ORIGINAL ARTICLE

Sonographic evaluation of diaphragmatic thickness and excursion as a predictor for successful extubation in mechanically ventilated preterm infants

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Abstract

Sonographic assessment of diaphragmatic thickness and excursion has been found to be an accurate tool in predicting successful extubation of adult patients from invasive mechanical ventilation. We aimed to evaluate the accuracy of sonographic assessment of diaphragmatic thickness and excursion in predicting successful extubation of preterm infants from invasive conventional mechanical ventilation. Preterm infants less than 32 weeks gestation who required invasive conventional mechanical ventilation were evaluated by diaphragmatic sonography within 1 h of their planned extubation. Infants were classified into successful or failed extubation groups based on their ability to stay off invasive mechanical ventilation for 72 h after extubation. Inspiratory and expiratory thickness plus excursion of the right and left hemidiaphragm as well as diaphragmatic thickening fraction (DTF) measures were compared between groups. We included 43 eligible infants, of whom 34 infants succeeded and 9 infants failed extubation. Infants in the successful extubation group had a significantly higher expiratory thickness of the right and left hemidiaphragm, excursion of the right and left hemidiaphragm, inspiratory thickness of the left hemidiaphragm, and DTF of the left hemidiaphragm compared with infants who failed extubation. The receiver-operating characteristic curves showed that excursion of the right and left hemidiaphragm has the highest significant accuracy in predicting successful extubation of preterm infants among all diaphragmatic parameters (AUC is 0.98 and 0.96, respectively; *p* value < 0.001 for both).

Conclusion: We conclude that diaphragmatic excursion is a useful indicator for successful extubation of preterm infants from mechanical ventilation.

What is Known:
• *Invasive mechanical ventilation induces ventilator induced diaphragmatic dysfunction (VIDD) particularly when used for long time.*
• *Assessment of diaphragmatic dimensions and functional activity has been a valuable tool in predicting successful extubation of adult patients from invasive mechanical ventilation.*

What is New:
• *Sonographic assessment of diaphragmatic dimensions can be used to predict successful extubation of preterm infants from mechanical ventilation.*
• *Sonographic assessment of diaphragmatic excursion shows the highest sensitivity and specificity in predicting successful extubation of preterm infants.*

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Abbreviations
AUC   Area under the curve
CPAP   Continuous positive airway pressure
DTF   Diaphragmatic thickening fraction
NICU   Neonatal intensive care unit
VIDD   Ventilator induced diaphragmatic dysfunction
FiO_2 Fraction of inspired oxygen

Introduction

The decision to extubate preterm infants from mechanical ventilators is mainly based on clinical assessment, blood gases, and ventilator settings [7]. Researchers attempted to evaluate different parameters as predictors for successful extubation of preterm infants from mechanical ventilation [26, 28]. However, up to 30% of preterm infants who are extubated based on the clinical assessment require re-intubation indicating a poor correlation with infants' readiness for extubation [3, 28].

The diaphragm represents the main respiratory muscle in infancy. It contributes to generation of an estimated three-fourths of the infant's tidal volume during resting inspiration in the supine position [23]. Continuous positive airway pressure (CPAP) affects the crura of diaphragm by shortening the muscle and decreasing excursion through maintaining end expiratory lung volume [21]. Moreover, prolonged mechanical ventilation triggers myofibrillar contractile dysfunction and myofilament protein loss of the diaphragmatic muscles which later results in loss of diaphragmatic force-generating capacity, poor activity, and unloading of the diaphragm [10]. This phenomenon of ventilator-induced diaphragmatic dysfunction (VIDD) has raised the attention of investigators to the correlation between duration of mechanical ventilation and failure to extubate preterm infants from mechanical ventilation [27]. However, the diagnosis of this diaphragmatic dysfunction can be hindered by the lack of appropriate quantitative assessments of neonatal diaphragm function [1].

Accurate assessment of diaphragm function in the neonate could aid to the diagnosis of respiratory distress, evaluation of therapeutic interventions, and identification of infants ready to wean from mechanical ventilation [20]. Monitoring the electrical activity of the diaphragm in infants and children has shown that higher diaphragmatic activity in relation to tidal volume indicates a better preserved diaphragmatic function and a better chance of passing the extubation readiness test [29]. However, the tools needed for monitoring the electrical activity of the diaphragm are invasive, expensive, and require trained personnel for proper interpretation. Sonographic evaluation of the diaphragm is ubiquitous in medical facilities, requires no radiation, can be used at the infant's bedside, and useful in assessing diaphragmatic mobility and excursion [13].

We hypothesized that assessment of diaphragmatic dimensions and excursion, before planned extubation, may be helpful in predicting successful extubation of preterm infants from mechanical ventilation. We aimed to study sonographic assessment of the diaphragmatic dimensions and excursion for mechanically ventilated preterm infants as a predictor for success of extubation.

