



ULTRASONOGRAPHIC EVALUATION OF DIAPHRAGM THICKNESS DURING MECHANICAL VENTILATION IN INTENSIVE CARE PATIENTS

By Colin Anthony Francis, MSc, Joaquín Andrés Hoffer, PhD, and Steven Reynolds, MD, FRCPC

Background Mechanical ventilation is associated with atrophy and weakness of the diaphragm. Ultrasound is an easy noninvasive way to track changes in thickness of the diaphragm.

Objective To validate ultrasound as a means of tracking thickness of the diaphragm in patients undergoing mechanical ventilation by evaluating interobserver and interoperator reliability and to collect initial data on the relationship of mode of ventilation to changes in the diaphragm.

Methods Daily ultrasound images of the quadriceps and the right side of the diaphragm were acquired in 8 critically ill patients receiving various modes of mechanical ventilation. Thickness of the diaphragm and the quadriceps was measured, and changes with time were noted. Interoperator and interobserver reliability were measured.

Results Intraclass correlation coefficients between operators and between observers for thickness of the diaphragm and quadriceps were greater than 0.95, indicating excellent interoperator and interobserver reliability. Patients receiving assist-control ventilation ($n = 4$) showed a mean decline in diaphragm thickness of 4.7% per day. Patients receiving pressure support ventilation ($n = 8$) showed a mean increase in diaphragm thickness of 1.5% per day. Quadriceps thickness declined in all participants ($n = 8$) at a mean rate of 2.0% per day.

Conclusions Use of ultrasound to measure thickness of the diaphragm in 8 intensive care patients undergoing various modes of mechanical ventilation was feasible and yielded reproducible results. Ultrasound tracking of changes in thickness of the diaphragm in this small sample indicated that the thickness decreased during assist-control mode and increased during pressure support mode. (*American Journal of Critical Care*. 2016;25:e1-e8)

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Ventilator-induced diaphragmatic dysfunction contributes to unsuccessful weaning in patients undergoing mechanical ventilation.¹⁻³ We seek to understand how diaphragmatic atrophy is associated with duration and mode of mechanical ventilation.⁴ Among noninvasive methods for measuring muscle dimensions, ultrasonography is preferred over radiography or computed tomography because it avoids radiation exposure⁵⁻⁷ (Appendix 1). Studies requiring serial evaluations demand a technique that eliminates the risk of repetitive radiation exposure; thus ultrasound is the most appropriate choice. We evaluated interoperator and interobserver reproducibility and reliability at obtaining daily ultrasound images, in order to establish a foundation for future ultrasound studies to elucidate natural history and determinants of diaphragmatic atrophy.

Materials and Methods

We evaluated diaphragm thickness in critically ill patients in the intensive care unit at Royal Columbian Hospital in New Westminster, BC, Canada. Our protocol was approved by the research ethics boards at Fraser Health Authority and Simon Fraser University and required informed consent from a surrogate decision maker.

Eligible patients had no history of diaphragmatic or neuromuscular disease or of morbid obesity (body mass index [calculated as weight in kilograms divided by height in meters squared] >40).

Diaphragm thickness was measured once daily until day 14 after inclusion in the study, extubation, discharge, or death.

The thickness of patients' quadriceps

muscle also was measured daily with ultrasound to track overall changes in patients' muscle size.

Information captured included time spent in each ventilation mode, daily fluid volume, daily positive end-expiratory pressure (Appendix 2) and Sequential Organ Failure Assessment score.

Movement of the diaphragm was recorded by using B-mode ultrasonography (Echo Blaster 128,

Telemed Ltd) with 0.1-mm resolution and a linear 5- to 10-MHz ultrasound transducer (HL9.0/60/128Z).

Diaphragm thickness was measured at the zone of apposition between the eighth or ninth intercostal spaces on the right side in the midaxillary line. For quadriceps imaging, patients were supine with legs relaxed and knees extended. Scans were performed midway between the anterosuperior iliac spine and the proximal part of the patella, with the transducer perpendicular to the femur under firm compression.⁸⁻¹⁰ Specific procedures are detailed in Appendix 3.

