The influence of muscle strength on different muscle groups and its influence on progressive mobility in the adult, critically ill patient on mechanical ventilation has not been examined. Identifying muscle strength in this patient population can benefit overall muscle health and minimize muscle deconditioning through a progressive mobility plan.

Objectives: To describe muscle strength in different muscle groups and to describe the influence of muscle strength on mobility in critically ill adult patients on mechanical ventilation.

Methods: Fifty ICU patients were enrolled in this descriptive, cross sectional study**.** Abdominal core, bilateral hand grip and extremity strength was measured using three measurement tools. Mobility was measured using the following scale: 0=lying in bed; 1=sitting on edge of bed;

2=sitting on edge of bed to standing; 3=walking to bedside chair and 4=walking >7 feet from the standing position. Predictors of mobility were examined using stepwise regression.

Results: Abdominal core, bilateral hand grip and extremity strength demonstrated statistically significant relationships with all variables. Extremity strength accounted for 82% of the variance in mobility and was the sole predictor (β=0.903; F=212.9; p=0.000). Future research addressing the outcomes of implementing a mobility protocol in this patient population and prioritizing when such a protocol should be implemented would be beneficial to ongoing plans to decrease MV, ICU and hospital days.

Conclusions: Muscle strength tests implemented at the bedside are crucial to implementing a progressive mobility plan for critically ill adults while they are on MV therapy.

Background/Significance

Muscle weakness, prevalent in the critically ill patient, is multi-factorial in its causes and may be compounded by neuromuscular, cardiovascular, pulmonary, psychological, pharmacological and equipment barriers (De Jonghe et al., 2007; Schweichert & Hall, 2007; Winkelman, 2007). Despite the dissemination of literature promoting the importance of progressive mobilization in the critically ill patient receiving mechanical ventilation (MV) therapy, there is a lack of research that has explored the influence of muscle strength on progressive mobility in this patient population. Numerous patients admitted to an intensive care unit (ICU) setting acquire a syndrome described as a neuromuscular dysfunction, which is characterized as generalized limb and respiratory muscle weakness (Bolton, 2005). This syndrome, which has come to be known as critical illness neuromyopathy (CINM), occurs in critically ill patients without previous neuromuscular disease, indicating its simultaneous development with the critical illness and/or treatments (De Jonghe B. et al., 2002; Schweichert &

Hall, 2007; Stevens et al., 2007). The peripheral neuromyopathy weakness component of CINM, which has come to be described as ICU-acquired weakness (ICU-AW) (De Jonghe, Lacherade, Sharshar, & Outin, 2009), has raised awareness of its clinical significance in the critically ill adult. The prevalence of muscle weakness in patients who regain normal consciousness after > 1 week of MV therapy is 25% - 60% (De Jonghe et al., 2009). These patients have demonstrated muscle waste peaking during the first 3-weeks of ICU stay, indicating progressive mobility in this patient population can benefit overall muscle health and minimize muscle deconditioning (Gruther et al., 2008).

Despite the increasing amount of research on progressive mobility in the ICU patient population, there remains a gap in knowledge on the influence of muscle strength on progressive mobilization in the adult ICU patient receiving mechanical ventilation. There is a lack of knowledge regarding how to evaluate muscle strength for the bedside clinician and its influence on determining progressive mobility in this patient population. Further research is needed with regards to measuring muscle strength for clinical application and the integration of this measure into the development of a protocol that will standardize progressive mobility in this patient population. Therefore, the purpose of this study is two-fold: (a) to describe muscle strength in different muscle groups in critically ill adults on mechanical ventilation, and (b) to describe the influence of muscle strength on progressive mobility

Methods

Design, Sample and Setting

A descriptive, cross-sectional design was used to assess muscle strength and ability to mobilize. The sample size was determined from a previous systematic review (Roberson, Starkweather, Grossman, Acevedo, & Salyer, 2018) with a goal of achieving 80% power for rejecting the false null hypothesis. A convenience sample of fifty adult participants were enrolled from the