Methods

The present study was placed at the Neonatal Intensive Care Unit (NICU) of Mansoura University Children's Hospital, Mansoura, Egypt, between January 2017 and November 2019. The study was approved by the Institutional Review Board, Mansoura Faculty of Medicine, and a fully informed written consent was obtained from the parent or infant's guardian before enrolment in the study.

Study designs

This was a prospective, observational, cohort study assessing diaphragmatic thickness and excursion for preterm infants prior to planned extubation from invasive conventional mechanical ventilation.

Participants

Preterm infants less than 32 weeks gestation who were supported by invasive conventional mechanical ventilation for a diagnosis of respiratory distress syndrome, as evident by clinical and radiological findings, and planned for extubation were eligible for this study. Preterm infants with chromosomal aberrations, hepatosplenomegaly, pleural effusion, congenital heart or lung disorders, or congenital anomalies related to diaphragm as diaphragmatic hernia and diaphragmatic paralysis were excluded from the study.

Intervention

Eligible preterm infants had sonographic assessment of diaphragmatic thickness and excursion within 1 h of planned extubation from invasive conventional mechanical ventilation to non-invasive respiratory support. Preterm infants were extubated from mechanical ventilation if they fulfilled the following criteria: spontaneous respiratory effort, presence of cough or gag induced by suctioning, acceptable arterial blood

gases (pH more than 7.25, $PaCO_2$ less than 60 mmHg, and base deficit less than 8 mEq/L) on a mean airway pressure less than 8 cm H_2O and respiratory rate of less than 30/min, saturation more than 90% on fraction of inspired oxygen (FiO_2) less than 30% in the preceding 24 h, and the decision of extubation was taken by the attending physician who was blinded to the results of sonographic measurements.

Sonographic diaphragmatic parameters were measured while infants were on spontaneous pressure support ventilation mode with a support pressure of 4 cm H_2O over an end expiratory pressure of 4 cm H_2O for 1 h prior to the sonographic assessment as an accommodation. The total duration on pressure support ventilation mode and sonographic diaphragmatic assessment was 2 h at most to avoid infant exhaustion. Sonographic evaluation was performed prior to the time of next feed, while infant's stomach is empty, to avert any interference of a full stomach on diaphragmatic mobility and measurements. All infants were extubated to nasal CPAP using the Infant Nasal CPAP Assembly system (Fisher & Paykel Healthcare, Auckland, New Zealand) at a pressure of 5 cmH$_2$O and FiO_2 between 21% and 30% to keep infant's saturation between 90% and 95%.

Sonographic diaphragmatic assessment technique

Ultrasonographic examinations were performed by one operator, who had ten years of experience in diaphragm sonography, using a portable Doppler ultrasonography (Micro-Maxx; SonoSite, Bothell, WA, USA) with a micro-convex transducer array (10 to 5 MHz). Diaphragmatic sonography was performed while the infant is in supine position after ensuring quiet regular breathing. For visualization of the right hemidiaphragm, the convex probe was placed over the right subcostal and lower intercostal spaces between the anterior axillary and the midclavicular lines with the probe directed cranially, dorsally, and medially so the radial beam came to be perpendicular to the posterior third of the right hemidiaphragm. For visualization of the left hemidiaphragm, the same technique, position, and direction of the probe as the right hemidiaphragm were performed apart from the probe was placed between the left anterior axillary and midaxillary lines.

At first, the two-dimensional mode was screened to detect the appropriate exploration image for each hemidiaphragm in which the diaphragm appeared as a hypoechoic line that was placed between two echogenic lines, the upper one was the reflection of the parietal pleura and the lower was for the peritoneum. After that, the M-mode ultrasonography was screened and the image was frozen after ensuring regular up and down movement of the diaphragmatic line that reflects regular breathing. The thickness of the diaphragmatic line during inspiration (upward slope) and expiration (downward slope) represents the diaphragmatic inspiratory and expiratory

thickness, respectively. The perpendicular distance between the most caudal point of this line during inspiration and the most caudal point during expiration represents the diaphragmatic excursion. Diaphragmatic thickness and kinetics measures can be affected by the irregular breathing pattern, high respiratory rate, breath to breath variability, and small diaphragmatic dimensions by using M-mode technique in preterm infants. To overcome this technical limitation, the investigator observed for regular up and down movements of the diaphragmatic line in M-mode and cine for 1 min to ensure an epoch of quiet regular breathing, and then diaphragmatic measurements were obtained [2]. The technique and measurements were repeated up to 3 respiratory cycles for each hemidiaphragm, and the average one was recorded [5]. Avoidance of diaphragmatic measurements during infant's crying or sighing movement was taken in consideration.

