**Name of Journal: *World Journal of Critical Care Medicine***

**Manuscript NO: 34404**

**Manuscript Type: ORIGINAL ARTICLE**

***Prospective Study***

**Reproducibility of diaphragm thickness measurements by ultrasonography in patients on mechanical ventilation**

Dhungana A *et al*. Diaphragm USG during mechanical ventilation

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**Author contributions:** Dhungana A, Khilnani G and Hadda V are guarantors of the paper, be responsibility for the integrity of the work. Khilnani G and Hadda V conceived the idea; Dhungana A was involved in performing ultrasonography, data collection, manuscript drafting and revision; Hadda V contributed to performing ultrasonography, manuscript drafting and revision; Guleria R was involved in drafting and revising the manuscript.

**Institutional review board statement:** This study was reviewed and approved by institutional review board of All India Institute of Medical Sciences.

**Informed consent statement:** All study participants, or their legal guardian, provided written consent prior to enrollment into the study.

**Conflict-of-interest statement:** None of the authors have any conflict of interest.

**Data sharing statement:** There is no additional data available.

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**Manuscript source:** Unsolicited manuscript

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**Telephone:** +977-98-41860457

**Received:** April 20, 2017

**Peer-review started:** April 21, 2017

**First decision:** July 18, 2017

**Revised:** July 26, 2017

**Accepted:** September 3, 2017

**Article in press:**

**Published online:**

**Abstract**

***AIM***

To prospectively evaluate the reproducibility of diaphragm thickness measurement by ultrasonography at the bedside by critical care physicians in patients on invasive mechanical ventilation.

***METHODS***

In a prospective observational study of 64 invasively ventilated patients, diaphragmatic thickness measurement was taken by 2 different observers at the same site. Three measurements were taken by each observer and averaged. The intraobserver and interobserver variability was assessed by estimation of intraclass correlation coefficient. The limits of agreement were plotted as the difference between two observations against the average of the two observations in Bland and Altman analysis.

***RESULTS***

The mean diaphragm thickness at the functional residual capacity was 2.29 ± 0.4 mm and the lower limit of the normal *i.e.* the 5th percentile was 1.7 mm (95%CI: 1.6-1.8). The intraclass correlation coefficient for intraobserver variability was 0.986 (95%CI: 0.979-0.991) with a *P* value of < 0.001. The intraclass correlation coefficient for interobserver variability was 0.987 (95%CI: 0.949-0.997) with a *P* value of < 0.001. In Bland and Altman analysis, both intraobserver and interobserver measurements showed high limits of agreement.

***CONCLUSION***

Our study demonstrates that the measurement of diaphragm thickness by ultrasound can be accurately performed by critical care physicians with high degree of reproducibility in patients on mechanical ventilation.

**Key words**:Diaphragm; Ultrasonography; Mechanical ventilation

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**Core tip:** Ultrasonography (USG) is a cheap, cost effective and non-invasive bedside tool for evaluation of diaphragm thickness during mechanical ventilation. Measurement of diaphragm thickness by USG can be accurately performed by critical care physicians with high degree of reproducibility. USG should be used more often by the physicians in the intensive care unit for the assessment of the diaphragm.

Dhungana A, Khilnani G, Hadda V, Guleria R. Reproducibility of diaphragm thickness measurements by ultrasonography in patients on mechanical ventilation. *World J Crit Care Med* 2017; In press

**INTRODUCTION**

Invasive mechanical ventilation causes progressive decline in diaphragm bulk and strength in a phenomenon called ventilator induced diaphragm dysfunction[1]. Diaphragm movement and function can be assessed by various methods which include chest X-ray, supine vital capacity, maximum inspiratory pressure, electromyography and magnetic phrenic nerve stimulation. Ultrasonography (USG) is a cheap, cost effective and non-invasive bedside tool for evaluation of diaphragm thickness. It has been used successfully to measure diaphragm thickness and movement in ambulatoryin dividuals[2,3]. Diaphragm thickness is a surrogate of its strength and helps to predict the outcome of extubation in patients on mechanical ventilation[4,5]. However, localization and measurement may be more difficult in critically ill ventilated patients in the intensive care unit (ICU) due to significant subcutaneous edema and supine position. The variability may also be due to variation in image acquisition and interpretation.