Video-format data files were saved for analysis. Diaphragm thickness was measured during the end-expiratory pause, when muscle fibers are longest.¹¹ Ultrasound exaggerates thicknesses of pleural and peritoneal membranes¹²; hence, measurements were made from the midpleural line to the midperitoneal line^{12,13} (Appendix 3). Three measurements were recorded and means were reported to 0.1 mm. Patients in whom imaging was not possible on 2 consecutive days were excluded from further analysis.

To assess interoperator reproducibility, in 6 patients, baseline scans were repeated by 2 additional operators (Joy Walcott-Francis, MA [Operator B] and Suzette Willems, RN [Operator C]) after a short training session. The operators were blinded to each other's scans.

To test interobserver reliability, 10 previously acquired images of the diaphragm and quadriceps were randomly selected and renamed to blind observers from patients' information. Observers measured all selected files and were blinded from each other's results (Appendix 4).

Statistical Analysis

Interrater reliability was evaluated for all operators and all readers by using interclass correlation coefficients. Reliability indices between observers and between operators were calculated.

Descriptive statistics included mean (SD) and median for continuous variables and counts and

Ultrasonography is preferred among noninvasive methods for measuring muscle dimensions.

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Table 1
Reproducibility of ultrasound measurements of thickness of diaphragm: interoperator and interobserver reliability

Comparison	Mean difference in thickness, ^a mm		Interclass correlation coefficient (95% CI)	
	Diaphragm	Quadriceps	Diaphragm	Quadriceps
Interoperator (A vs B; n = 6)	0.08 (P = .86)	0.18 (P = .90)	0.976 (0.856-0.997)	0.995 (0.969-0.999)
Interoperator (A vs C; n = 6)	0.05 (P = .91)	0.41 (P = .92)	0.982 (0.893-0.997)	0.998 (0.990-1.000)
Interobserver (A vs B; n = 10)	0.01 (P = .97)	0.06 (P = .97)	0.992 (0.971-0.998)	0.999 (0.997-1.000)
Interobserver (A vs C; n = 10)	0.03 (P = .91)	0.13 (P = .94)	0.995 (0.980-0.999)	0.999 (0.997-1.000)

^a Difference between mean diaphragm thickness measured by each operator and each observer. Significance was tested by using independent *t* test.

frequencies for categorical variables. Statistical analysis was performed by using SPSS v19.0 for Windows. Statistical significance was set at *P* less than .05.

Results

Of 18 patients for whom consent was obtained, 10 were excluded (7 had poor image quality due to edema; 3 were extubated by day 2). Mean fluid balance was +21 870 mL for patients in whom imaging failed versus +8257 mL in successfully imaged patients (*P* < .001).

Reliability and Reproducibility of Ultrasound Measurements

Interoperator reliability was assessed between 2 pairs of operators (C.F. [Operator A]/Operator B and Operator A/Operator C). Interclass correlation coefficients were estimated by using a 1-way random effect model, and mean measures were reported. Interclass correlation coefficients and indices of reliability for diaphragm and quadriceps thickness were greater than 0.95 (Table 1).

Interobserver reliability was assessed between 2 pairs of observers (C.F. [Observer A]/Joy Walcott-Francis, MA [Observer B] and Observer A/Ming Fong Wong, BSc [Observer C]). Interclass correlation coefficients and indices of reliability were greater than 0.95 (Table 1).

Diaphragm and Quadriceps Thickness

All data were acquired while the patient was receiving either pressure support ventilation (PSV) or assist-control ventilation (ACV). Of 8 patients included in the analysis, 4 were maintained on PSV for the duration of the study (mean [SD], 6.8 [5.6] days on PSV) and 4 were initially on ACV (4.5 [4.4] days) followed by PSV (4.3 [2.6] days). For all 8 patients, mean (SD) time on PSV was 5.5 (4.3) days. Total patient-days were 18 on ACV and 44 on PSV.