Medical Respiratory ICU (MRICU) at Virginia Commonwealth University Health System in Richmond, Virginia, an 824-bed, level I trauma center. The MRICU is a 28-bed unit for adults with complex illnesses, including sepsis, diabetes, kidney and liver diseases and respiratory failure. Inclusion criteria for this study comprised of adult patients $\geq$ 18 years old, admitted the MRICU service, on MV therapy for $\geq$ 24 hours with the plan to remain on MV therapy for $\geq$ 24 hours; alert and oriented to person, place and time; and demonstrate a 0-2 score on the attention screening examination of the Confusion Assessment Method used in the ICU setting (CAM-ICU) (Ely et al., 2001) and $\geq$ -1 on the Richmond Agitation Sedation Scale (RASS) (Sessler et al., 2002). Exclusion criteria included participants receiving neuromuscular blocking, anesthetic or inotropic/vasopressor agents for the past 24 hours or those who were hemodynamically unstable or required intracranial pressure monitoring and had a history of vestibular deficits (e.g., vertigo, inner ear problems). Additional exclusion criteria encompassed pre-existing musculoskeletal diseases/conditions, abdominal surgery within the past three months, and any limitations to assessing muscle strength and hand grip function. Once enrolled, participant withdrawal was voluntary and could occur at any time before or during the study.

Variables and Measures

The Manual Muscle Test (MMT), Medical Research Council Scale (MRC), Maximum Inspiratory Pressure (MIP) and Hand-Held Dynamometry (HHD) are commonly used measures to determine muscle strength (Ali et al., 2008; C. E. Baldwin & Bersten, 2014; Claire E. Baldwin, Paratz, & Bersten, 2013). The MMT compares the patient’s muscle strength in six different muscles groups in the upper and lower extremities bilaterally and is measured to determine the MRC, a 0-5 score, which has been deemed a reliable and valid test to assess muscle strength (Ali et al., 2008; C. E. Baldwin & Bersten, 2014; Claire E. Baldwin et al., 2013;

Burtin et al., 2009; De Jonghe et al., 2007; Efstathiou, Mavrou, & Grigoriadis, 2016; Lee et al., 2012; Nordon-Craft, Schenkman, Ridgeway, Benson, & Moss, 2011; Vanpee, Hermans, Segers, & Gosselink, 2014; Vanpee et al., 2011; Yosef-Brauner, Adi, Ben Shahar, Yehezkel, & Carmeli, 2015). MIP is the maximum amount of inspiratory pressure generated when a patient inhales and is indicative of the inspiratory muscles that promote ventilation and respiratory muscle strength (ERS, 2002; Efstathiou et al., 2016). MIP has also shown to be a potential surrogate parameter to assess muscle strength, which will promote early detection of ICU-AW (Tzanis et al., 2011). Hand-grip strength was measured using HHD and has been used in studies involving the critically ill patient population (Burtin et al., 2009; Vanpee et al., 2014, 2011). For the purposes of data analysis and interpretation, negative MIP numbers were recoded to positive integers and average right and left HHD score and an average HHD was used. The dependent variable, mobility, was assessed based on the activity level the participant was able to perform. This variable used a 0-4 scale based on the participant's mobility, to include 0 = remaining supine in the bed, 1 = supine to sitting on the edge of the bed, 2 = sitting on the edge of the bed to standing, 3 = walking to a bedside chair and sitting in the chair, or 4 = walking greater than seven feet from the standing position.

