Lung (2020) 198:499–505
https://doi.org/10.1007/s00408-020-00352-3

LUNG ULTRASOUND

The Utility of Diaphragm Ultrasound in Reducing Time to Extubation

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Received: 12 March 2020 / Accepted: 30 March 2020 / Published online: 13 April 2020

Abstract

Purpose Prediction of optimal timing for extubation of mechanically ventilated patients is challenging. Ultrasound measures of diaphragm thickness or diaphragm dome excursion have been used to aid in predicting extubation success or failure. The aim of this study was to determine if incorporating results of diaphragm ultrasound into usual ICU care would shorten the time to extubation.

Methods We performed a prospective, randomized, controlled study at three Brown University teaching hospitals. Included subjects underwent block randomization to either usual care (Control) or usual care enhanced with ultrasound measurements of the diaphragm (Intervention). The primary outcome was the time to extubation after ultrasound, and the secondary outcome was the total days on the ventilator. Only intensivists in the Intervention group would have the ultrasound information on the likelihood of successful extubation available to incorporate with traditional clinical and physiologic measures to determine the timing of extubation.

Results A total of 32 subjects were studied; 15 were randomized into the Control group and 17 into the Intervention group. The time from ultrasound to extubation was significantly reduced in the Intervention group compared to the Control group in patients with a $\Delta tdi\% \geq 30\%$ (4.8 ± 8.4 vs 35.0 ± 41.0 h, $p = 0.04$). The time from ultrasound to extubation was shorter in subjects with a normally functioning diaphragm ($\Delta tdi\% \geq 30\%$) compared to those with diaphragm dysfunction ($\Delta tdi\% < 30\%$) (23.2 ± 35.2 vs 57.3 ± 52.0 h $p = 0.046$). When combining the Intervention and Control groups, a value of $\Delta tdi\% \geq 30\%$ for extubation success at 24 h provided a sensitivity, specificity, PPV and NPV of 90.9%, 86.7%, 90.9%, and 86.7%, respectively.

Conclusions Diaphragm ultrasound evaluation of $\Delta tdi\%$ aids in reducing time to extubation.

Keywords Diaphragm ultrasound · Mechanical ventilation · Extubation · Critical care

Introduction

Determining the optimal timing for extubation of mechanically ventilated patients continues to be a challenge for clinicians. Extubating the patient too early may result in increased cardiovascular and respiratory stress or complications related to carbon dioxide (CO_2) retention and hypoxemia [1, 2] Delaying extubation can increase the risk of developing complications such as ventilator associated pneumonia and ventilator induced diaphragm atrophy [3–5]. Using subjective measures alone to determine the timing of extubation can be fraught with error with the decision to extubate biased toward ventilator dependency [6]. Incorporating measures of tidal volume and breathing frequency into a rapid shallow breathing index aids in making the decision as to when mechanical ventilation can be discontinued [7–9]. However, these parameters are limited when subjects are assisted using pressure support [10–12].

Ultrasound can be used either to assess motion of the diaphragm dome [13–16] or changes in diaphragm thickness as it contracts [11]. Both parameters have been used to determine the likelihood of extubation success. Ultrasound measures of the diaphragm dome evaluate its effectiveness in displacing the rib cage and abdomen, whereas ultrasound measures of diaphragm thickness in the zone of apposition of the diaphragm to the rib cage (ZOA) allow the clinician to directly assess diaphragm musculature. These prior studies

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indicate that diaphragm ultrasound can aid in predicting extubation success or failure; however, they do not address whether using diaphragm ultrasound can aid in decreasing the time to extubation. The aim of this study was to determine if incorporating results of diaphragm ultrasound into usual ICU care would shorten the time to extubation. In addition, we re-examined the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of measures of percent change in diaphragm thickness between end-expiration and end-inspiration (Δtdi%) in predicting extubation outcomes.