In patients on ACV (*n* = 4), mean diaphragm thickness declined 0.4 (SD, 0.4) mm (from 2.8 [SD, 0.7] to 2.4 [SD, 0.8] mm, mean decline = 21.2% [SD, 10.8%]; 95% CI, 0.05-0.79 mm) over 4.5 (SD, 4.4) days (mean daily decrease = 0.1 [SD, 0.1]

mm; 4.7% [SD, 5.7%] per day; see Figure, part C). Patients supported on ACV at baseline and first measured on day 1 or day 2 after intubation (*n* = 3; see Figure, part C) showed similar declines in diaphragm thickness.

In patients on PSV (*n* = 8), mean overall diaphragm thickness increased 0.23 (SD, 0.03) mm (from 2.5 [SD, 0.7] mm to 2.7 [SD, 0.76] mm, mean increase = 8.4% [SD, 3.9%]; 95% CI, 0.21-0.25 mm) over 5.5 [SD, 4.3] days (mean daily increase = 0.04 [SD, 0.03] mm; +1.5% [SD, 1.4%] per day; see Figure, part D). Table 2 shows mean daily changes in diaphragm thickness across all patients on PSV versus ACV.

Mean decline in quadriceps thickness for all participants (*n* = 8) was 2.4 (SD, 2.6) mm (from 15.5 [SD, 5.5] mm to 13.2 [SD, 5.1] mm, 95% CI, 0.58-4.16 mm; 14.4% [SD, 13.6%]) over 7.1 (SD, 4.7) days (mean [SD], -2.0% [2.7%] per day). The rate of change in quadriceps thickness was not significantly different (*P* = .17) between ACV and PSV patients.

Data were acquired while the patient was receiving pressure support ventilation or assist-control ventilation.

Discussion

Daily use of ultrasonography to evaluate diaphragm thickness in critically ill patients undergoing mechanical ventilation proved feasible and reliable, except in patients with gross edema. Operators with no prior experience in ultrasonography were able to accurately reproduce images and measurements of diaphragm and quadriceps thickness with high interoperator reliability (interclass correlation coefficient > 0.95).

We were unable to acquire images in cases of gross edema.¹⁴ Edema is known to decrease ultrasound sensitivity and may limit the utility of ultrasound in the intensive care unit.^{13,15}

In patients supported on ACV, diaphragm thickness declined at a mean rate of 4.7% (SD,