Data Collection Procedures

Approval for this study was obtained through Virginia Commonwealth University (VCU) Institutional Review Board (IRB). Prior to enrollment, the study was explained to potential participants, and a signed consent was obtained. For the purposes of this study, the participant's medical and surgical history, physical examination, laboratory test results, progress notes, and medication administration records were reviewed and used to characterize health status. To ensure accurate data collection using instruments measuring muscle strength, the investigator's data collection performance was validated by an expert clinician for each measurement. Once participants were enrolled, each instrument used in muscle strength evaluation was explained. The first instrument used determined maximum inspiratory pressure (Negative Inspiratory Force meter [NIFometer], Mercury Medical, Clearwater, Florida, USA). A demonstration was provided on how to take deep breaths once the instrument was attached to the endotracheal tube (ETT), after disconnecting the corrugated ventilator tubing. A total of three MIP measures were collected and an average score was calculated. Next, the use of the JAMAR Plus + Hand Dynamometry device was demonstrated (Sammons Preston, Bolingbrook, Illinois, USA). The participant then provided three return demonstrations with each hand, alternating hands, starting with their dominate hand. A score for each attempt was documented and the average of the three attempts was the final hand grip score for each hand. Last, the MMT procedures were demonstrated as follows. With the participant in bed and the head of the bed elevated to 70 degrees, the investigator tested the upper extremities, dominate side first, then their lower extremity muscles. The following muscle movements were tested: shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension and ankle dorsiflexion on both the left and right side. This study modified the protocol developed by Ciesla et al (2011) and graded the movement based on the MRC scale of 0-5 (Figure 1). Upon completing the muscle strength evaluation, the participants demonstrated their ability to mobilize, based on their pre-hospitalization mobility. Participants were given as much time as needed to safely mobilize.

Data Analysis

Descriptive statistics were used to analyze demographic and clinical characteristics, and medical-surgical history. Categorical variables were described using frequency and percent.

Continuous variables were summarized using mean ($\bar{x}$), standard deviation (SD) and range. The independent sample t-test was used to describe the mean differences between males and females in demographic, clinical characteristics, abdominal core strength (MIP), hand-grip strength (HHD), muscle strength of all extremities (MRC) and mobility. Correlational analysis (Pearson's *r*) was used to establish the strength and direction of the relationships among the independent and dependent variables. Multiple stepwise linear regression described the associations and variance between the independent variables and the outcome. Level of significance was set at $p \leq 0.05$. SPSS software for Windows, version 24, was used for all statistical analyses.

Results

Sample Characteristics

A convenience sample of fifty participants were enrolled and completed this study. The mean age was 56.0 (SD = 16.7) years, ranging from 18-88 years (Table 1). While there were more female (54%) than male (46%) participants, there was no statistically significant difference in age between females (57.6; SD =16.12) and males (54.2; SD = 17.50). Participants were in the MRICU for an average of 6.7 (SD = 5.71) days, ranging from 1-24 days and, on average, 4.6 (SD =4.15) of those days were on MV therapy. Ninety percent of the participants were on a spontaneous intermittent mode of ventilation and the remaining participants were on assist-control mode of MV therapy.

Pulmonary diseases accounted for 76% of the participants medical-surgical history, with asthma and chronic obstructive pulmonary diseases (18% each) most commonly observed (Table 2). Hypertension was the predominant cardiovascular disease found, accounting for 44%. Chronic diseases, diabetes mellitus and kidney dysfunction, represented 42% and 40%, respectively. Gastrointestinal diseases, such as gastro-esophageal reflux disease, liver disease, and pancreatitis were seen in 16%. Substance abuse (e.g., drugs, smoking and alcohol abuse) was found in 24% of the participants. Thyroid disease, primarily hypothyroidism (12%), was noted in 14%. A history of cancer (14%) - which included non-Hodgkin's lymphoma (4%), endometrial, prostate, throat, tonsil and lung cancers (2% each) - was also noted.

Descriptive Statistics

There was no difference in age between males and females (t = -0.711, p = 0.481). Male participants had a higher abdominal core strength, bilateral hand grip strength, and extremity strength than females, but these differences were non-significant. There were significant differences between males and females in hand grip strength. Both males and females had stronger right hand grip strength (t = 3.65, p = 0.001) than left hand grip strength (t = 3.34, p = 0.002). See Table 3.