Methods

Study Subjects

The study was conducted from November 2013 to May 2014. We performed a prospective, randomized, controlled study at three Brown University teaching hospitals. Subjects who were included in the study were those who were in the medical intensive care unit; had an age of 18 years or older; were able to provide informed consent or had a medical decision maker who could provide informed consent; had been on mechanical ventilation more than 48 h; were ready to undergo a spontaneous breathing trial; were on minimal sedation; and were on a positive end-expiratory pressure (PEEP) < 8 cmH2O and FiO2 of < 50% with an oxygen saturation > 92%. Exclusion criteria are as follows: pregnancy, current incarceration, right-sided diaphragmatic paralysis, severe neurological injury, planned terminal extubation, prolonged intubation for more than 2 weeks duration, and Do-not-Re-intubate status.

Included subjects underwent block randomization to either usual care alone (Control), where the intensivist evaluates traditional indices for extubation and determines appropriateness for extubation or usual care enhanced with ultrasound measurements of the diaphragm (Intervention). The ICU attending was responsible for all clinical decisions. The ICU attendings in the intervention group were immediately communicated with the ultrasound results. If Δtdi% was ≥ 30%, the intensivist would be given the following message: "Your patient has a 91% chance of successful extubation within the next 48 h". If Δtdi% was < 30%, the intensivist would be told that diaphragm contraction was impaired and this will lower the success of extubation. The intensivist then determined appropriateness for extubation.

Based on the time from diaphragm ultrasound to extubation data in our previous study [11], the estimated sample size, assuming the time from ultrasound to extubation in the control group to be 36 h and in the intervention group to be 24 h with a standard deviation of 18 h, was 36 subjects for an alpha of 0.05 and power of 80% to detect a difference in outcome. A total of 44 subjects provided consent to participate in the study. Figure 1, 12 were excluded before they could be studied (five died prior to any weaning attempt, five were extubated and two underwent tracheostomy) (Fig. 1) Of the remaining 32 subjects, fifteen were randomized to the usual care group (Control group) and 17 were randomized into the usual care+ultrasound group (Intervention group). All had diaphragm thickness measured with ultrasound while intubated during a spontaneous breathing trial with pressure support of 5 cm H2O (PS Δ5/5). The primary outcome was time to extubation after diaphragm ultrasound, and the secondary outcome was the total days on the ventilator. Demographic data were recorded for the subjects who participated in the study. (Table 1) The Institution Review Board at Rhode Island Hospital, Memorial Hospital of Rhode Island and Miriam Hospital approved of the study.

Diaphragm Ultrasonography

Diaphragm thickness was measured in millimeters using a 7–10 MHz linear ultrasound probe (LOGIQ Book, GE Healthcare, Waukesha, Wisconsin, USA). The B mode was used to image the right hemidiaphragm in the mid axillary line between the 8th and 10th intercostal space. The diaphragm muscle was visualized as the echogenic space between the pleura and peritoneum as previously described [11]. Diaphragm thickness (tdi) was measured at end-expiration and end-inspiration. The Δtdi% was calculated as (tdi end-inspiration—tdi end-expiration / tdi end-expiration) × 100. The Δtdi% for each patient represented the mean of 3–5 breaths. Images were obtained within the first 5 to 10 min of the spontaneous breathing trial (SBT). One individual performed all the ultrasound exams at all sites.

