The predictive value of diaphragm ultrasound for weaning outcomes in critically ill children

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Abstract

Background: Multiple studies have shown that diaphragmatic ultrasound can better predict the outcome of weaning in adults. However, there are few studies focusing on children, leading to a lack of sufficient clinical evidence for the application of diaphragmatic ultrasound in children. The purpose of this study was to investigate the predictive value of diaphragm ultrasound for weaning outcomes in critically ill children. Methods: Study included 50 cases whose mechanical ventilation(MV) time > 48 h, and all eligibles were divided into either the weaning success group (n = 39) or the weaning failure group (n = 11). Diaphragm thickness and diaphragmatic excursion (DE) were measured in the zone of apposition. The maximum inspiratory pressure (PImax) was also recorded. Results: The ventilatory treatment time (P = 0.002) and length of PICU stay (P = 0.013) in the weaning failure group was longer than the success group. Cut-off values of diaphragmatic measures associated with successful weaning were ≥ 21% for DTF with a sensitivity of 0.82, and a specificity of 0.81, whereas it was ≥ 8.40 mm for DE with a sensitivity of 0.62, and a specificity of 0.91. The linear correlation analysis showed that DTF had no significant correlation with PImax in children (P = 0.31). Conclusions: Diaphragm ultrasound has great value in predicting the weaning outcome of critically ill children. DTF and DE presented better performance than other diaphragmatic parameters. However, PImax has limited value in terms of reflecting the inspiratory muscle function of children with MV. Trial Registration: The trial 'Early rehabilitation intervention for critically ill children' has been registered at http://www.chictr.org.cn/showproj.aspx?proj=23132. Registration number: ChiCTR1800020196. Key words: Paediatric; mechanical ventilation; diaphragm; ultrasound; weaning; PImax

Introduction

Mechanical ventilation (MV) technology is widely used in paediatric critical care. About 30% of children in the paediatric intensive care unit (PICU) receive MV support.[1] However, MV support is not the end of the treatment, and our ultimate goal is to help patients wean off of MV support. An international consensus conference on weaning from MV in 2007 proposed that weaning should be categorized into three groups: simple weaning, difficult weaning, and prolonged weaning.[2] A multicentre study has shown that 10% of patients with MV had a difficult weaning duration of more than 1 day and less than 1 week, and 9% had a prolonged weaning duration of 1 week or more.[3] Failure to wean (FTW) is generally defined as difficult and prolonged weaning. FTW has significantly worse clinical outcomes. Studies have shown that FTW is an independent risk factor for mortality in ICU patients and prolonged length of ICU stay, and it is also associated with the occurrence of intensive care unit-acquired weakness (ICU-AW) and ventilator-induced diaphragmatic dysfunction (VIDD).[4-6] Therefore, weaning from mechanical ventilation represents a crucial step for every patient. The optimal timing of weaning can shorten the duration of MV and reduce complications. Weaning predictors – such as rapid shallow breathing index (RSBI), airway occlusion pressure 0.1 s (P0.1), maximum inspiratory pressure (PImax), and the weaning index – have been used to improve the rate of successful weaning in adult studies.[7-9] Unfortunately, in terms of weaning success in children, there is an insufficient amount of data to suggest the usefulness of predictors being superior to clinical judgment.[10]

Diaphragm ultrasound as a new technology in recent years allows for the direct visualisation of the diaphragmatic function of patients,[11-13] which has the advantages of being noninvasive, rapid, and easy to perform at the bedside. Therefore, it is suitable for application in patients with MV in ICU.[12, 13] Multiple adult studies have shown that diaphragmatic ultrasound can better predict the outcome of weaning, which has great value of guiding weaning in patients with MV.[14-16] However, there are few studies of diaphragmatic ultrasound in the field of paediatric critical medicine, leading to diaphragmatic ultrasound data being insufficient. In addition, the respiratory physiology and anatomical characteristics of children are different from that of adults. Therefore, the conclusions of adult studies may not be applicable to children, and more studies in children are needed to confirm the effectiveness of diaphragmatic ultrasound in predicting the outcome of weaning. To the best of our knowledge, this paper is the first study to investigate the predictive value of diaphragm ultrasound for weaning outcomes in critically ill children.