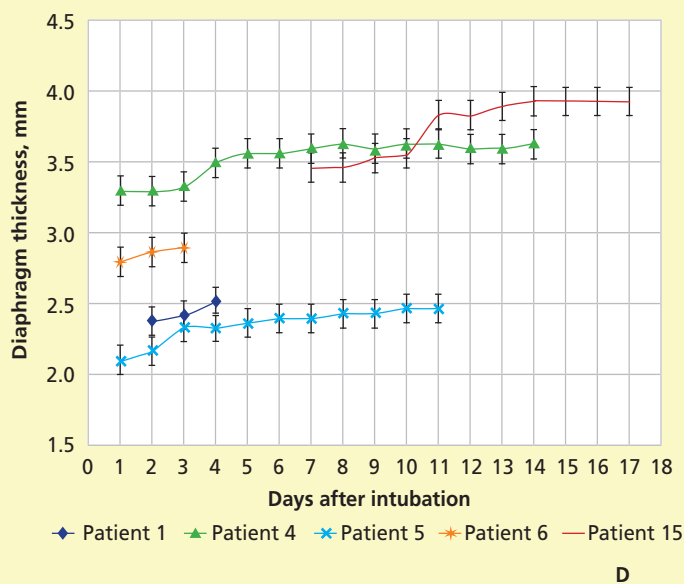
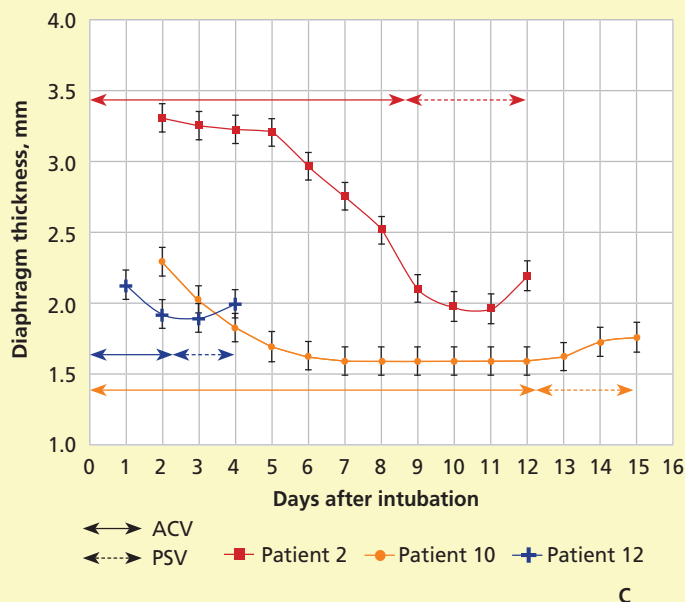
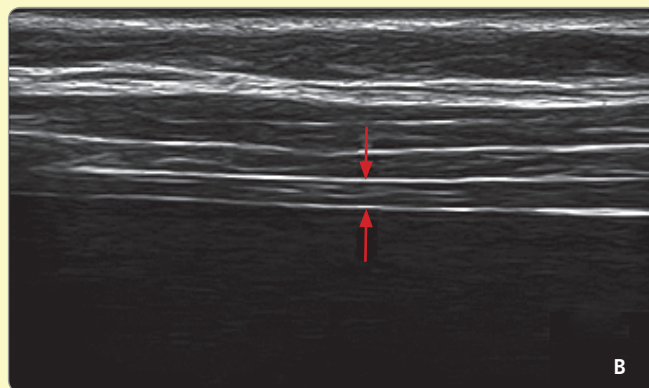
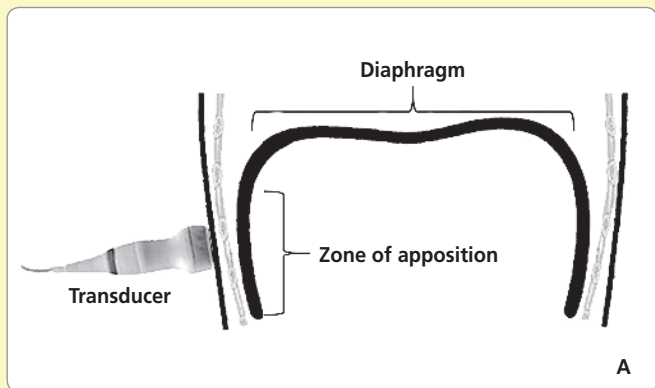


Figure (a) Transducer placement in the zone of apposition to the ribcage. (b) Echogenic lines (arrows) representing the pleural and peritoneal membranes overlying the diaphragm. (c) Trends in diaphragm thickness versus time from intubation for patients predominantly on assist control ventilation (ACV). Solid horizontal arrows indicate period when each patient was on ACV. Dashed arrows indicate time period when patient was on pressure support ventilation (PSV). (d) Trends in diaphragm thickness versus time from intubation for patients predominantly on PSV.

5.7%) per day. This finding is consistent with rapid atrophy of the diaphragm due to mandatory modes of mechanical ventilation that inactivate the diaphragm.^{5,16,17} Total thickness loss may have been greater than we measured, as the decline may have already started before the patients' entry into our study 24 to 48 hours after intubation.