The mean mobility level was 2.3 (SD = 1.33) with ten (20%) participants achieving this level. A total of fourteen (28%) participants achieved mobility levels one and two. Most participants, however, were able to achieve the third mobility level (n = 16; 32%) – walking to a bedside chair and sitting in this chair (Table 4). Mobility in males and females was not significantly different (t = 0.23, p = 0.817). The mean mobility level achieved in males was 2.35 (SD = 1.3) and in females was 2.26 (SD = 1.4) (Table 3). No adverse events occurred during mobilization.

Correlation Analysis

All independent variables demonstrated positive linear relationships that were statistically significant (Table 5). Extremity strength correlated strongly with abdominal core (r = .625, p = .000), right hand grip (r = .670, p = .000), and left hand grip (r = .662, p = .000) strengths.

Abdominal core strength was strongly correlated to mobility (*r* = .622, *p* = .000) and extremity strengths (*r* = .903, *p* = .000).

Regression analysis

A multiple linear regression model was used for prediction analysis (Table 6). Through a series of stepwise multiple linear regression analyses, the extremity strength, which was measured by the MRC score (β = .903), was determined to be the best predictor of mobility (R^2= .816, $F(1,48)$ = 212.92, *p* = .000). In this study, about 82% of the variance in mobility is accounted for by extremity strength.

Discussion

Most of the participants (48%) in this study were between the ages of 50 – 69 years, with a mean age of 56.0 (SD = 16.7) years. Studies done by Wunsch et al (2011) and Wunsch et al (2013) used national databases to describe the ICU populations in the United States, which demonstrated similar mean ages, 60.4 (SD = 18.6) and 59.8 (SD = 18.3) years, respectively. Although our study had a small number of participants, our participant characteristics were similar to the national databases referenced in the above studies.

The participants in this study were on MV therapy for 4.6 days and averaged 6.7 days in the MRICU setting. The Society of Critical Care Medicine (SCCM) has identified respiratory failure with ventilator support as a primary diagnoses for adult ICU admissions, with other medical conditions, such as pulmonary edema, respiratory failure, renal failure and diabetes, as additional conditions requiring high ICU use (Critical Care Statistics, 2018). Similarly, the SCCM has cited that 20-30% of ICU admissions require MV support (Critical Care Statistics, 2018). In our study, 58% of the participants had a medical-surgical history of pulmonary disease and 42% and 40% of the participants had diabetes or renal disease, respectively.

Ninety percent of study's participants required spontaneous intermittent MV (SIMV) or SIMV with pressure support. Identifying patient-centered care that promotes MV therapy discontinuation is critical to patient outcomes. Early and aggressive efforts to identify and minimize muscle weakness while on MV therapy can improve the critically ill patient's overall strength and promote return to their baseline mobility. Further, this study's results can be generalized to other ICU settings with similar patients requiring MV therapy and those with similar medical characteristics.

The performance of repeated hand grip measures may have been tiring, hence, these participants may have experienced fatigue on their third hand grip attempt. Identifying a specific rest period for the participant before performing the next hand grip test could minimize fatigue. Establishing a protocol which more clearly defines the number of attempts the participant should perform of each hand grip, as well as the amount of time needed for the participant to rest between hand grips would be beneficial. Male participants having a higher hand grip score is reflected in the normative grip strength guidelines, which indicates greater strength in males than females across all age groups (Sammons Preston, Patterson Medical Co., Illinois).

Although abdominal core, hand grip and extremity strength have been used as single measures in previous studies to explain muscle strength, this is the first time all three of these measures have been used to both examine muscle strength and predict mobility in critically ill adults on MV therapy. Our findings indicate that relationships are among these three muscle strength measures and mobility, suggesting that as the participant's overall muscle strength increased, so did their mobility ability. The mean mobility level indicates, on average, the participants were able to mobilize from sitting on the edge of the bed to a standing position. Most participants, however, demonstrated a higher mobility level – that of walking to a bedside chair and sitting. Safely maximizing muscle strength during a patient's critical illness while on MV therapy may enhance their ability to mobilize to greater levels while they remain in the ICU setting.