Methods

Patients

This prospective study was conducted in the paediatric intensive care unit of First Hospital of Jilin University, Changchun, China. Study subjects included 61 consecutive patients between January 2019 and May 2019, who were aged less than 18 years. The institutional ethics committee of the hospital approved the study protocol (ChiCTR1800020196). The parents or guardians of the eligible children provided written informed consent. An information sheet was provided for the parents or guardians of all the participants.

All children who received mechanical ventilation support for ≥ 48 h and met standard criteria for weaning readiness (improvement in the cause of primary disease, $P_{aO2}/F_{iO2} > 200$, positive end-expiratory pressure(PEEP) ≤ 5–10 cm H_2O, $F_{iO2} \leq 50\%$, and hemodynamically stable in the absence of vasopressors) were included in the study.[17] If the child experienced a known neuromuscular disease (such as amyotrophic lateral sclerosis, Guillain-Barre, or myasthenia gravis), cervical spinal cord injury, pneumothorax, death during mechanical ventilation, or if there was an unwillingness of the parents or guardians to participate in the study, then that child was excluded from the study.

Study Design

All eligibles underwent the spontaneous breathing test (SBT), which was performed using pressure support trials with a pressure support (8 cm H_2O) and 5 cm H_2O PEEP using Drager Evita 4 ventilator for 30 min.[2] Ultrasound measurements and PImax were taken at the fifth minute after the start of SBT. The patient passed the SBT if the exhaled tidal volume was equal to or above 5 mL/kg of ideal body weight, and if respiratory rate remained within the targeted range for age (< 6 months 20–50 breaths/min; 6 months – 2 yr. 15–45 breaths/min; 2 yr. – 5 yr. 15–40 breaths/min; > 5 yr. 10–35 breaths/min).[18] All patients accepted the Venturi inside the mask for oxygen therapy after passing the SBT. Successful weaning was defined as the ability to maintain spontaneous breathing for > 48 h.

PImax Measurement

The measurement of PImax was occluding the airway at end expiration through a unidirectional valve, and maintained for approximately 10 breaths or 20 s.[19] Finally, the maximum negative pressure displayed by the ventilator was recorded.

Ultrasonographic Measurements

All patients were placed in a semi-recumbent position with the head of the bed at a 30-degree angle. Two experienced sonographers performed ultrasound measurements by using the same portable ultrasound machine (Mindray, M7 series, China), and the evaluators were blinded to the results of the SBT prior to measurement. In our study, only the right hemidiaphragm was measured because the right hemidiaphragm was more feasible and repeatable compared with the left hemidiaphragm.[20] Diaphragm thickness (Tdi) was measured by using a 10 MHz linear probe at the zone of apposition at the right eighth or ninth intercostal space, between the anterior axillary and the midaxillary lines. The direction of the ultrasound probe was perpendicular to the diaphragm. At this position, the diaphragmatic ultrasound image was a hypoechoic structure between two echoic lines (the diaphragmatic pleura and the peritoneal membrane) in the B-mode (Fig. 1). In the same position, M-mode ultrasonography was used to measure resting Tdi at end-expiration (Tdi-exp) and end-inspiration (Tdi-insp), respectively (Fig. 2). The Tdi measurement was the inner edge of the peritoneal membrane to the inner edge of the diaphragmatic pleura. The calculation formula of diaphragmatic thickening fraction (DTF) was (Tdi-insp - Tdi-exp)/Tdi-exp.

For the measurement of diaphragmatic excursion (DE), a 5 MHz probe was placed at the junction of the right mid-clavicle line and the right subcostal margin, where the probe direction paralleled the diaphragmatic movement. The diaphragmatic movement toward the probe during inspiration was recorded as an upward motion of the M-mode tracing, and the movement was opposite during expiration. In a breathing cycle, the amplitude of DE was the maximum point that moved vertically downward to the lowest point in M-mode (Fig. 3).[21, 22] The DE was continuously measured for 3 times in free breathing, and then the average was taken.