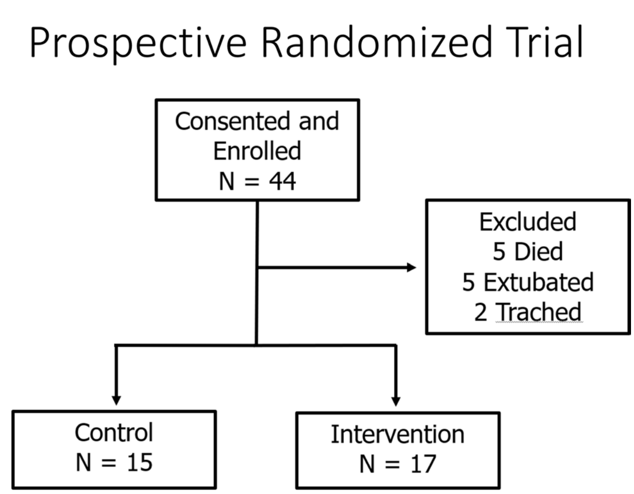

Fig. 1 Flow chart demonstrating the allocation of subjects in the study

Table 1 Baseline characteristics

Variables	Overall ($n=32$)	Control ($n=15$)	Intervention ($n=17$)	P value
Age (years)	55.8 ± 14.8	56.5 ± 17.3	55.3 ± 12.8	0.83
Male (%)	17 (53.1)	11 (73.3)	6 (35.3)	0.03
Body-mass Index (kg/m^2)	33.8 ± 10.8	31.3 ± 9.9	35.9 ± 11.3	0.23
End-expiratory Tdi (cm)	0.25 ± 0.1	0.25 ± 0.1	0.26 ± 0.1	0.72
End-inspiratory Tdi (cm)	0.34 ± 0.1	0.36 ± 0.1	0.32 ± 0.1	0.30
Extubation within 24 h (%)	22 (59.5)	10 (62.5)	12 (57.1)	0.74
Extubation within 48 h (%)	26 (70.3)	13 (81.3)	13 (61.9)	0.20

All continuous variables are expressed in mean ± standard deviation, and categorical variables were expressed as percentages

US ultrasound, *Tdi* diaphragm thickness

Only the right hemidiaphragm was examined because it is easier to visualize than the left in the ZOA due to the liver providing an excellent acoustic window [17].

Perception of Diaphragm Ultrasound for Extubation

The following Likert scale was used to assess the intensivist's perception of the utility of diaphragm ultrasound: 1. Not at all helpful, 2. Slightly helpful, 3. Somewhat helpful, 4. Very helpful, and 5. Extremely helpful.

Statistical Analyses

Descriptive analysis was performed on the demographic data. Continuous data were presented as mean and standard deviation (mean ± SD), and categorical variables were presented as counts and percentages. For continuous variables, comparisons between the control and intervention groups were performed using unequal variances *t* test (Welch's *t* test). Comparisons between categorical variables were performed using Chi-squared test for proportions.

Sensitivity and specificity were calculated using the Δtdi% in relation to the success of extubation within 24 h and 48 h. A receiver operating characteristic (ROC) curve was constructed, and the area under the curve and the cutoff for the change in tdi were determined. The cutoff for the change in tdi was chosen based on a sensitivity and specificity of approximately 80%. A 2-tailed p value of < 0.05 was considered significant. All statistical analyses were performed using Stata/IC version 15 (StataCorp, College Station, Texas).

Results

Fifteen subjects were randomized into the usual care (Control) group and 17 into the usual care+ultrasound (Intervention) group. The most common admitting diagnosis for both groups was pneumonia. The mean age for the Control group was 56 years and for the Intervention group 55 years.

For subjects with a Δtdi% ≥ 30%, the time from ultrasound to extubation, which was the primary outcome, was significantly reduced in the Intervention group when compared the Control group. (4.8 ± 8.4 vs 35.0 ± 41.0 h, $p = 0.04$) (Table 2). However, the total number of days on the ventilator, which was the secondary outcome, for subjects with a Δtdi% ≥ 30% was similar for both the Intervention and Control groups. (6.9 ± 4.3 vs. 7.1 ± 5.1 days). For subjects with diaphragm dysfunction, a Δtdi% < 30%, the time from

Table 2 Extubation outcomes of usual care (Control) or usual care with diaphragm ultrasound (Intervention)

Variables	Overall ($n=32$)	Control ($n=15$)	Intervention ($n=17$)	P value
Time to extubation after US (h)	38.1 ± 45.9	44.4 ± 54.3	32.5 ± 37.9	0.48
Time to extubation after US in those with Tdi < 30% (hr)	57.3 ± 52.0	70.4 ± 83.2	52.0 ± 38.6	0.69
Time to extubation after US in those with Tdi ≥ 30% (h)	23.2 ± 35.2	35.0 ± 41.0	4.8 ± 8.4	**0.04**
Time on ventilator (days)	7.5 ± 4.3	7.3 ± 4.8	7.6 ± 4.0	0.87
Time on ventilator in those with Tdi < 30% (days)	8.1 ± 3.9	8.0 ± 4.2	8.1 ± 4.0	0.97
Time on ventilator in those with Tdi ≥ 30% (days)	7.0 ± 4.7	7.1 ± 5.1	6.9 ± 4.3	0.92