Of great importance is that this study demonstrated that extremity strength was the best predictor of mobility in critically ill adults on MV therapy. As such, development and implementation of mobility protocols and translation into the patients' overall plan of care may provide the opportunity for them to return to their pre-hospitalization mobility level, discharged out of the ICU setting sooner and return to their home setting. Promoting extremity strength, despite concerns of dislodging lines and tubes (Morris, 2007) and traditional beliefs of allowing ICU patients to rest, is paramount in the recovery of ICU patients. Consistent with other studies' citations, mobilization of participants who had lines, tubes and various monitoring devices was safe. The risks and benefits of implementing extremity strength and overall muscle conditioning should be assessed to determine the safest, individualized mobility plan for a patient. Whether promoting extremity strength through passive motion (Burtin et al., 2009) or actively, this association with mobility must be actualized to impact MV, ICU, and hospital days.

Future Research

Further study is needed to explore the effects of extremity strength on clinical characteristics, such as MV, ICU and hospital days, as well as the patient's return to their baseline mobility level and their perception of their quality of life. In addition, future studies should assess standardizing progressive mobility protocols, specifically around the timeliness of introducing the protocol and assessing the readiness of the patient to participate in the plan. Last, using more interprofessional rehabilitation therapies in the ICU setting vs. placing most of these tools and resources in the non-ICU settings or select ICU settings should be explored to maximize patient outcomes.

While evidence exists to support the need to mobilize patients in a medical respiratory ICU setting (Thomsen, Snow, Rodriguez, & Hopkins, 2008), further study is needed to determine if other ICU-types of patients would demonstrate similar mobility outcomes using these specific muscle strength tests. This study excluded various types of patients who could be found in the ICU setting (e.g., trauma patients, patients with neurological disorders, surgical patients); however, this study was inclusive of patient medical characteristics, which can be found across a variety of ICU settings. Another area that requires further study is the integration of these muscle strength tests into clinical practice. It took approximately 30-minutes to complete all three measures, a considerable amount of time for the bedside nurse to use to assess muscle strength.

While the focus of this study did not include addressing cost factors and length of stays (LOS) in the ICU setting and on MV therapy, addressing such is crucial in health care costs discussions. According to the Agency for Healthcare Research and Quality, respiratory system with ventilatory support less than 96 hours is attributed to 24.4% of total ICU charges, with a mean hospital charge of $61,800 for a patient discharged with an ICU stay, compared to $25,200 for a patient without an ICU stay (Statistical Brief #185, Healthcare Costs and Utilization Project [HCUP], 2014). Strategies for addressing costs and LOS are multifaceted, requiring an interprofessional approach at local and national arenas to ensure safe and quality patient-centered care remains the top priority.

Limitations

Despite having a small sample from one type of ICU setting, the results of the investigation show great promise for having an impact on future studies and practice. To provide additional support for our findings, a more robust design, conducted in a variety of ICU settings would improve the generalizability of the findings. A repeated measures or longitudinal design would capture multiple assessments of the participant's muscle strength, as well as their progression towards returning to their pre-hospital baseline. This design, however, could potentially lead to loss of participants due to extubations or transfer/discharge out of the ICU.

Conclusion

The purpose of this study was to describe muscle strength in different muscle groups and to describe the influence of muscle strength on early mobility in adult, critically ill patients on mechanical ventilation. This study showed that abdominal core, hand grip and extremity strengths had a relationship within groups and with mobility. The only predictor of mobility in critically ill adult patients on MV therapy was extremity strength. Muscle strength tests implemented at the bedside are crucial to implementing a progressive mobility plan for critically ill adults while they are on MV therapy. The clinical use of muscle strength tests, specifically, extremity strength tests that can be performed by bedside practitioners could contribute to improved clinical decision-making regarding mobility for critically ill adult patients on MV therapy and, subsequently, to overall improved patient outcomes.