Our results agree with the estimate by Grosu et al⁵ of a 6% daily decline in diaphragm thickness in patients undergoing mandatory mechanical ventilation. Additionally, in patients where the ventilation mode was switched from ACV to PSV, we measured small consistent increases in thickness of the diaphragm, presumably in response to increased voluntary activation of the diaphragm during weaning. Increases in diaphragm thickness were detected in the 5 patients who entered the

study while on PSV, as well as the 3 patients who entered the study while on ACV and subsequently were switched to PSV. These findings suggest that PSV may help attenuate and reverse the course of diaphragm atrophy in patients previously receiving mandatory mechanical ventilation.

Thinning of the quadriceps indicates that muscle decline in critically ill patients undergoing mechanical ventilation was not limited to the diaphragm; however, the rate of decline was faster for the diaphragm in our small sample.

Limitations of our study included an inability to obtain timely consent to initiate ultrasound evaluation on the day of intubation, the small sample size, an inability to assess patient-ventilator synchrony, and the exclusion of morbidly obese and edematous patients owing to poor imaging quality.

Table 2
Mean change in thickness of diaphragm: pressure support ventilation versus assist-control ventilation

Days after intubation	Pressure support ventilation		Assist-control ventilation	
	Mean difference in thickness, mm	No. of patients per data point	Mean difference in thickness, mm	No. of patients per data point
0				
1	2.7	3	2.1	1
2	2.7	4	2.5	3
3	2.7	4	2.6	2
4	2.8	3	2.5	2
5	3.0	2	2.5	2
6	3.0	2	2.3	2
7	3.2	3	2.2	2
8	3.2	3	2.1	2
9	3.2	3	1.6	1
10	3.2	3	1.6	1
11	3.3	3	1.6	1
12	3.7	2	1.6	1
13	3.8	2		
14	3.8	2		
15	3.9	1		
16	3.9	1		
17	3.9	1		

Conclusions

This pilot study demonstrates the feasibility and reproducibility of using ultrasound to measure diaphragm thickness in ICU patients receiving various modes of mechanical ventilation. We confirmed that diaphragm thickness decreases progressively during ACV, and found that the thickness of the diaphragm subsequently increases during PSV. Daily ultrasound monitoring of diaphragm thickness may help predict successful clinical outcomes and liberation from mechanical ventilation.

Appendix 1: Rationale for Using Ultrasonography to Track Changes in Diaphragm Thickness

For assessing body composition, new technologies that can quantify the thickness and distribution of both fat and muscle, such as computed tomography (CT), X-ray absorptiometry, and ultrasound, have advantages over older methods such as measurement of skinfolds and bioelectrical impedance analysis. In order to produce an accurate measurement of subcutaneous fat and overcome the problem of fat compression that is inherent in the skinfold technique, X-ray technology may be used.¹⁸⁻²⁰ However, the applicability of X-ray technology for serial evaluations is limited because of cumulative radiation exposure. Studies requiring serial evaluations

demand a technique that eliminates the risk of repetitive exposure to radiation. For studies of this nature, ultrasound is the most appropriate choice.

Acquiring body tissue images via ultrasonography has the same advantages as X-ray or CT scan technology in that fat and muscle thicknesses can be accurately visualized without compression of the tissue. However, ultrasonography is unique in that radiation exposure is eliminated. Another important advantage specific to this study is the ease with which real-time images of soft tissue can be obtained, making ultrasound the ideal technique for evaluating highly functional muscles such as the diaphragm.

Appendix 2: Positive End-Expiratory Pressure (PEEP) and Diaphragm Atrophy

All patients in this study were on PEEP, and all measurements were done at mean PEEP levels ranging between 5 cm H₂O and 13 cm H₂O. Skeletal muscles atrophy faster when inactive in the shortened position, and the increased lung volume at the end of expiration with the use of PEEP puts the passive diaphragm in a relatively shortened position, so it is possible that the diaphragm atrophied at a relatively faster rate than in patients not on PEEP. However, because PEEP is the standard of care in our institution, we had no control patients to whom we could refer in order to investigate whether PEEP affects rate of atrophy in critically ill patients.