**MATERIAL AND METHODS**

This was a prospective observational study done in mechanically ventilated patients admitted to the Pulmoanry Medicine ICU, All India Institute of Medical Sciences, New Delhi. Ethical clearance was obtained from the Institute Ethics Committee and written informed consent was obtained in all patients. Diaphragm measurements were taken within the 1st 24 h of ICU admission.

***Inclusion criteria***

(1) Patients aged > 18 years and requiring endotracheal intubation and mechanical ventilation; (2) Admitted to the ICU within 72 h of initiation of mechanical ventilation.

***Exclusion criteria***

(1) Mechanical ventilation for more than 72 h before admission; (2) Any form of mechanical ventilation in the preceding 3 mo or those who are on home non-invasive or invasive ventilation; (3) Surgical dressings over the right lower rib cage; and (4) Surrogates of the patient not willing for consent.

***Observer training***

Both observers who conducted the ultrasonography were provided training in ultrasonographic measurement of diaphragm thickness by a radiologist in 3 sessions, each session lasting 30 min.

***Measurement of diaphragm thickness***

All ultrasound examinations were done with Sonosite Micromaxx Portable Ultrasound Machine (Sonosite, Inc. United States) using the B-mode and a 5-10 MHz linear transducer. Patients were put in a supine position at 0 ℃ of incline. The same incline was used for all subsequent measurements for a given patient. Diaphragm thickness was measured in right hemi diaphragm in the zone of apposition. USG probe was positioned at the 8th or 9th right intercostal space with vertical orientation in the mid-axillary line and adjusted until the diaphragm was properly visualised. The distal end of the transducer was marked with permanent ink. The diaphragm was identified as the last set of parallel lines, the pleural and peritoneal membranes overlying the less echogenic muscle. Figure 1 shows an USG sample image of a patient taken at end expiration. Three measurements of the diaphragm thickness were taken and averaged to report the mean. In 10 randomly selected patients, diaphragm thickness was re-measured on the same day by 2nd observer who was blinded to the results of the 1st observer. The results of diaphragm measurements were not revealed to the treating physician nor it was taken into consideration in any clinical decision-making or management of the patients.

***Statistical analysis***

The primary outcome was intraobserver and interobserver variability of the measurements. The intraobserver variability was assessed by estimation of intraclass correlation coefficient using the three observations in the same patient by the 1st observer. Interobserver variability was tested between observations made by the 1st and the 2nd observers in the same subjects. The limits of agreement were plotted as the difference between two observations against the average of the two observations in Bland and Altman analysis. Data was analysed using International Business Machine (IBM) SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.

**RESULTS**

***Baseline characters***

A total of 106 patients admitted to the ICU were assessed for eligibility and inclusion into the study. Forty two of the 106 were excluded as they did not meet the eligibility criteria. Right hemidiaphragm localisation for measurement of thickness was successful in 64 out of 66 (97%) subjects. The flow of the patients enrolled into the study is shown in Figure 2.

The mean age of the study population was 54.5 ± 15.3 years. The mean diaphragm thickness at the functional residual capacity was 2.29 ± 0.4 mm and the lower limit of the normal *i.e.,* the 5th percentile was 1.7 mm (95%CI: 1.6-1.8).The baseline characteristic of the study population is depicted in Table 1.

***Intraobserver variability***

The intraclass correlation coefficient was 0.986 (95%CI: 0.979-0.991) with a *P* value of < 0.001. In Bland and Altman plots, 2 out of 64 observations were outside the limits of agreement when first and second measurements were compared. Similarly 1 out of 64 observations was outside the 95% limit of agreement when the second and third or first and third measurements were compared.

***Interobserver variability***

The intraclass correlation coefficient of interobserver variability was 0.987 (95%CI: 0.949-0.997) with a *P* value of < 0.001. In Bland and Altman analysis, no measurements were outside the limit of agreement. Bland and Altman plots of intraobserver and interobserver agreement are shown in Figure 3.