The diaphragmatic thickening fraction (DTF) was calculated and recorded using the following formula: DTF = [(inspiratory thickness − expiratory thickness) / expiratory thickness] × 100 [8].

The intra-observer reproducibility was evaluated by repeated measurements of sonographic diaphragmatic parameters by the same investigator with 30 min in between measurements. Ten clinically stable preterm infants, age and sex cross-matched with the studied group, were randomly selected for this purpose.

Study end point

The primary study end point was successful extubation from invasive mechanical ventilation defined as being off mechanical ventilation with transmission to oxygen therapy or non-invasive respiratory support, for at least 72 h post-extubation [12]. The indications for re-intubation were specified as follows: more than six episodes of apnea requiring stimulation within 6 h, or more than one significant episode of apnea requiring bag and mask ventilation, respiratory acidosis ($PaCO_2 > 65$ mmHg and pH < 7.25) or $FiO_2 > 60\%$ to maintain saturation in the target range (90–95%) [12].

Sample size calculation

Sample size calculation was based on the area under the receiver-operating characteristic curve that was 0.79 for predicting successful extubation of mechanical ventilation retrieved from previous research [4]. Using MedCalc for Windows, version 15.0 (MedCalc Software, Ostend, Belgium), sample size calculation using area under ROC curves with null hypothesis = 0.5, α-error = 0.05, power of the study = 80% ratio of positive to negative cases which will be considered as 3.3. The total calculated sample size will be 43 cases.

Statistical analysis

Statistical analysis was performed using SPSS statistical software (version 21; IBM Corporation, Armonk, NY, USA). Student's t test was used to compare continuous parametric variables. Mann–Whitney U test was used for continuous non-parametric variables. Chi-square test or Fisher's exact test was used for categorical variables when appropriate. Shapiro–Wilk test was done to examine the distribution of data. Pearson's correlation coefficient test was used to correlate between duration of invasive mechanical ventilation and different diaphragmatic measures. The accuracy of different diaphragmatic measurements for predicting successful extubation from invasive mechanical ventilation was evaluated using receiver-operating characteristic (ROC) curves. A p value of < 0.05 is considered to be statistically significant. Data are expressed as mean ± standard deviation, median (inter-quartile range), or number (percentage) unless otherwise stated. Reproducibility of the diaphragmatic measurements was assessed by Bland–Altman analysis and Pearson's correlation coefficient.

Results

Of the 164 preterm infants who were at less than 32 weeks gestation admitted to our NICU during the study period, 62 infants required invasive conventional mechanical ventilation, 43 were included in the study, and 19 were excluded due to various causes (Fig. 1). A total of 34 infants succeeded and 9 infants failed extubation. Infants in the failed extubation group had significantly higher postnatal age at extubation, longer duration of invasive mechanical ventilation, higher pre-extubation mean airway pressure, and higher pre-extubation FIO$_2$ compared with infants in the successful extubation group (Table 1). Of the 9 infants who failed extubation, 6 infants were reintubated for increased work of breathing in association with hypoxia, two infants were reintubated for increased work of breathing in association with hypercapnia, and one infant was reintubated for apnea which was preceded by increased work of breathing. The mean time for reintubation was 43.5 ± 13.5 h with a minimum of 29 and a maximum of 66 h, respectively. Measurements were highly reproducible with a high degree of agreement between diaphragmatic dimensions as assessed by Pearson's correlation coefficient and Bland–Altman analysis. Pearson's correlation coefficient values were above 0.9, and p values were < 0.001 for all measured diaphragmatic indices.

Infants in the successful extubation group had a significantly higher expiratory thickness of the right and left hemidiaphragm, excursion of the right and left hemidiaphragm, inspiratory thickness of the left hemidiaphragm, and DTF of the left hemidiaphragm compared with infants who failed extubation to nasal CPAP (Table 2) (Fig. 2). The duration of invasive mechanical ventilation had a significant negative correlation with inspiratory and expiratory thickness of the right and left hemidiaphragm, excursion of the right hemidiaphragm, and DTF of the right and left hemidiaphragm (Table 3).