Statistical Analysis

Analyses were carried out using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp, Armonk, NY). Depending on whether distribution was normal or non-normal, continuous variables were described as mean ± SD or median (interquartile range). Categorical variables were described as n(%). Continuous variables were compared with Student’s t-test or Mann-Whitney U test. Depending on sample size, categorical variables were compared with Chi-squared test or Fisher's exact test. The correlation analyses are conducted using the Pearson method to test the relationship between DTF, PImax, and DE. To determine the best cut off for DE and DTF to predict weaning success, we calculated area under the receiver operating characteristic curve (ROC). For all final comparisons, a p-value less than or equal to 0.05 was considered statistically significant.

Results

Sample Characteristics

61 patients underwent mechanical ventilation support during the study period. Eleven cases were excluded – ten cases passed away during mechanical ventilation, and one case had pneumothorax. Finally, 50 patients met the inclusion criteria. Eligibles were divided into either the weaning success group (n = 39) or weaning failure group (n = 11) (Figure 4).

All patient characteristics are summarized in Table 1. Ventilatory treatment time ($P = 0.002$) and length of PICU stay ($P = 0.013$) in the weaning failure group was significantly longer than the success group. Three cases passed away in the failure group, the in-hospital mortality was 27.3% (3/11), and there was one case that passed away in the success group. The DTF ($P < 0.001$) and DE ($P = 0.009$) were significantly higher in the weaning success group than the failure group. However, it should be noted that there were no differences in Tdi or PImax between the weaning success and failure groups (Table 2).

Diaphragmatic parameters predict the value of weaning success

Of the 39 patients who were categorized as having successful weaning, 32 had a DTF of ≥ 21%. Of the 11 who failed weaning, 9 had a DTF < 21%. The resulting positive predictive value (PPV) and negative predictive value (NPV) was 94% and 56%, respectively. 24 cases with DE ≥ 8.40 mm in the 39 patients who were successfully weaning, and 10 cases had a DE < 8.40 mm of the 11 who failed weaning, had a resulting PPV and NPV of 96% and 40%, respectively.

An ROC curve was used to assess the diagnostic accuracy of DTF and DE in predicting weaning success. A cut-off value of DTF ≥ 21% was associated with weaning success with a sensitivity of 82%, and a specificity of 81%. A cut-off value of DE ≥ 8.40 mm was associated with weaning success with a sensitivity of 62%, and a specificity of 91%, as shown in Table 3. The area under the ROC curve for DTF was 0.89 (95% confidence interval [0.78 to 0.99]) (Figure 5A), and for DE it was 0.77 (95% confidence interval [0.64 to 0.91]) (Supplemental Figure 5B).

Correlation analysis within DTF, PImax, and DE

We performed a Pearson linear correlation analysis within DTF, PImax, and DE (Table 4). The results showed that DTF had no significant correlation with PImax ($r = 0.15$, $P = 0.31$). We also performed the same analysis between DTF and DE. The results showed that there was no significant correlation between DTF and DE ($r = 0.17$, $P = 0.24$).

Discussion

This paper is the first study to investigate the predictive value of diaphragm ultrasound for weaning outcomes in critically ill children. Our findings demonstrated that the DTF and DE of patients in the group of weaning failure were significantly lower than those in the successful group, which is consistent with previous study results.[20, 23, 24] indicating that the patients with weaning failure generally had diaphragmatic dysfunction (DD). At the same time, the study also demonstrated that the duration of MV in the failed group was significantly longer than that in the successful group, suggesting that the prolonged MV had promoted the occurrence of DD. Respiratory muscle weakness in critically ill patients was associated with difficulty in weaning from mechanical ventilation.[25] Therefore, monitoring diaphragm function during SBT was important for predicting the outcomes of weaning.

