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Ultrasonography in the intensive care setting can be used to detect changes in the quality and quantity of muscle and is related to muscle strength and function

Selina M. Parry PhD, Doa El-Ansary PhD, Michael S. Cartwright MD, MS, Aarti Sarwal MD, Sue Berney PhD, René Koopman PhD, Raquel Annoni PhD, Zudin Puthuchearu PhD, Ian R. Gordon PhD, Peter E. Morris MD, Linda Denehy PhD

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Authors:

Selina M Parry^{1*} PhD, Doa El-Ansary¹ PhD, Michael S Cartwright² MD MS, Aarti Sarwal² MD, Sue Berney³ PhD, René Koopman⁴ PhD, Raquel Annoni^{1,8} PhD, Zudin Puthuchear⁵ PhD, Ian R Gordon⁶ PhD, Peter E Morris⁷ MD, Linda Denehy¹ PhD

¹ Department of Physiotherapy, The University of Melbourne, Victoria, Australia

² Department of Neurology, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA

³ Department of Physiotherapy, Austin Health, Melbourne, Australia

⁴ Department of Physiology, The University of Melbourne, Victoria, Australia

⁵ Division of Respiratory and Critical Care Medicine, National University Health System, Singapore

⁶ Statistical Consulting Centre, The University of Melbourne, Victoria, Australia

⁷ Department of Pulmonology and Critical Care, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA

⁸ CAPES Foundation, Ministry of Education of Brazil, Brasília-DF, Brazil.

* **Corresponding Author:** Dr Selina M Parry

Postal Address: The University of Melbourne, Department of Physiotherapy, School of Health Sciences

Level 7 Alan Gilbert Building, 161 Barry Street, Parkville Victoria 3010, Australia

Telephone: +61 3 8344 6171; Fax number: +61 3 8344 4188

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ABSTRACT

Purpose: This study aimed to: (1) document patterns of quadriceps muscle wasting in the first ten days of admission and (2) determine the relationship between muscle ultrasonography and volitional measures.

Materials and Methods: Twenty-two adults ventilated > 48 hours were included. Sequential quadriceps ultrasound images were obtained over the first ten days and at awakening and ICU discharge. Muscle strength and function were assessed at awakening and ICU discharge.

Results: A total of 416 images were analysed. There was a 30% reduction in vastus intermedius (VI) thickness, rectus femoris (RF) thickness and cross-sectional area within ten days of admission. Muscle echogenicity scores increased for both RF and VI muscles by +12.7% and +25.5% respectively (suggesting deterioration in muscle quality). There was a strong association between function and VI thickness ($r = 0.82$) and echogenicity ($r = -0.77$). There was a moderate association between function and RF cross-sectional area ($r = 0.71$).

Conclusions: Muscle wasting occurs rapidly in the ICU setting. Ultrasonography is a useful surrogate measure for identifying future impairment. Vastus intermedius may be an important muscle to monitor in the future as it demonstrated the greatest change in muscle quality and had the strongest relationship to volitional measures.

Key words: ultrasound; critical illness; intensive care; muscle wasting; functional outcomes; echogenicity; muscle strength; intensive care unit-acquired weakness

Introduction

Survivorship will become the defining challenge of the 21st century for patients admitted to intensive care units (ICUs) [1], due to ongoing significant impairments in muscle strength, function, and difficulties in resuming family and societal roles [2, 3]. The timely identification of individuals who are at highest risk of developing intensive care unit-acquired weakness (ICU-AW) is challenging. Traditionally ICU-AW is diagnosed using volitional strength testing according to the Medical Research Council sum-score (MRC-SS) (<48/60) [4, 5]. However there is often a delay in the diagnosis of ICU-AW due to patients not being alert and able to follow commands to enable accurate volitional strength testing [6]. Measures such as muscle biopsy and nerve conduction testing are used to identify individuals with ICU-AW [7]. However, these measures are invasive, expensive and require significant expertise; and are not always readily available in the clinical setting. To date there are no proven relationships of these invasive tests to ICU patient strength and function [8]. The ability for a testing modality to differentiate potential ICU-AW patients early in their course may prove especially important since the majority of muscle changes occur within the first ten days [9].