**DISCUSSION**

Diaphragm is the principal muscle of respiration and its proper functioning is the critical determinant of the ability of a patient to be successfully weaned from mechanical ventilation. Assessment of diaphragm thickness and function is relevant to clinical practice because diaphragm dysfunction is an important cause of complications in mechanically ventilated patients[1,4]. We were able to successfully measure diaphragm thickness in 64 of the 66 (97%) patients who were eligible to participate in the study. This finding is important as measurement of diaphragm thickness by USG is an easy to learn, non-invasive bedside tool and is hazard free. It also avoids the hassle of shifting the patients out of the ICU and the associated complications.

Previous studies have shown that USG measurements of diaphragm thickness and movement have high degree of reproducibility in both spontaneously breathing and mechanically ventilated patients[6-8]. In the study by DiNino *et al*[5] diaphragm thickness was measured by an intensivist after an initial training of three to five sessions lasting ten to 15 min each. The intra-observer variability after such training was less than 10%. Similarly, in the study by Schepens *et al*[9] the coefficient of reproducibility was high (0.945 for intra-observer and 0.971 for inter-observer variability). Francis *et al*[10] also demonstrated both to be greater than 0.95. The intraclass correlation coefficients of both intra and inter observer variability in our study was high. Our study demonstrates that the measurement of diaphragm thickness by ultrasound can be accurately performed by critical care physicians after a short training with high degree of reproducibility.

The mean diaphragm thickness in our cohort was 2.29 ± 0.4 mm and the lower limit of normal was 1.7 mm (95%CI: 1.6-1.8). Prior studies have reported a diaphragm thickness in the range of 1.5 to 3.2 mm in normal healthy population[6,11,12]. The diaphragm thickness and contractility are minimally affected by age, body habitus and smoking history and may differ in different population. Majority of the patients in our study had underlying chronic respiratory disorder, as the most common diagnoses were chronic obstructive pulmonary disease (COPD), post tuberculosis sequelae, interstitial lung disease, asthma and lung cancer. The mean diaphragm thickness in COPD patients, as reported by Baria *et al*[12] was 2.8 mm and the lower limit of normal was 1.4 mm. The diaphragm thickness in COPD population was lesser than the normal controls. There was also a wider deviations of diaphragm thickness from the mean in those with COPD as compared to the controls (SD = 1.6 *vs* 1.3 mm for COPD and controls respectively).

Our study also has some limitations. Though we analysed the intraobserver variability of diaphragm thickness measurements in all included patients, interobserver variability was only evaluated in 10 randomly selected patients in the study cohort. This was due to technical difficulties in performing ultrasonography twice in all patients. Hence, the results of interobserver agreements may need to be replicated in a larger cohort. All the measurements were taken by physicians trained in critical care ultrasonography and the radiologist was only involved in the initial training of the observers. Another limitation of the study is that we only used B mode for the measurement of diaphragm thickness. M mode USG has also been suggested by some authors as an alternative modality to assess diaphragmatic excursions[2,8]. Reproducibility compared to a radiologist derived measurement would have added more value to the results.

In conclusion, the results of our study indicate that the measurement of diaphragm thickness by ultrasound can be accurately performed by critical care physicians with high degree of reproducibility. Hence, USG should be used more often by the physicians in the ICU for the assessment of the diaphragm.

**COMMENT**

***Background***

Ultrasonography (USG) is a cheap, cost effective and non-invasive bedside tool for evaluation of diaphragm thickness and function during mechanical ventilation. However, there may be variability in the measurement of diaphragm thickness by USG due to variation in image acquisition and interpretation.

***Research frontiers***

The reproducibility of diaphragm thickness measurement by critical care physicians at bedside needs to be further explored. The results from this study suggest that the intraobserver and interobserver agreements of the measurements by critical care physicians after adequate training is high.

***Innovations and breakthroughs***

This study adds to the current literature of evidence that USG can be used at the bedside to measure diaphragm thickness during mechanical ventilation even by critical care physicians, and can be used as a guide to assess weaning outcomes.