Among the 50 patients in our study, the rate of weaning success was 78% (39/50), and the rate of weaning failure was 22% (11/50), which was lower than the previous study (30%).[26] The areas under the ROC curve of DTF and DE for patients with weaning success were 0.89 and 0.77, respectively. An optimal cut-off value for predicting weaning success of DTF and DE were 21% and 8.40 mm. Our study showed that DTF ≥ 21% was associated with weaning success with a sensitivity of 0.82, and a specificity of 0.81, and DE ≥ 8.40 mm was associated with weaning success with a sensitivity of 0.62, and a specificity of 0.91. Both have good value for predicting weaning success of children, but the predictive value of DTF is better than that of DE. A study by Ferrari established that a DTF of 36% predicted successful weaning in patients requiring long-term ventilator support.[27] Farghaly et al. have showed that DTF% ≥ 34.2% was associated with successful extubation.[22] The results of the above studies are all adults, and our results (DTF ≥ 21%) are lower than the above studies. The main reasons for consideration are as follows: the thickness and strength of human skeletal muscle fibres vary with age, and the diaphragm is a skeletal muscle that also conforms to this physiological change,[28] thus the DTF of children will be less than that of adults. In addition, the majority of patients in adult studies were elderly chronic obstructive pulmonary disease(COPD) patients, whose diaphragmatic muscle fibres had a chronic oxidative remodelling process,[29] leading to diaphragm compensatory ability weakness. Accordingly, more extensive contraction was needed to meet the ventilation. Further, most patients for studies that focus on children suffered mostly from acute respiratory diseases such as severe pneumonia and laryngitis – whose diaphragm had no chronic oxidative remodelling process and had good compensatory ability. The above may be the main reasons for the differences found between our study results and those of adults.

PImax is often used in the assessment of respiratory muscles, which can indirectly react to inspiratory muscle strength. The study conducted by Ferrari et al.[27] demonstrated that PImax was positively correlated with DTF in adults with mechanical ventilation ($r = 0.71$, $P < 0.05$). Ueki et al.[30] have provided a similar result ($r = 0.82$, $P < 0.01$). However, our study has found no significant linear correlation between DTF and PImax. In the process of measuring PImax, we found that the cooperation of children was significantly lower than that of adults, resulting in insufficient inspiratory effort. In addition, PImax is the result of a combination of all inspiratory muscles, however, the development of intercostal muscles and sternocleidomastoid muscles in children was immature.[31] The above factors will reduce the accuracy of PImax measurement. Therefore, PImax may not be a preferred weaning predictor for children compared with DTF.

There are several limitations in this study. First, we studied a relatively small population, especially since 11 patients failed to wean, the ability to predict weaning success within our study was not sufficiently provided. Second, DE and diaphragm thickness will change with age,[28] but there is no relevant research report on whether DTF conforms to the same trend. Third, because there is currently no reference value of DTF and DE in children, we do not know whether the initial diaphragmatic function of our enrolled children is abnormal or not. Finally, though diaphragmatic endurance is also important for weaning from mechanical ventilation, our study only assessed the diaphragm muscle strength. Therefore, the diaphragmatic time-tension index and other indicators can be used to explore the relationship between diaphragmatic endurance and weaning outcome.

Conclusion

Diaphragm ultrasound has great value in predicting weaning outcome of critically ill children. DTF and DE showed better performance in predicting weaning outcomes than other diaphragmatic parameters. However, PImax has limited value on reflecting the inspiratory muscle function of children with MV.

Abbreviations

PICU: pediatric intensive care unit; MV: mechanical ventilation PCIS: pediatric critical illness score; ICU-AW: intensive care unit-acquired weakness; FTW: failure to wean; VIDD: ventilator-induced diaphragmatic dysfunction; RSBI: rapid shallow breathing index; P0.1: airway occlusion pressure 0.1s; PImax: maximum inspiratory pressure; SBT: spontaneous breathing test; Tdi: diaphragm thickness; DTF: diaphragmatic thickening fraction DE: diaphragmatic excursion; VT: Tidal volume; PPV: positive predictive value NPV: negative predictive value; AUC: area under curve; IQR: interquartile range SD: Standard Deviation; PEEP: positive end-expiratory pressure; COPD: chronic obstructive pulmonary disease

Declarations

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Availability of data and materials:

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

Yang Xue conceived the study design and data collection. Zhen Zhang participated in the study design. Chu-Qiao Sheng performed statistical analyses. Yu-Mei Li participated in Literature search. Fei-Yong Jia performed review of manuscript. All authors interpreted the data, contributed to the intellectual content, reviewed the manuscript, and approved the final version.