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Muscle Groups	Medical Research Council Score					
	0 No palpable contraction	1 Palpable contraction without limb movement	2 Movement of limb but not against gravity	3 Movement against gravity and no resistance	4 Movement against gravity and moderate resistance	5 Movement against gravity and resistance
Shoulder Abduction L / R						
Elbow Flexion L / R						
Wrist Extension L / R						
Hip Flexion L / R						
Knee Extension L / R						
Ankle Dorsiflexion L / R						

Figure 2: Manual Muscle Test and MRC Scoring Tool

	f (%)	Mean (SD)	Range
Age		56.0 (16.7)	18 - 88
18 - 29 years	4 (8)		
30 - 39 years	5 (10)		
40 - 49 years	7 (14)		
50 - 59 years	12 (24)		
60 - 69 years	12 (24)		
70 - 79 years	7 (14)		
≥80 years	3 (6)		
Gender			
Female	27 (54)		
Male	23 (46)		
MV Days		4.6 (4.2)	1- 19
ICU Days		6.7 (5.7)	1- 24
Hospital Days		12.4 (11.5)	1- 51
Body Mass Index		30.0 (11.3)	16.1 – 82.9
Systolic BP (mmHg)		125.0 (20.8)	93.0 – 195.0
Diastolic BP (mmHg)		71.3 (11.2)	54.0 – 95.0
Mean Arterial Pressure (mmHg)		87.5 (11.3)	68.0 – 113.0
Heart Rate (bpm)		88.2 (20.3)	49.0 – 132.0
Fraction of inspired oxygen (%)		.41 (.10)	.30 - .80
Ventilatory Respiratory Rate (bpm)		15.5 (5.2)	10 - 28
Modes of Mechanical Ventilation			
Spontaneous Intermittent Mechanical Ventilation	28 (56)		
-with Pressure Support	17 (34)		
Assist/Volume Control	4 (8)		
-with Pressure Control	1 (2)		
Tidal Volume (ml)		442.9 (77.7)	300 - 750
SpO2 (%)		96.9 (3.1)	86 – 100
Abdominal Core (MIP) Average (cm H2O)		57.1 (16.84)	24 - 87
Hand Grip (HHD) – R (kg)		39.98 (14.30)	18.20 – 64.50
Hand Grip (HHD) – L (kg)		35.8 (14.22)	15.60 – 62.47
Manual Muscle Test Sum		47.9 (12.52)	24 - 60
Extremity Strength (MRC) Score		3.996 (1.04)	2 - 5
Mobility Level		2.30 (1.33)	0 - 4

Table 3: Demographic and Clinical Characteristics

Variables	*f*	(%)
Pulmonary Disease:	29	58%
- Asthma	9	18%
- Chronic obstructive pulmonary disease (COPD)	9	18%
- Pneumonia	4	8%
- Lung resection/removal	3	6%
- Sarcoidosis	2	4%
- Pulmonary hypertension	1	2%
- Pulmonary embolism	1	2%
Cardiovascular Disease:	27	54%
- Hypertension	22	44%
- CAD/HF	5	10%
Diabetes Mellitus	21	42%
Kidney Disease	20	40%
Gastrointestinal Disease	16	32%
- Gastro-esophageal Reflux	7	14%
- Liver	5	10%
- Other (pancreatitis, Cholecystectomy, gastric bypass)	4	8%
Substance Use/Abuse	12	24%
- Smoking	6	12%
- Alcohol	3	6%
- Drugs	3	6%
Thyroid Disease	7	14%
- Hypothyroidism	6	12%
- Hyperthyroidism	1	2%
Cancer	7	14%
- Non-Hodgkin's Lymphoma	2	4%
- Other (Endometrial, Throat, Prostate, Tonsil, Lung)	5	10%
Anemia	4	8%
Obesity	4	8%
Psychological Disorder(s)	3	6%