Ultrasonography is a new and promising non-volitional measure, which enables identification of changes in muscle structure and morphology. It can be performed at the bedside, is non-invasive, inexpensive, shows good inter and intra-observer reliability [10, 11] and is readily available in most hospitals [12]. Reliability for the measurement of quadriceps muscle thickness, and echogenicity have been demonstrated in individuals with critical illness in several recent studies [13-15]. One study demonstrated excellent intra and inter-rater reliability for echogenicity assessment of quadriceps musculature regardless of level of expertise [13].

Whilst it is known that muscle wasting can occur quickly in the ICU admission, [9] no studies have examined the different muscles that make up the quadriceps complex to determine if there are different wasting patterns. The four muscles which form the quadriceps complex: Rectus Femoris (RF), Vastus Intermedius (VI), Vastus Lateralis (VL), Vastus Medialis (VM) have different fibre type compositions and functional roles. For example, RF is predominantly made up of Type II fibres and is a bi-articular muscle, which is often described as a power muscle designed to assist in fast movements such as kicking a ball [16-18]. This is in contrast to VI which is a deep stabiliser uni-articular muscle and is predominantly made up of Type I fibres [18]. It may be that there is a preferential loss of certain

musculature, which is important to delineate as this may affect how rehabilitation strategies are developed. Further and importantly, no studies have determined the relationship between ultrasound parameters and volitional measures of muscle strength and function.

The aims of this study were to determine: (1) the rate of muscle wasting of the quadriceps muscles; RF VI and VL in individuals with critical illness during the first ten days of an ICU admission; and (2) the relationship between muscle ultrasound parameters and measures of muscle strength and function at ICU awakening and ICU discharge.

Materials and Methods

Study Design: Single centre prospective observational study conducted at a mixed medical/surgical ICU in Melbourne, Australia. Institutional ethical approval was obtained and patient consent was waived for this study.

Screening and Eligibility: Adults expected to be mechanically ventilated (MV) > 48 hours and remain in the ICU $\geq$ four days were included. Individuals with spinal cord injury, other primary neuromuscular disease or new intracranial process were excluded.

Ultrasonography Imaging Procedure: A Voluson eBT09 Ultrasound (GE Healthcare, Yokogawa Medical Systems Ltd., Japan) was used with an 8.5MHz linear transducer to obtain images at baseline (as soon as possible after ICU admission), days three, five, seven, ten, awakening and ICU discharge. Device settings were kept constant between subjects and across time-points with one experienced assessor acquiring all images. Subjects were assessed in supine with their knee in passive extension and neutral rotation. A water-soluble transmission gel was applied to the ultrasound head to allow acoustic contact without depressing the dermal surface. Two images were acquired in each leg for each subject: (1) *Anterior imaging:* transducer placed perpendicular to the long axis of the anterior thigh, two-thirds distance from the anterior superior iliac spine to the superior patella border [10], and (2) *Lateral imaging:* 5cm laterally from the first imaging point. The lateral image was obtained in an extended field of view mode over a distance of 10cm running in a caudal-cephalad direction. To enable replication of image location on repeat ultrasound assessments a mark was drawn on the subject's legs. Images were saved onto the ultrasound hard-drive and transferred for further analysis onto a computer using ImageJ software (NIH, Bethesda, MD) [19].

Outcome Measures: Baseline demographic data included: reason for ICU admission, APACHE II score, MV hours, ICU and hospital length of stay (LOS), discharge destination and mortality.