Appendix 3: Procedures for Acquiring Images and Measuring Muscle Thickness

Diaphragm Thickness

Real-time movement of the diaphragm was recorded by B-mode ultrasonography using an Echo Blaster 128 Kit (UAB Telemed, Darius ir Gireno str. 42, Vilnius LT-02189, Lithuania— resolution of 0.1 mm) fitted with a 5- to 10-MHz ultrasound linear transducer (HL9.0/60/128Z; Figure 1).

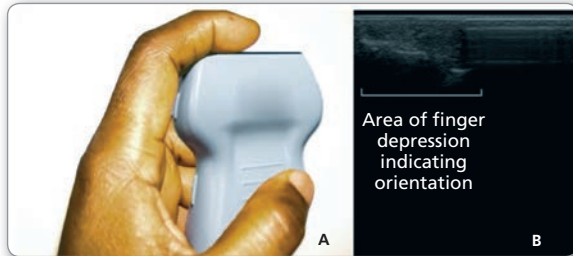


Figure 1 Orientation of transducer. A, Using finger to push on the marker side of transducer. B, Aberration from pushing on one side of transducer. The ultrasound image that appears on the screen should correspond to the same side as the finger applying pressure to the transducer. If not, the transducer is rotated so that the same side that is depressed on the transducer is the side where the aberration appears on the screen.

Locate the Diaphragm in the Zone of Apposition to the Ribcage. Patients were in the supine position.

- Precautions were taken to ensure that the patient was lying flat on his or her back.
- The head of the bed was lowered to 0° of incline.
- In cases where the head of the bed could not be laid completely flat because of the patient's condition, the degree of incline (usually between 10° and 20°) during baseline measurement was noted and the same degree of incline was set for all subsequent measurements.

The probe was oriented with the screen image by applying pressure to one end and noting the position of the aberration generated on screen (Figure 1).

The probe was placed in the eighth or ninth right intercostal space in the midaxillary or anterior axillary line (see part A of Figure in Results section).

The ultrasound beam was directed perpendicular to the diaphragm; that is, the probe was positioned perpendicular to the chest wall in a long-axis configuration with the left end cephalad.

The probe position was adjusted until the diaphragm was clearly visualized and then was carefully held, as small changes in orientation of the probe from its ideal position could result in distortion or loss of image.

Once a clear image of the diaphragm was obtained, an indelible ink marker was used to mark the skin at the caudal end of the transducer (Figure 2).

All ultrasound images were acquired with the transducer in the same position.

Files were stored in video format and named according to patient number and day of exam (eg, "patient#1.diaphragm.day2").

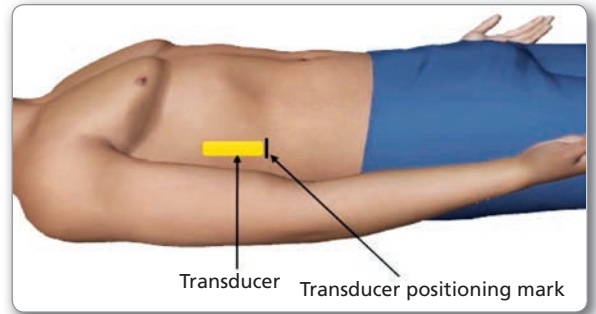


Figure 2 Placement of transducer positioning mark.

Identify the Diaphragm. The diaphragm was identified as the last set of parallel lines on the image, corresponding to the pleural and peritoneal membranes overlying the less echogenic muscle (see part B of Figure in Results section).

Once identified, real-time movement of the diaphragm was recorded on B-mode ultrasonography.

If the patient was triggering the ventilator (as was usually the case in assist modes of ventilation) and diaphragmatic contractions were visible, at least 6 consecutive respiratory cycles were recorded.

End-expiratory diaphragm thickness was measured in 3 consecutive respiratory cycles at 3 points along the zone of apposition during the end-expiratory pause, just before inspiration (Figure 3).