Significant p value for the comparison between control and intervention groups indicated in bold

All continuous variables are expressed in mean ± standard deviation, and categorical variables were expressed as percentages

US ultrasound, *Tdi* diaphragm thickness ultrasound to extubation was similar in the Intervention and Control groups (52.0 ± 38.6 vs 70.4 ± 83.2 h, $p = 0.69$) as well as the total number of days on the ventilator. (8.1 ± 4.0 vs 8.0 ± 4.2 days)

Overall, the time from ultrasound to extubation was shorter in subjects with a normally functioning diaphragm compared to those with diaphragm dysfunction (23.2 ± 35.2 vs 57.3 ± 52.0 h for Δtdi% $\geq$ 30% and Δtdi% < 30%, respectively; $p = 0.046$) (Table 3). This difference primarily can be attributed to a shorter time from ultrasound to extubation in those with a normally functioning diaphragm in the Intervention group (4.8 ± 8.4 vs 52.0 ± 38.6 h for Δtdi% $\geq$ 30% and Δtdi% < 30%, respectively; $p = 0.004$). (Table 3) By contrast, the time from ultrasound to extubation was similar for subjects with and without diaphragm dysfunction in the Control group (70.4 ± 83.2 vs 35.0 ± 41.0 h for Δtdi% < 30% and Δtdi% $\geq$ 30%, respectively; $p = 0.46$). There were two failed extubations in Intervention group and one in the Control group. These subjects had findings consistent with diaphragm dysfunction and underwent tracheostomy.

The ROC curves for Δtdi% for predicting extubation success at 24 and 48 h are shown in Fig. 2a, b, respectively. A Δtdi% $\geq$ 30% for extubation success at 24 h provided a sensitivity, specificity, PPV and NPV of 90.9%, 86.7%, 90.9%, and 86.7%, respectively. A Δtdi% $\geq$ 30% for extubation success at 48 h provided a sensitivity, specificity, PPV and NPV of 80.8%, 90.9%, 95.5%, and 66.7%, respectively. Clinicians perceived the utility of diaphragm ultrasound as being between "slightly useful" and "somewhat useful" (score of 2.53).

Discussion

We found that incorporating results of diaphragm ultrasound into usual ICU care decreased the time from US to extubation in subjects with a normally functioning diaphragm. We noted a high prevalence of subjects with diaphragm dysfunction, as defined by a Δtdi% < 30%, in our study. Those individuals had a longer interval from ultrasound to extubation irrespective of being in the Intervention or Control group. In addition, we found that the PPV, NPV and ROC area for a Δtdi% $\geq$ 0.30% for predicting extubation outcomes was similar to those values reported previously for Δtdi% $\geq$ 20% and Δtdi% $\geq$ 30%.

Table 3 Time to extubation by change in diaphragm thickening

Variables	Tdi < 30%	Tdi ≥ 30%	*P* value
Time to extubation after US in all subjects (h)	57.3 ± 52.0	23.2 ± 35.2	**0.046**
Time to extubation after US in control group (h)	70.4 ± 83.2	35.0 ± 41.0	0.46
Time to extubation after US in intervention group (h)	52.0 ± 38.6	4.8 ± 8.4	**0.004**

Significant *p* values for the comparison between control and intervention groups are indicated in bold