Ethics approval and consent to participate

The study was approved by The institutional ethics committee of the hospital, the First Hospital of Jilin University (ChiCTR1800020196). The parents or guardians of the eligible children provided written informed consent. An information sheet was provided for the parents or guardians of all the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

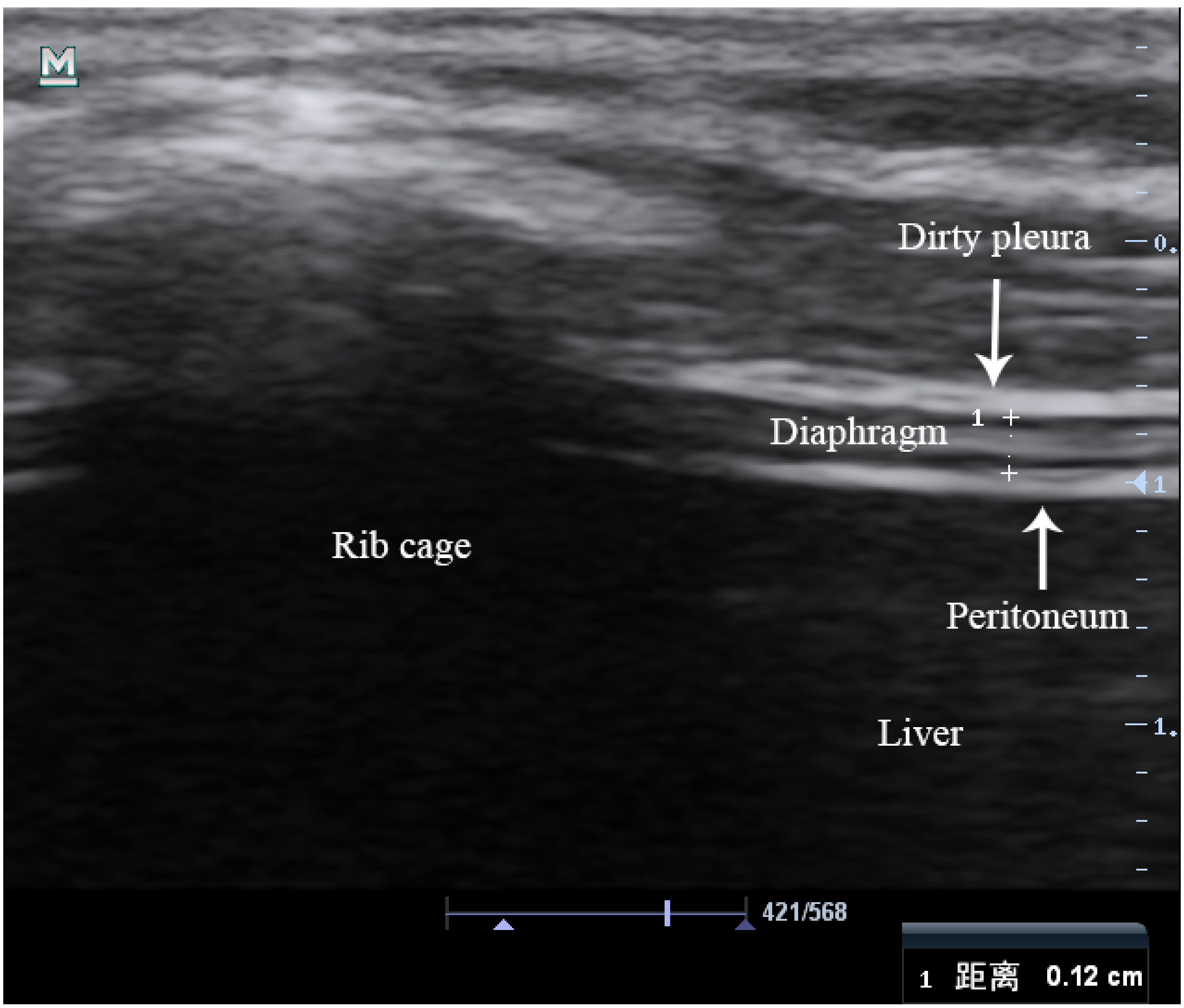

Figure 1

Ultrasound B-mode using a 10 MHz probe in the zone of apposition.