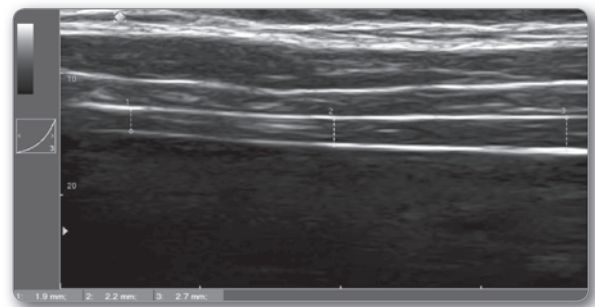


Figure 3 Measuring end-expiratory diaphragm thickness by using "distance" measuring tool.

- The diaphragm thickens as it contracts,²¹ hence great efforts were made to ensure that all thickness measurements were made during the end-expiratory pause (when the diaphragm is relaxed).

The thicknesses of the pleural and peritoneal membranes are exaggerated by ultrasound.²² Therefore, to obtain the most accurate measurement of diaphragm thickness, measurements were made from the middle of the pleural line to the middle of the peritoneal line.²²

Measurements were averaged, and the means were reported to the nearest 0.1 mm.

Failure to Acquire Image. Failure to acquire image was defined as the inability of 2 different operators to acquire a discernible image on 2 consecutive days. All patients for whom image acquisition failed were excluded from the study.

Measuring Quadriceps Thickness

The ultrasound technique used to measure thickness of the quadriceps muscle in this study has been described

and validated by Freilich et al²³ with modifications to reduce interoperator variability. Briefly, the thickness of the quadriceps muscle was measured by using the same Echo Blaster 128 Kit and 5- to 10-MHz linear array transducer previously described. Patients were positioned supine with the knees extended and the legs in the neutral position and completely relaxed. Scans were obtained at the midhigh level, defined as the midpoint between the superior aspect of the patella and the anterior superior iliac spine (Figure 4). The distance between the anterior superior iliac spine and the superior aspect of the patella was measured and the midpoint determined.

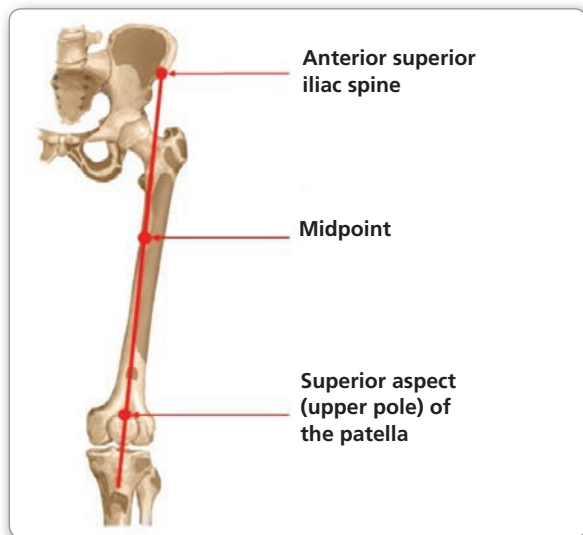


Figure 4 Midpoint between the anterior superior iliac spine and the superior aspect of the patella.

Using an indelible ink marker, a mark was placed on the patient's skin at the midpoint (Figure 5A). The transducer was positioned over the midpoint mark perpendicular to the longitudinal axis of the femur (Figure 5B). Once the transducer was positioned over the midpoint mark, a second mark was placed at the distal edge (Figure 5B) to ensure that all consequent measurements were made from the same position. To ensure consistency, the patient's legs were placed in the neutral position before each ultrasound examination.

The quadriceps was visualized by using a generous amount of gel and, using the transducer, maximal compression was applied before imaging in order to mitigate interoperator variability (Figure 6).

Thickness was measured, using the machine's electronic calipers, as the distance between the femur and the posterior border of the fascia lata (Figure 7). The scans were completed in approximately 5 minutes.