All continuous variables are expressed in mean ± standard deviation

US ultrasound, *Tdi* diaphragm thickness

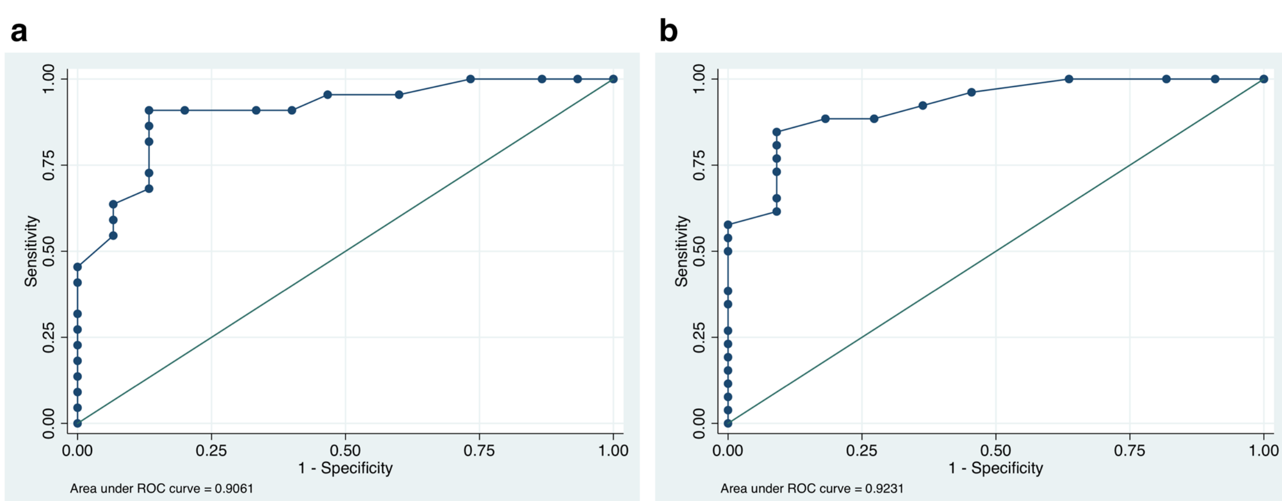

Fig. 2 (**a**) ROC curve for Δtdi% > 30% in relation to extubation success within 24 hours. (**b**) ROC curve for Δtdi% > 30% in relation extubation success within 48 hours

Ultrasound measures of diaphragm thickening in the zone of apposition give insight into diaphragm function. When the diaphragm contracts, it shortens and thickens. Absence of thickening with inspiration is consistent with diaphragm paralysis, whereas the presence of thickening by more than 20% is consistent with a functioning diaphragm. Clinical application of measures of diaphragm thickening include evaluating diaphragm function post-op, predicting extubation outcomes and documenting the presence of and recovery from diaphragm paralysis. It also has been used to determine the prevalence of diaphragm dysfunction in mechanically ventilated subjects, a condition which may occur within 36 h of the initiation of mechanical ventilation [4, 15, 18]. This condition may be prevented when the level of ventilator support is reduced to allow diaphragm thickening during inspiratory efforts [19].

Ultrasound measures of Δtdi% as well as measures of diaphragm dome excursion can be used to predict extubation failure or success. DiNino et al. found that a Δtdi% ≥ 30% had a PPV for extubation success of 91% in subjects undergoing spontaneous breathing trials with low levels of pressure support (PS of Δ5/5) [11]. Blumhof et al. reported similar results when extending these observations to levels of pressure support as high as Δ10/5 [12]. However, when PS was raised to Δ15/5, the PPV and NPV deteriorated significantly. At the lower levels of PS, a Δtdi% ≥ 20% predicted extubation success with a positive predictive value of 85% and extubation failure with a NPV of 75%. The current study echos these observations with similar values for PPV, NPV, and ROC area for Δtdi% ≥ 30%. By contrast, Vivier et al. found that Δtdi% was not useful in distinguishing between subjects who were and were not successfully extubated [19]. Their study differs from prior studies evaluating Δtdi% as their subjects were mechanically ventilated for at least one week (prolonged mechanical ventilation), were older (aged > 65 years) and were at high risk for re-intubation. In addition, they studied both hemidiaphragms and found unilateral dysfunction in 140 of 160 subjects [20].