All ultrasonography measurements were performed in triplicate with the average of the scores used in final analyses. On *anterior imaging* muscle thickness and echogenicity of VL, RF, subcutaneous tissue thickness and RF cross-sectional area (CSA) were evaluated. All thickness parameters were measured in cm, CSA in cm squared and were measured at the widest point of the muscle, and echogenicity was reported in pixels. Echogenicity was determined using computer-assisted quantitative greyscale analysis. A standard square 2x2cm for analysis of RF and VL muscles separately was used to determine the region of interest (ROI) (Figure 1a). The square method has stronger inter-rater reliability compared to the trace method (where the assessor highlights all visible muscle area excluding the surrounding epimysium and artefacts) for defining the ROI [13]. If the area to be analysed was smaller than 2x2cm, the largest possible square within the anatomic boundaries of the muscle was examined. Mean and standard deviation echogenicity of this ROI was calculated by using the histogram function of ImageJ software (NIH, Bethesda, MD) and expressed as a value between 0 (=black) and 255 (=white) [20] (Figure 1a). On *lateral imaging* measures included: VL thickness and VL pennation angle (angle in degrees between muscle fibre fascicles and the deep muscle aponeurosis) (Figure 1b).

Muscle strength and function outcomes were evaluated on awakening and at ICU discharge. Ultrasonography measurements were also evaluated at awakening and at ICU discharge. The day of awakening was defined as the first day the subject was alert with a Riker Sedation Agitation Scale score between three and five [21] and able to follow at least three of the *De Jonghe* five-command criteria [4]. Muscle strength was assessed using the MRC-SS [4] and function was assessed using the physical function in intensive care test scored (PFIT-s) [22] and ICU mobility scale (IMS) [23]. The incidence of ICU-AW was defined according to the MRC-SS if individuals scored less than 48 out of 60 on awakening [4].

Sample Size and Statistical analyses: A pragmatic sample size of 20 was identified for this pilot study. Data from all patients were analysed using Minitab 16 Statistical Software (2013) [Computer Software], State College PA: Minitab, Inc. and GenStat for Windows 16th Edition, VSN International,

Hemel Hempstead, UK. Descriptive statistics are reported as mean and standard deviation (SD) or median and interquartile range (IQR). Changes over time for the ultrasound parameters were examined using a linear random coefficient regression model. Within the model an interaction between time and explanatory variables including age, gender, number of days in ICU at time of the first ultrasound measure, and ICU LOS were examined. Pearson's correlation coefficient was used to assess bivariate relationships between ultrasonography and volitional measures. Coefficients were interpreted as little (0.00-0.25), fair (0.25–0.50), moderate (0.50–0.75) and strong (0.75–1.0) association [24].

Results

Table 1 demonstrates the baseline characteristics of the 22 included subjects. Fifty-nine percent ($n=13/22$) were male with a mean $\pm$ SD age of 56 ± 18 years, and they represented a severely critically ill cohort (APACHE II mean $\pm$ SD 23 ± 8). The time to first ultrasound measurement was median [IQR] 2.2 [0.9-2.9] days compared to time to first strength measurement which was median [IQR] 10 [7-16] days (Table 1). Ultrasonography took less than 10 minutes to set-up and complete image acquisition and less than 10 minutes per image to complete measurement analysis in all patients. Sixteen individuals were still in ICU at day ten (73%). A total of 416 images were analysed across the 22 subjects. The incidence of ICU-AW on awakening was 45% ($n=9/20$) (two subjects did not undertake strength testing due to delirium).

Change in muscle quantity and quality measured with ultrasonography

Baseline mean $\pm$ SD scores for RF, VI and VL thickness were: 2.44 ± 0.76 cm, 1.91 ± 0.73 cm and 2.31 ± 0.57 cm respectively. Rectus Femoris CSA was mean $\pm$ SD 4.42 ± 0.52 cm². During the ICU admission period 21% of the time (22/107 occasions) it was not possible to quantify pennation angle due to deterioration of the muscle structure and inability to visualise the individual fascicles in relation to the deep aponeurosis in order to calculate pennation angles. Baseline mean $\pm$ SD subcutaneous thickness was 1.89 ± 0.61 cm. The average rate of change per day for muscle thickness, subcutaneous thickness and pennation angle are reported in the online supplementary material (Supplementary Figure 1).

There was no interaction between measures of muscle thickness, CSA, echogenicity or pennation angle with explanatory variables including gender, age, LOS or time from admission to first ultrasound

measurements within the linear random coefficient regression modelling (Supplementary Online Material).