The ROC curves showed that expiratory thickness of the right and left hemidiaphragm, excursion of the right and left hemidiaphragm, inspiratory thickness of the left hemidiaphragm, and DTF of the left hemidiaphragm had significant accuracies in predicting successful extubation of preterm infants (Fig. 3). Excursion of the right and left hemidiaphragm showed the highest accuracy among all diaphragmatic parameters. A right hemidiaphragmatic excursion of 2.75 mm was associated with 94% sensitivity and 89% specificity in predicting successful extubation. A left hemidiaphragmatic excursion of 2.45 mm was associated with 94% sensitivity and 89% specificity in predicting successful extubation.
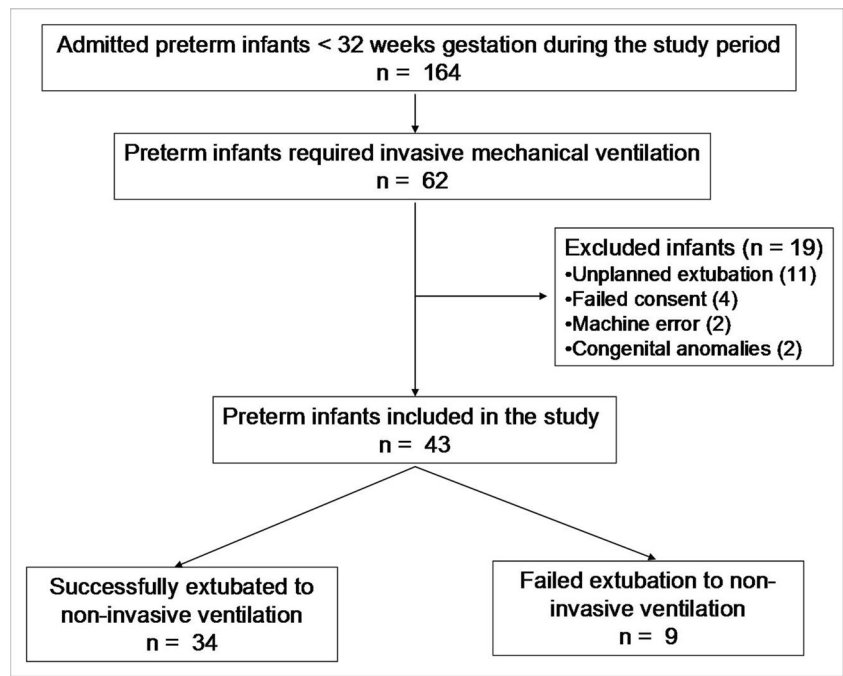
Discussion

Sonographic assessment of the lungs and diaphragm has gained the interest of neonatologists nowadays. Sonographic assessment of the lungs has shown a high sensitivity and specificity in diagnosing various respiratory disorders in neonates [24]. Ultrasound has been recently used to assess diaphragmatic thickness and excursion of diaphragmatic dome in stable spontaneously breathing infants [5]. We aimed to assess the accuracy of sonographic assessment of diaphragmatic thickness and excursion as a predictor for successful extubation of preterm infant from invasive conventional mechanical ventilation. The main finding of our study is that excursion of the right and left hemidiaphragm has the highest accuracy in predicting successful extubation of mechanically ventilated preterm infants. Diaphragmatic excursion was significantly higher in preterm infants successfully extubated from invasive conventional mechanical ventilation compared with infants who failed extubation.

Diaphragmatic activity as a predictor for successful extubation was evaluated in pediatric age group through monitoring of diaphragmatic electrical activity. Assessment of diaphragmatic electrical activity has shown that infants and children who generated higher diaphragmatic activity in relation to tidal volume had a better chance of passing the extubation readiness test as opposed to infants and children who generated lower diaphragmatic activity in relation to tidal volume [29]. Authors in this study stated that diaphragmatic activity in relation to tidal volume indicates a better preserved diaphragmatic function [29].

To the best of our knowledge, this study is the earliest to report the accuracy of assessing diaphragmatic activity by using diaphragmatic ultrasound in prediction of successful

Fig. 1 Diagram showing the flow of participants in the study

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│ Admitted preterm infants < 32 weeks gestation during the      │
│ study period                                                  │
│ n = 164                                                       │
└─────────────────────────────────────────────────────────────┘
                          │
┌─────────────────────────────────────────────────────────────┐
│ Preterm infants required invasive mechanical ventilation      │
│ n = 62                                                        │
└─────────────────────────────────────────────────────────────┘
                          │          ┌──────────────────────────────────┐
                          │────────→ │ Excluded infants (n = 19)         │
                          │          │ •Unplanned extubation (11)        │
                          │          │ •Failed consent (4)               │
                          │          │ •Machine error (2)                │
                          │          │ •Congenital anomalies (2)         │
                          │          └──────────────────────────────────┘
┌─────────────────────────────────────────────────────────────┐
│ Preterm infants included in the study                         │
│ n = 43                                                       │
└─────────────────────────────────────────────────────────────┘
              ╱                              ╲
┌──────────────────────────┐    ┌──────────────────────────┐
│ Successfully extubated to │    │ Failed extubation to non- │
│ non-invasive ventilation  │    │ invasive ventilation      │
│ n = 34                    │    │ n = 9                     │
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extubation in preterm infants. Over 400 participants between 1 month and 16 years, sonographic assessment of the diaphragm has shown a high accuracy in assessing diaphragmatic thickness and excursion [5]. Rehan and colleagues reported normal diaphragmatic excursion in 34 preterm infants between 26 and 37 weeks gestation to be 5.5 ± 0.2 mm at 26