The advantage of assessing Δtdi% rather than dome excursion is that it provides an image of the diaphragm muscle itself, whereas diaphragm dome excursion reflects motion of the central tendon and the diaphragm's coupling to the abdomen and rib cage. Nonetheless, diaphragm dome excursion also can be used to predict extubation outcomes. In general, diaphragm excursion during a spontaneous breathing trial of less than 1.0 cm is associated with extubation failure and excursion greater than 1.05 cm is associated with extubation success [14, 15, 21, 22]. Measurements of diaphragm excursion at 5 and 30 min of a spontaneous breathing trial may improve the specificity and sensitivity of this parameter [23] Dome excursion during spontaneous breathing trial has also been compared to dome excursion during triggered- assist/control ventilation [24]. The smaller the difference between diaphragm dome excursion measured during triggered-assist/control ventilation and breaths at 30 min of a SBT, the more likely the patient would be successfully extubated.

Although prior studies have evaluated the utility of diaphragm ultrasound in predicting extubation failure or success, they have not evaluated its utility in reducing the time to extubation. The current study found that the time from ultrasound to extubation in subjects with a Δtdi% ≥ 30% was significantly shorter in the Intervention group than in the Control group and that subjects with diaphragm dysfunction in the intervention group (Δtdi% < 30%) had longer time from ultrasound to extubation. These findings suggest that clinicians who incorporate US measures with other clinical and physiologic features may feel more confident and act sooner to extubate a patient. Furthermore, knowledge that the diaphragm was not functioning allowed for better discrimination between individuals with and without diaphragm dysfunction in the intervention group and allowed for more caution in these individuals.

We expected that shortening the time from US to extubation would shorten the total number of ventilator days. However, we did not find a difference in the total ventilator days between the Control and Intervention groups. This lack of a difference may be related to the greater incidence of diaphragm dysfunction in the intervention group. There were more than twice as many subjects with diaphragm dysfunction in the intervention group (10/17) than in the control group (4/15). As expected, subjects with diaphragm dysfunction had a significantly longer time between ultrasound and extubation. Two of the subjects with diaphragm dysfunction had repeat ultrasound measurements in the intervention group. Both were found to have functioning diaphragms and both were successfully extubated. This observation was not included in our data analysis and is presented only to show that patients on mechanical ventilation can recover diaphragm dysfunction.

Shortening the time to extubation has financial and medical implications. Prolonged mechanical ventilation stresses health care resources and increases financial expenditures related to the development of co-morbid conditions [25–28]. The hospital costs of subjects receiving prolonged mechanical ventilation (> 96 h) in the United States of America as of 2003 were three times that for subjects being ventilated for less than 36 h. In addition, hospital length of stay was nearly triple for the prolonged mechanical ventilation and these subjects are less likely to be discharged home and more likely to be transferred to a skilled nursing care facility [26]. If diaphragm ultrasound can assist the clinician in extubating a patient sooner and reduce the ICU length of stay, this can result in considerable cost savings. A study evaluating the impact of an early mobility program in a trauma ICU suggested that a reduction in ICU length of stay of 1.31 days resulted in a cost savings of $8,239 per patient [29].

The major limitation of our study is the small number of subjects studied. However, despite the small number, there was a significant reduction in the time from ultrasound to extubation in subjects who were deemed ready to be extubated when clinicians had knowledge of the ultrasound results. We had only one ultrasonographer who visited the three hospitals to study all the subjects. The advantage of having one ultrasonographer is that it ensures reproducibility in US measurements among subjects. However, having ultrasound measurements made by a single individual limits the generalizability of this study and speaks to the need to have more individuals trained in point-of-care diaphragm ultrasonography.

Conclusion

Predicting the optimal time for extubation is challenging, especially in patients with underlying diaphragm dysfunction. Incorporating ultrasound information on diaphragm function into usual care allowed clinicians to identify patients with a normally functioning diaphragm and decreased the time from ultrasound to extubation.

Authors Contributions All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Franklin Dennis McCool, Dennis Oyieng'o, and Patrick Koo. The first draft of the manuscript was written by Franklin Dennis McCool and Patrick Koo and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability All available data have been included in the article.

Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest to disclose.

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