There was a 30% reduction in RF and VI thickness as well as RF CSA within the first ten days (Table 2), which was in contrast to VL thickness (14% reduction) (Table 2). Changes in RF thickness and CSA occurred at a relatively linear rate from baseline to day ten (Table 2). The rate of wasting for muscle thickness was fastest for the RF muscle (9%) compared to VI (1%) and VL (0.2%) musculature in the first three days (Table 2). Reductions in VI thickness was most pronounced between days three and five with a 17% decrease; this accounted for 57% of the total reduction in VI thickness seen in the first ten days (Table 2). Subcutaneous thickness increased significantly over the ten-day period by 39% (Table 2).

Rectus femoris and VI echogenicity increased over the ten-day period by 13% and 25% respectively (Table 2). There was for the echogenicity scores for VI and RF muscles (Figure 2, Supplementary Figure E1 respectively). In some subjects VI echogenicity increased over time (for example: subjects 3, 7, and 21) whereas in some subjects VI echogenicity remained constant or decreased (Subject 2, 13, and 16) (Figure 2). The subjects whose echogenicity increased (worsened) over time had MRC-SS on awakening between 10 to 17 out of 60, and a PFIT-s of zero out of 10. The subjects whose echogenicity scores remained constant or decreased over time had MRC-SS between 36 and 56 out of 60, and a PFIT-s between 3.2 and 7.1 out of 10 on awakening (Supplementary Figure 2).

Correlation between muscle strength and function with muscle ultrasonography

At ICU awakening there was a strong correlation between VI thickness and functional outcomes as measured by the PFIT-s ($r = 0.82$, $p < 0.001$) and IMS at ICU discharge ($r = 0.84$, $p < 0.001$) (Table 3). There was a moderate correlation between VI echogenicity and PFIT-s ($r = -0.55$; $p = 0.01$) and IMS ($r = -0.65$, $p = 0.002$) (Table 3), a moderate negative correlation between VI echogenicity and MRC-SS ($r = -0.57$, $p = 0.04$) and a strong negative correlation with PFIT-s ($r = -0.77$, $p = 0.001$) and IMS ($r = -0.73$, $p = 0.003$) at ICU discharge (Table 3). A moderate correlation between RF CSA and PFIT-s was also observed ($r = 0.71$, $p = 0.02$). Finally there was a strong correlation between VL pennation angle and PFIT-s at ICU discharge ($r = 0.81$, $p = 0.008$) (Table 3). There was no correlation between subcutaneous thickness and volitional measures at awakening or ICU discharge ($r < 0.2$, $p > 0.05$).

Discussion

Our study confirms muscle wasting occurs early and rapidly over the first ten days of critical illness in line with a recent landmark study [9], but more importantly demonstrates the association with subsequent impaired function. Ultrasonography is both a feasible and time-efficient tool for use in the clinical setting. At baseline, levels of muscle thickness and CSA were similar to that previously reported in studies examining healthy individuals [12, 25, 26]. Muscle wasting occurred in this study despite usual care rehabilitation being provided. Diminished contractility and loss in muscle mass may occur independently and thus ICU-AW and muscle atrophy should not be construed to be synonymous or interchangeable [27]. A recent retrospective study demonstrated muscle mass at ICU admission was an independent predictor of mortality [28]. Lower admission muscle mass was also associated with increased disability and higher frequency of discharge to a nursing home [28]. One study demonstrated individuals with “thicker” muscles on admission to ICU had a more significant reduction in thickness compared to individuals with “thinner” muscles [29]. However, it remains unclear whether it is the change in muscle size from baseline or the absolute score on admission, which is the most important predictor of functional outcome and mortality [30]. Going forward, this highlights the need to simultaneously measure muscle strength and muscle mass in future studies investigating ICU-AW.