Table 1 Baseline characteristics of the studied groups

Characteristics	Successful extubation group ($n = 34$)	Failed extubation group ($n = 9$)	p value
Gestational age (weeks)	29.5 ± 1.7	29.2 ± 1.7	0.66
Birth weight (g)	1206 ± 249	1111 ± 123	0.28
Male sex	10 (29%)	3 (33%)	0.98
Apgar score			
• 1 min	5 (3–6)	4 (4–6)	0.62
• 5 min	8 (6–9)	8 (7–8)	0.86
Mode of delivery			
• Vaginal delivery	9 (26%)	4 (44%)	0.41
• Cesarean section	25 (74%)	5 (56%)	
Small for gestational age	3 (9%)	1 (11%)	0.98
Antenatal steroid therapy	30 (88%)	8 (89%)	0.98
Surfactant therapy	10 (29%)	5 (56%)	0.24
Culture proven early-onset neonatal sepsis	0 (0%)	0 (0%)	1.0
Caffeine therapy	33 (97%)	9 (100%)	0.98
Postnatal age at extubation (days)	13 (10.5–15.5)	16 (14.5–17)	0.02
Body weight at extubation (g)	1177 ± 245	1047 ± 146	0.1
Duration of invasive mechanical ventilation (days)	6.5 (4–9)	10 (7.5–11.5)	0.04
Pre-extubation mean airway pressure (cm H_2O)	6.3 ± 0.5	6.6 ± 0.3	0.03
Pre-extubation fraction of inspired oxygen (FiO_2)	21.1 ± 0.6	23.6 ± 2.0	<0.001

Data expressed as mean $\pm$ SD, median (inter-quartile range), or number (percentage)

Table 2 Sonographic diaphragmatic parameters of the studied groups

Characteristics	Successful extubation group (n = 34)	Failed extubation group (n = 9)	p value
Inspiratory thickness of the right hemidiaphragm (mm)	1.38 ± 0.10	1.32 ± 0.07	0.07
Expiratory thickness of the right hemidiaphragm (mm)	1.29 ± 0.13	1.19 ± 0.04	0.02
Excursion of the right hemidiaphragm (mm)	3.43 ± 0.41	2.37 ± 0.37	< 0.001
Inspiratory thickness of the left hemidiaphragm (mm)	1.35 ± 0.14	1.23 ± 0.14	0.03
Expiratory thickness of the left hemidiaphragm (mm)	1.24 ± 0.10	1.16 ± 0.07	0.03
Excursion of the left hemidiaphragm (mm)	3.08 ± 0.36	2.0 ± 0.53	< 0.001
Diaphragm thickening fraction (DTF) of the right hemidiaphragm (%)	38.4 ± 9.4	32.1 ± 7.5	0.07
Diaphragm thickening fraction (DTF) of the left hemidiaphragm (%)	35.4 ± 14.2	23.3 ± 15.1	0.03