Appendix 4: Reproducibility of Ultrasound Measurements

In a subset of participants, baseline scans were repeated by 2 additional operators (Operator B and Operator C) in order to assess interoperator reproducibility of the method. The operators were blinded to each other's scans. As neither of the additional operators had previous ultrasound

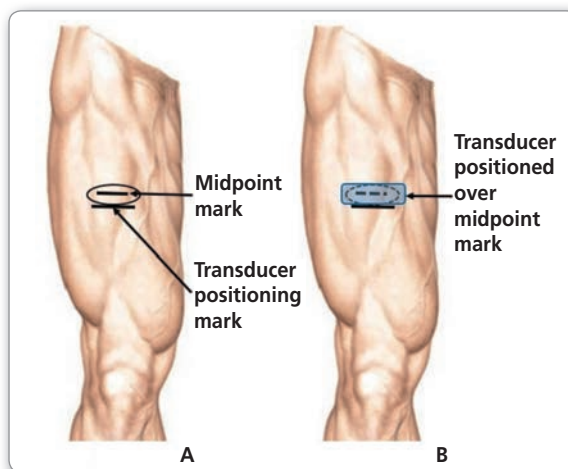


Figure 5 A, Mark placed at midpoint of the thigh over which the transducer would be positioned. B, Transducer positioned over midpoint mark with transducer positioning mark placed at the distal edge of the transducer.

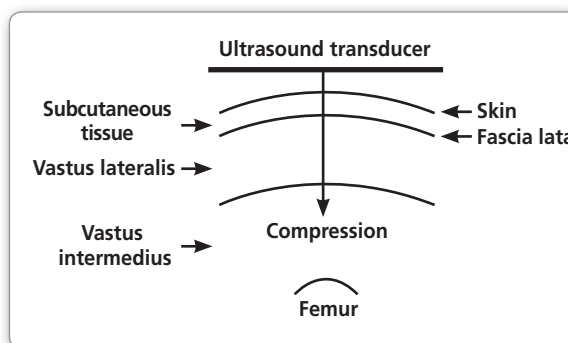


Figure 6 Maximal compression was applied during image acquisition.²³

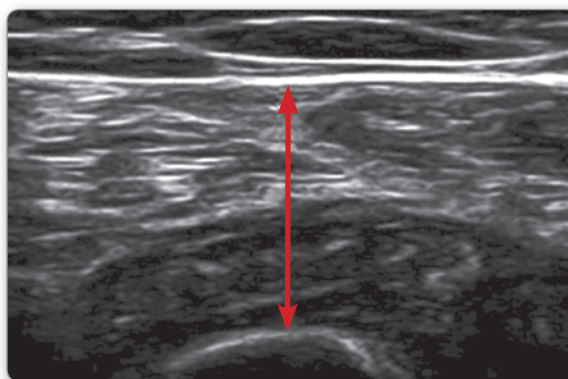


Figure 7 Measuring quadriceps thickness.

experience, a short training session (~1 hour) was conducted, following which competency was gained in performing the examinations independently. Training included image acquisition and techniques for measuring muscle thickness. Ultrasound images were acquired from study

participants by each operator within a week following training and at least 30 minutes apart on the day of image acquisition. Skin markings were removed following image acquisition by the first operator. To ensure that the operators were blinded to each other's results, each operator made measurements of muscle thickness on their images immediately following image acquisition (in the absence of the second operator) using the Telemed Echo Wave II software. Results were recorded on the form provided and submitted for analysis.

Interobserver reliability was assessed between two pairs of observers (Observer A vs Observer B, and Observer A vs Observer C). Previously acquired measurements of patients' diaphragm and quadriceps were randomly selected and the files were renamed to blind the observers to the patient number and the date when the information was acquired. The observers were also blinded to each other's results. Each observer was presented with all the selected patients' data files and made measurements on all ultrasound images using the Telemed Echo Wave II software. The data were recorded on the provided form and submitted for analysis.

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FINANCIAL DISCLOSURES

None reported.

eLetters

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