In this study, muscle echogenicity increased (worsened) for RF and VI muscles with a two-fold increase in VI compared to RF, by day ten (+25% versus +13% for RF). There is growing interest in the measurement of changes in the quality (echogenicity) of muscles particularly in the ICU setting. Different tissues have unique appearances on ultrasonography. Normal muscle is relatively hypoechoic (dark) [31]. An increase in echogenicity as seen in this study results in the muscle appearing whiter or brighter (hyperechoic) [31, 32]. We hypothesise the increase in echogenicity may be representative of muscle necrosis and infiltration of fatty and connective tissue in replacement of muscle fibres. Several studies, albeit not in the ICU, have demonstrated a strong correlation between echogenicity and measurements of fibrosis and intramuscular fat from muscle biopsies [32, 33]. Therefore changes in muscle echogenicity may be reflective of disruption of muscle architecture at a cellular level. The validity of ultrasonography for evaluating changes in the overall quality of muscle in individuals with critical illness may need to be determined in comparison to muscle biopsy. A recent study by Puthucherry and colleagues correlated ultrasound echogenicity with muscle biopsy measurement of

muscle necrosis within the ICU setting [34] adding further support to the proposed hypothesis that echogenicity may be representative of muscle necrosis and architectural destruction at a cellular level. Echogenicity scores did not follow a consistent trend or pattern across all included participants within this study. In some participants echogenicity scores increased, while in others it remained constant or decreased. Individuals who had an increase in echogenicity scores (i.e. greater disruption to the muscle architecture) had poorer awakening strength and functional capability. Our sample was small and measurement of echogenicity warrants further investigation for individuals who are critically unwell as it may be a useful parameter to identify weak and less functional muscles.

It is also interesting to examine the differences in the rate of muscle wasting between the different muscles, which make up the quadriceps complex, in particular RF and VI. There was initially faster reduction in RF thickness compared to VI (day 3 RF -9% versus VI -1%). Rectus Femoris is often described as a power muscle designed to assist in fast movements such as kicking a ball. In contrast, VI functions as a stabilising muscle, and is important for maintaining dynamic balance in standing and walking. Immobilisation studies have demonstrated preferential loss of Type II fibres, and conversion of fibre typing from Type I to Type II in postural muscles. This may therefore explain the faster rate of muscle loss observed in RF muscle and partly explain changes in the echointensity (quality) of the VI muscle. The other key consideration for the differences in muscle wasting patterns may lie in RF being a bi-articular muscle and VI a uni-articular muscle [35]. It is important to consider which muscles are affected as it may mean in the future rehabilitation needs to factor in specificity with respect to the type of muscle predominantly affected (VI-postural or RF-power) in addition to considering the timing of rehabilitation.

Traditionally the presence of ICU-AW or functional impairments is diagnosed after awakening which is often delayed due to the volitional nature of the tests. This was indeed the case in our study with baseline assessment of volitional strength and function assessed at a median of 9 days compared to baseline ultrasonography, which was assessed earlier, at a median of 2.2 days (this timeframe is extremely short given the many tests and assessments administered for patients on admission to the ICU). Due to the nature of critical illness, sedative medications and inability to follow commands accurately it is not possible often within the ICU setting to obtain ICU admission strength and function measures. Therefore ultrasonography may be a useful outcome to enable early and timely

identification of individuals who may develop future impairment in strength and function. This is the first study to report a relationship between ultrasonography measures and volitional tests in the ICU setting. The strongest correlation was observed for the VI muscle and thus may be an important muscle to monitor in the future.

There are several limitations to this study. It involved a small sample size of 22 subjects and therefore precludes exploration of the patterns of muscle wasting in relation to specific disease entities or comorbidities. Future research needs to examine other variables, which may affect ultrasound measures (echogenicity, thickness) such as medications, functional comorbidity index score, history of diabetes mellitus, or poor premorbid function. This study did not examine these parameters given the small sample size. Although ultrasonography was performed by one trained clinician utilising the one ultrasound machine, this is reflective of clinical practice and results of this study in terms of muscle wasting are similar to previous research [36] within a different ICU setting. This study did not involve muscle biopsy or nerve conducting testing as they are not routinely performed in clinical practice within this institution. It is often challenging to obtain “true baseline” data in the ICU setting. The baseline ultrasonography measurements obtained were not necessarily from the first day of ICU admission. However ultrasonography is an attractive modality in the ICU as it can be performed close to admission and thus earlier than currently used clinical “volitional” tests.