Data expressed as mean ± SD

to 28 weeks gestation, 4.8 ± 0.2 mm in 29 to 31 weeks gestation, 4.6 ± 0.2 mm in 32 to 34 weeks gestation, and 4.4 ± 0.3 mm in 35 to 37 weeks gestation [22]. The difference between our measurements and Rehan's study is attributed to their inclusion of clinically stable preterm infants who have no evidence of any acute illness, no culture proven sepsis, not on
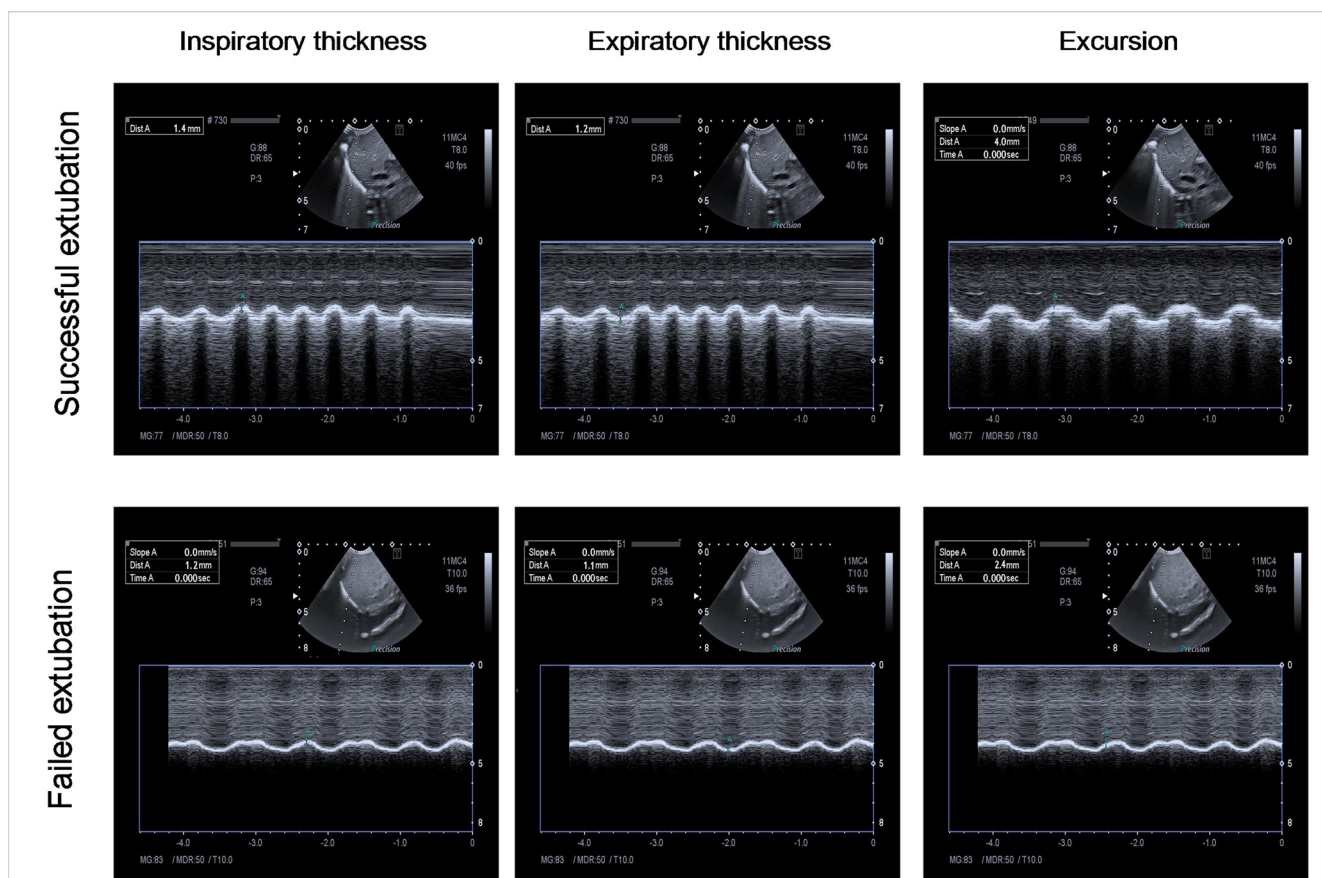
Fig. 2 Sonographic images showing M-mode measurements of inspiratory thickness, expiratory thickness, and excursion of the right hemidiaphragm in an infant (case number 5) from the successful extubation group and an infant (case number 11) from the failed extubation group

Table 3 Correlation between duration of pre-extubation (invasive) mechanical ventilation and sonographic diaphragmatic parameters of the studied groups

Characteristics	All infants ($n = 43$)	
	r	p value
Inspiratory thickness of the right hemidiaphragm (mm)	− 0.63	< 0.001
Expiratory thickness of the right hemidiaphragm (mm)	− 0.58	< 0.001
Excursion of the right hemidiaphragm (mm)	− 0.31	0.04
Inspiratory thickness of the left hemidiaphragm (mm)	− 0.64	< 0.001
Expiratory thickness of the left hemidiaphragm (mm)	− 0.53	< 0.001
Excursion of the left hemidiaphragm (mm)	− 0.25	0.09
Diaphragm thickening fraction (DTF) of the right hemidiaphragm (%)	− 0.61	< 0.001
Diaphragm thickening fraction (DTF) of the left hemidiaphragm (%)	− 0.64	< 0.001

any oxygen supplementation, and not on CPAP or ventilator support compared with our ventilated infants. Radicioni and colleagues tested the accuracy of a model that consists of the sonographic measurements of right diaphragmatic excursions during inspiration and expiratory phases plus the oxygen saturation/FiO$_2$ ratio as a predictor for CPAP failure in preterm infants with respiratory distress syndrome. The authors found that integration of both measures in this model has a high accuracy, with AUC 0.95, in predicting CPAP failure [19].