Table 4: Medical - Surgical History Characteristics

	Gender	N	Mean (SD)	t	p-value	95% Confidence Interval
Abdominal Core (MIP) Average	male	23	60.0 (17.3)	1.12	.270	-4.25 – 14.91
	female	27	54.7 (16.3)			
Hand Grip (HHD) - R	male	23	49.2 (12.4)	4.82	.000	8.91 – 21.66
	female	27	33.9 (9.98)			
Hand Grip (HHD) - L	male	23	44.3 (12.8)	4.25	.000	7.43 – 20.80
	female	27	30.2 (10.7)			
Manual Muscle Tests Sum	male	23	49.6 (13.5)	.86	.397	-4.12 – 10.21
	female	27	46.5 (11.7)			
Extremity Strength (MRC Score)	male	23	4.1 (1.1)	.84	.406	-.35 - .85
	female	27	3.9 (.98)			
Mobility	male	23	2.35 (1.3)	.23	.817	-.68 - .85
	female	27	2.26 (1.4)			

Table 5: Gender Differences Between Strength and Mobility

Mobility Levels	$\overline{x}$ = 2.30; SD = 1.33	n (%)
0 = Supine in bed		7 (14)
1 = Supine to sitting on the edge of bed		7 (14)
2 = Sitting on edge of bed to standing		10 (20)
3 = Walking to bedside chair		16 (32)
4 = Walking greater than seven feet		10 (20)

Table 6: Mobility Levels

		Hand Grip (HHD) - R	Hand Grip (HHD) - L	Extremity Strength (MRC Score)	Mobility
Abdominal Core (MIP) Average	Pearson's r	.470**	.404**	.625**	.622**
	p-value	.001	.004	.000	.000
Hand Grip (HHD) - R	Pearson's r	1	.966**	.670**	.558**
	p-value		.000	.000	.000
Hand Grip (HHD) - L	Pearson's r		1	.662**	.561**
	p-value			.000	.000
Extremity Strength (MRC Score)	Pearson's r			1	.903**
	p-value				.000
Mobility	Pearson's r				1
	p-value				

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

Table 7: Correlations of the Variables

Model	β	R square	Standard Error	95% Confidence Interval	
Extremity Strength (MRC Score)	0.903	0.816	0.576	0.992	1.309
F (1, 48) = 212.92, *p* = 0.000					

Dependent Variable: Mobility

Table 8: Regression Model of Predictive Analyses

Vita

Audrey Robin Lay Roberson was born on September 22, 1964 in New York City, New York and is an American citizen living in Chesterfield, Virginia with her husband, two children and mother. Following her graduation from high school in Amityville, New York, she received her Bachelor of Science degree in Nursing from New York University in May 1987. After relocating to Richmond, Virginia, she completed her Master of Science degree in Nursing, with a concentration in Adult Health, from Virginia Commonwealth University (VCU) in May 1992. Her 32-year professional nursing career has spanned across the roles of acute, progressive and critical care nurse, educator and leader. Clinical areas of practice have included medical-surgery, cardiovascular/transplant surgery, coronary intensive care, and post-anesthesia care. She has served as a reviewer for journals, poster and podium presentations and is the co-author of a book chapter in Perianesthesia Nursing: A critical care approach, both the 5th and 6th editions. She has been a presenter at the National Teaching Institute of AACN on education and clinical topics and a Clinical Consultant for "Auscultation Skills: Breath & Heart Sounds" 4th ed. She has held Course and Adjunct Faculty positions at VCU's SON in the undergraduate and graduate programs and worked as a legal nurse consultant.

In December 2007, she joined the Medical Respiratory ICU (MRICU) team as the Nurse Clinician and is currently the Nurse Manager of the MRICU at VCU Health System. She is the recipient of the Virginia Organization of Nurse Executives and Leaders' Sara Tatem Scholarship in 2013 and was has been awarded the Transformational Leadership and Excellence in Collaborative Practice Awards. She maintains her certification as a post-anesthesia nurse and memberships in AACN and Sigma Theta Tau, the International Honor Society of Nursing.