There have now been three negative randomised controlled trials of rehabilitation in individuals with critical illness [37, 38]. It is important to therefore consider “responders” to rehabilitation and who should receive targeted early rehabilitation [38]. The identification of phenotypes of intensive care unit acquired weakness may be another avenue to identify responders [39] particularly when resources are limited to enable provision of early rehabilitation. Ultrasonography in the future may provide a means by which potential responders to rehabilitation may be identified early in the ICU admission. We believe that ultrasound imaging may be a useful predictor of future physical impairment based on the findings within this study.

There is currently a lack of standardisation in terms of image acquisition along the length of the thigh, and how measurements should be calculated which limits the ability to compare findings between studies. The main limitation with quantitative measurement of echogenicity is that the findings are machine dependent [40]. Conversion algorithms are available which enable translation of results from

one machine to another but are not practical in the clinical setting, as they require access to a shared phantom platform with preprogrammed range of tissue pathologies [40]. New methods are currently being investigated for evaluating echogenicity such as calibrated backscatter analysis [41] and blob analysis, which would enable interpretation of findings between studies across different institutions and using different ultrasound machines.

Conclusions and Future Directions

Muscle wasting occurs early and rapidly within the first ten days of admission. Individuals with greater echogenicity changes had poorer function and strength, with the greatest amount of change observed for the VI muscle. There was a strong relationship between VI muscle thickness and echogenicity and measures of strength and function. Based on the findings of this study we recommend measurement of RF CSA and VI thickness and echogenicity in ultrasonography studies in the future.

Future research needs to focus on the most important predictors of functional outcome, morbidity and mortality using ultrasonography. Additionally, there needs to be combined examination of ultrasonography and patient-centred outcomes in conjunction with laboratory investigations to examine the molecular mechanisms involved. The ability to identify individuals most at risk early will subsequently enable investigation of interventional strategies, which can be delivered in the critical period to try to minimise these changes and their deleterious functional consequences.

Abbreviations: APACHE II, Acute Physiological and Chronic Health Evaluation 2; CI, confidence interval; cm, centimetres; CSA, cross-sectional area; ICU, Intensive Care Unit; ICU-AW, Intensive Care Unit-Acquired Weakness; IMS, ICU mobility scale; IQR, interquartile range; LOS, Length of Stay; MHz, Megahertz; MRC-SS, Medical Research Council sum-score; MV, Mechanical Ventilation; PFIT-s, Physical Function in Intensive Care Test scored; RF, Rectus Femoris; ROI, Region of Interest; SD, standard deviation; VI, Vastus Intermedius; VL, Vastus Lateralis; VM, Vastus Medialis.

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Figure 1a: Anterior ultrasound image of the quadriceps

The square boxes indicate the 2x2cm region of interest selected over the Rectus Femoris and Vastus Intermedius muscles, with insert representation of histogram analysis for computerised quantitative grey scale analysis. **Abbreviations:** RF, Rectus Femoris; VI, Vastus Intermedius

Figure 1b: Lateral ultrasound image of the quadriceps demonstrating measurement of pennation angle and muscle thickness

Abbreviations: VI, Vastus Intermedius; VL, Vastus Lateralis

Figure 2: Vastus intermedius mean echointensity by day of ICU stay, one subject per panel

Footnote: This figure represents individual subject data in a panel tabulation format. For each subject the y-axis represents rectus femoris mean echogenicity score (in pixels) and the x-axis is the time-point of assessment in days. The individual panels highlighted in a red box represent subjects who had an increase in echogenicity scores (Subjects 3, 7, 21) (worsening) whereas the individual panels highlighted in a blue box represent subjects whose echogenicity scores remained stable or decreased over time (Subjects 2, 13, 16).