In mechanically ventilated adults, sonographic assessment of diaphragmatic function showed that diaphragmatic excursion was significantly higher in the successful group compared with those who failed extubation [6]. Liu and colleagues found that diaphragmatic excursion had a sensitivity of 89.2% and a specificity of 75.0% with an AUC (ROC) of 0.849 in predicting successful extubation in mechanically ventilated adult patients. The cut-off value of diaphragmatic excursion for predicting successful extubation was determined to be 1.14 cm by ROC curve analysis [16]. Yoo et al. found that diaphragmatic excursion is more accurate than a change in the diaphragm thickness to predict extubation success in mechanically ventilated adults [31]. In a meta-analysis of 13 studies over 742 adults, Li and colleagues concluded that diaphragmatic excursion and thickness are accurate measures for predicting reintubation within 48 h of extubation despite having a large heterogeneities among the included studies [15].

In mechanically ventilated adults, McCool and colleagues [17] showed that the duration of mechanical ventilation was significantly shorter in patients diagnosed with normal diaphragmatic function as assessed by ultrasound measurement of diaphragmatic thickness and excursion. The authors stated that normal diaphragmatic function as assessed by ultrasound shows 90.9% sensitivity, 86.7% specificity, 90.9% positive predictive value, and 86.7% negative predictive value in predicting successful extubation from mechanical ventilation [17].

The proposed mechanism for diaphragmatic dysfunction in association with invasive mechanical ventilation is the loss of myofilament protein of diaphragmatic muscle which results in what is known as ventilator-induced diaphragmatic dysfunction (VIDD). A previous research revealed that only 18–24 h of invasive mechanical ventilation is sufficient to develop VIDD in both laboratory animals and humans [18]. In animal models, ventilator-induced diaphragmatic proteolysis and associated diaphragmatic atrophy occur due to increased diaphragmatic protein breakdown and decreased protein synthesis which is mediated by various proteases, such as calpain, caspase-3, autophagy, and the ubiquitin-proteasome system [18]. We have found that expiratory thickness of the right and left hemidiaphragm and inspiratory thickness of the left hemidiaphragm were significantly lower in infants who failed compared with infants who succeeded extubation from mechanical ventilation. Our results support previous results of ventilator-induced diaphragmatic atrophy which were retrieved by animal studies and human studies [11, 14]. This is further supported by our finding of negative correlation between the duration of mechanical ventilation with inspiratory and expiratory thickness of the right and left hemidiaphragm, excursion of the right hemidiaphragm, and DTF of the right and left hemidiaphragm. The possible cause of the absence of significant difference in the inspiratory thickness and thickening fraction of the right hemidiaphragm between successfully and failed extubated preterm infants can be attributed to the supporting effect of the liver to the right hemidiaphragm during inspiration which can mask minimal effects on the muscle mass of the right hemidiaphragm. Another possibility for this non-significant difference may be related to our use of M-mode technique during measurement. Compared with B-mode, M-mode may not obtain reliable measurements of the diaphragmatic thickness, due to the subtlety of the imaging line. However, we compensated for this by obtaining our M-mode measures over the most moving point of the hemidiaphragm on B-mode. Moreover, M-mode technique
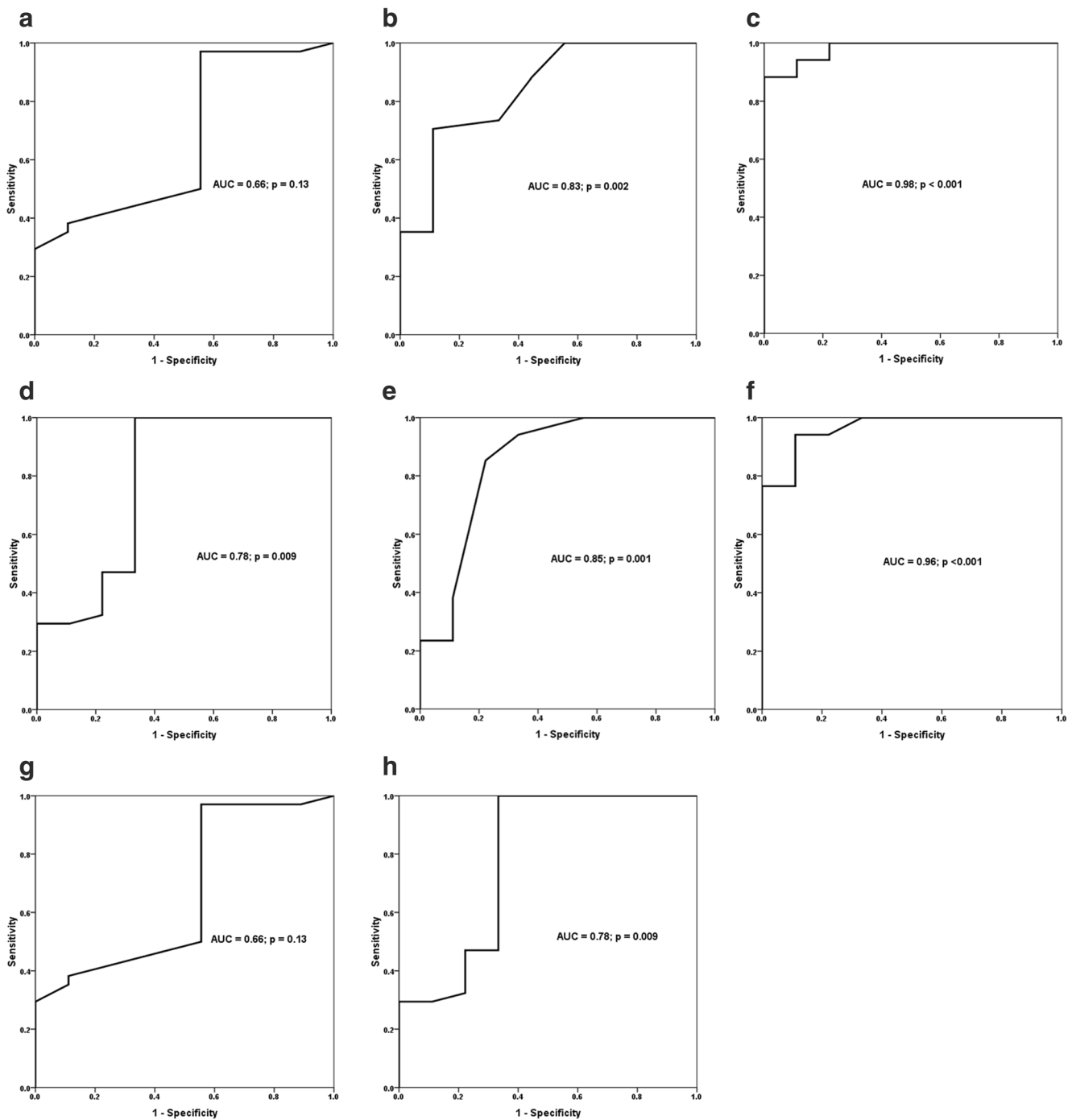
Fig. 3 Receiver-operating characteristic curves show area under the curve (AUC) and *p* value of significance for inspiratory thickness of the right hemidiaphragm (**a**), expiratory thickness of the right hemidiaphragm (**b**), excursion of the right hemidiaphragm (**c**), inspiratory thickness of the left hemidiaphragm (**d**), expiratory thickness of the left hemidiaphragm (**e**), excursion of the left hemidiaphragm (**f**), and diaphragm thickening fraction (DTF) of the right hemidiaphragm (**g**) and the left hemidiaphragm (**h**) in predicting successful extubation of preterm infants from mechanical ventilation