***Applications***

USG should be used more often by the physicians in the intensive care unit for the assessment of the diaphragm.

***Terminology***

USG: a technique using echoes of ultrasound pulses to delineate objects or areas of different density in the body. Diaphragm: the principal muscle of inspiration muscle that separates the chest (thoracic) cavity from the abdomen. Mechanical ventilation: the technique through which gas is moved toward and from the lungs through an external device connected directly to the patient.

***Peer-review***

The authors describe a study to evaluate the interobserver agreement of sonographic measurement of the diaphragm thickness in 64 ventilated patients.

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**P-Reviewer:** Muensterer OH, Zhang ZH, He HW **S-Editor:** Cui LJ

**L-Editor: E-Editor:**

**Specialty type:** Critical Care Medicine

**Country of origin:** India

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C, C

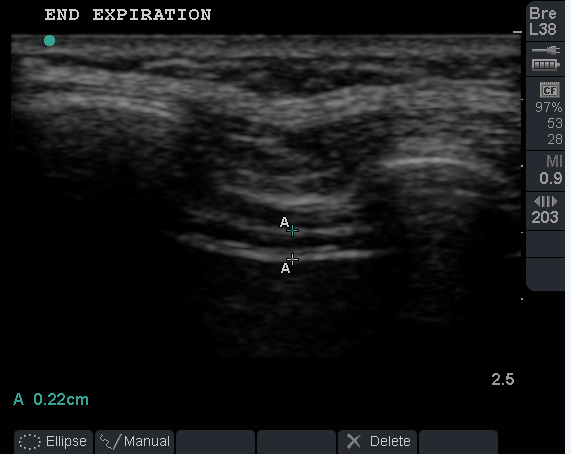
Grade D (Fair): 0

Grade E (Poor): 0

**Table 1 Baseline characters of the study population**

|  |  |
| --- | --- |
| **Classification** | **Quantity, *n* (%)** |
| Mean age, yr | 54.5 ± 15.3 |
| Male sex | 45 (70) |
| Diagnoses  COPD  Post tuberculosis sequelae  Interstitial lung disease  Asthma  Lung cancer  Others1 | 20 (31)  11 (17)  8 (13)  5 (8)  5 (8)  15 (23) |
| Mean apache II score at admission | 15.5 ± 5.3 |
| Mean diaphragm thickness at FRC (mm) | 2.29 ± 0.4 |

1Other diagnoses included chronic obstructive pulmonary disease, obstructive sleep apnea overlap syndrome, aspiration pneumonia, diabetic ketoacidosis and acute respiratory distress syndrome. COPD: Chronic obstructive pulmonary disease; FRC: Functional residual capacity.

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**Figure 1 Ultrasonography image of a patient taken at end expiration.** Diaphragm identified as the last set of parallel line, pleural and peritoneal membranes overlying the less echogenic muscle.

**Screened:** 106

**Excluded**

1. Mechanical ventilation for more than 72 h: 24
2. Receiving home non-invasive ventilation: 12
3. Right intercostal tube in situ: 3
4. Poor acoustic window: 2
5. Declined to participate: 1

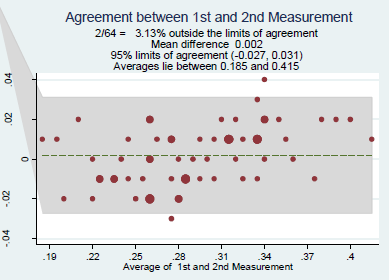
**Eligible for the study**: 64

**USG measurement of Diaphragm at end expiration by 1st observer within 24 hours of inclusion:** 64

10 **Randomly selected patients**

**USG measurement of diaphragm thickness by 2nd observer on the same day**

**Figure 2 Flow of the patient enrolled into the study.** USG: Ultrasonography.



A B



C D

**Figure 3 Bland and Altman plots of intraobserver agreement in diaphragm measurement.** The result of three occasions (A, B, C) and between two observers D.