Table 1: Demographics of the cohort

Characteristic	n (%) or median [IQR]
Male	13 (59)
Age, years mean $\pm$ SD	56 $\pm$ 18
MV time, days	7.2 [4.7-11.8]
APACHE II mean $\pm$ SD	23 $\pm$ 8
Admission category	
- Medical	13 (59)
- Surgical	9 (41)
Awakening time, days	9.0 [7.0-14.5]
Time to baseline ultrasound measures, days	2.2 [0.9-2.9]
Time to baseline strength measures, days	10 [7-16]
Total ICU LOS, days	11.5 [9.0-21.5]
Total hospital LOS, days	22.0 [12.8-43.5]
Overall in-hospital mortality	3 (14)
Return to home	11 (50)

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit; ICU-AW, intensive care unit-acquired weakness; IQR, interquartile range; LOS, length of stay; MV, mechanical ventilation; n, number; SD, standard deviation; %, percentage.

Table 2: Percentage change in ultrasound muscle parameters over the first ten days of the ICU admission

US muscle parameter measured	Day Three	Day Five	Day Seven	Day Ten
RF thickness	-8.7%	-16.6%	-24.9%	-30.4%
VI thickness	-1.3%	-18.1%	-20.0%	-29.7%
VL thickness	-0.2%	-5.7%	-6.0%	-14.1%
RF CSA	-1.0%	-11.8%	-16.8%	-29.9%
RF echogenicity	+2.8%	+8.8%	+9.6%	+12.7%
VI echogenicity	+4.0%	+7.1%	+13.6%	+25.2%
VL pennation angle	+4.9%	+18.9%	+1.4%	-7.3%
Subcutaneous tissue thickness	+7.3%	+15.7%	+30.4%	+39.4%

*Abbreviations; CSA, cross-sectional area; RF, rectus femoris; US, ultrasound; VI, vastus intermedius; VL, vastus lateralis; %, percentage. **Footnote:** Day Three measure is a % change from baseline.*

Table 3: Correlation between ultrasound parameters and measures of muscle strength and function at awakening and ICU discharge

Ultrasound parameter	Comparator	ICU awakening		ICU discharge	
		r value	p-value	r value	p-value
RF thickness	MRC-SS	0.30	0.22	0.35	0.24
	PFIT-s	0.27	0.25	0.58	0.03*
	IMS	0.30	0.20	0.63	0.02*
VI thickness	MRC-SS	0.22	0.37	0.56	0.05
	PFIT-s	0.19	0.41	0.82	<0.001*
	IMS	0.17	0.47	0.84	<0.001*
VL thickness	MRC-SS	0.41	0.09	0.46	0.12
	PFIT-s	0.49	0.03*	0.56	0.04*
	IMS	0.53	0.02*	0.55	0.04*
RF CSA	MRC-SS	0.47	0.06	0.53	0.14
	PFIT-s	0.44	0.07	0.71	0.02*
	IMS	0.34	0.17	0.68	0.03*
RF echogenicity	MRC-SS	-0.24	0.33	-0.51	0.08
	PFIT-s	-0.05	0.84	-0.34	0.23
	IMS	-0.25	0.30	-0.31	0.28
VI echogenicity	MRC-SS	-0.46	0.05	-0.57	0.04*
	PFIT-s	-0.55	0.01*	-0.77	0.001*
	IMS	-0.65	0.002*	-0.73	0.003*
Pennation angle	MRC-SS	0.26	0.35	0.59	0.12
	PFIT-s	0.36	0.18	0.81	0.008*
	IMS	0.45	0.08	0.61	0.08
Subcutaneous thickness	MRC-SS	-0.16	0.52	-0.003	0.099
	PFIT-s	-0.13	0.59	-0.12	0.68
	IMS	-0.29	0.21	-0.21	0.47

Abbreviations: CSA, cross-sectional area; ICU, intensive care unit; IMS, ICU Mobility Scale; MRC-SS, Medical Research Council Sum Score; PFIT-s, Physical Function in Intensive Care Test; RF, rectus femoris; VI, vastus intermedius; VL, vastus lateralis. * **significant results, $p < 0.05$. Pearson's correlation coefficient was used to determine correlations.**

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Author/s:

Parry, SM;El-Ansary, D;Cartwright, MS;Sarwal, A;Berney, S;Koopman, R;Annoni, R;Puthuchear, Z;Gordon, IR;Morris, PE;Denehy, L

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