has been successfully used in previous studies to measure diaphragmatic thickness in excursion in adults and pediatric age groups [9, 30].

A potential technical limitation to our study is the use of a micro-convex transducer rather than a high-frequency micro-linear transducer for imaging. The latter has better ability for visualization of the thin muscles and superficial structures, like hemidiaphragm. However, the micro-convex transducer gives a better in-between ribs view and wider angle of image "pie-shaped image" of the whole hemidiaphragm which allows for better identification of the most moving part of the hemidiaphragm in B-mode. We compensated for this

technical limitation by taking our M-mode measurements at the most moving part of hemidiaphragm in the B-mode view.

We acknowledge that the study is limited by the relatively small sample size, which is attributed to our adoption of the early administration of non-invasive respiratory support techniques to our preterm infants to minimize ventilator-induced lung injury which decreased the percentage of preterm infants who required invasive mechanical ventilation during the study period. The study is also limited by the lack of physiopathologic proof of respiratory etiology as a cause for extubation failure and the need for reintubation. It is of note that assessment of diaphragmatic function in infants who failed extubation due to non-respiratory causes, such as central apnea or poor respiratory drive, is less valuable. Moreover, our practice of extubation to a nasal CPAP of 5 cm H_2O represents another limitation given the new guidelines of extubating preterm infants to CPAP pressure of 7–9 cm H_2O [25]. Our low level of CPAP support may have resulted to an increased incidence of preterm infants who required reintubation. Future studies should consider evaluation of diaphragmatic thickness and excursion in relation of different modes and parameters of respiratory support to find out the appropriate approach for respiratory support in preterm infants that maintain adequate diaphragmatic stimulation and prevent VIDD.

In conclusion, sonographic assessment of diaphragmatic thickness and excursion represents a promising sensitive and specific easily applicable tool to predict successful extubation of preterm infants from invasive conventional mechanical ventilation.

Compliance with ethical statements

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