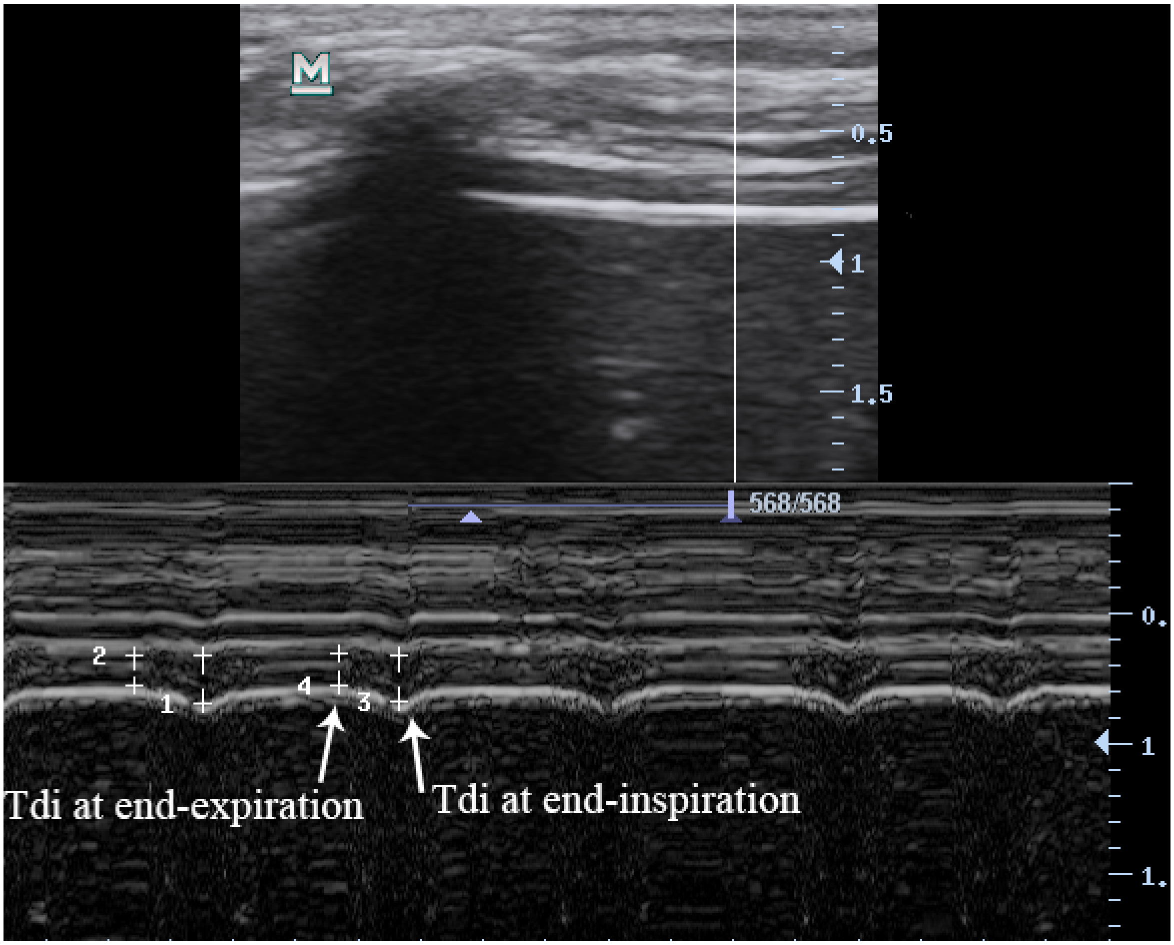

Figure 2

Ultrasound M-mode using a 10 MHz probe in the zone of apposition.

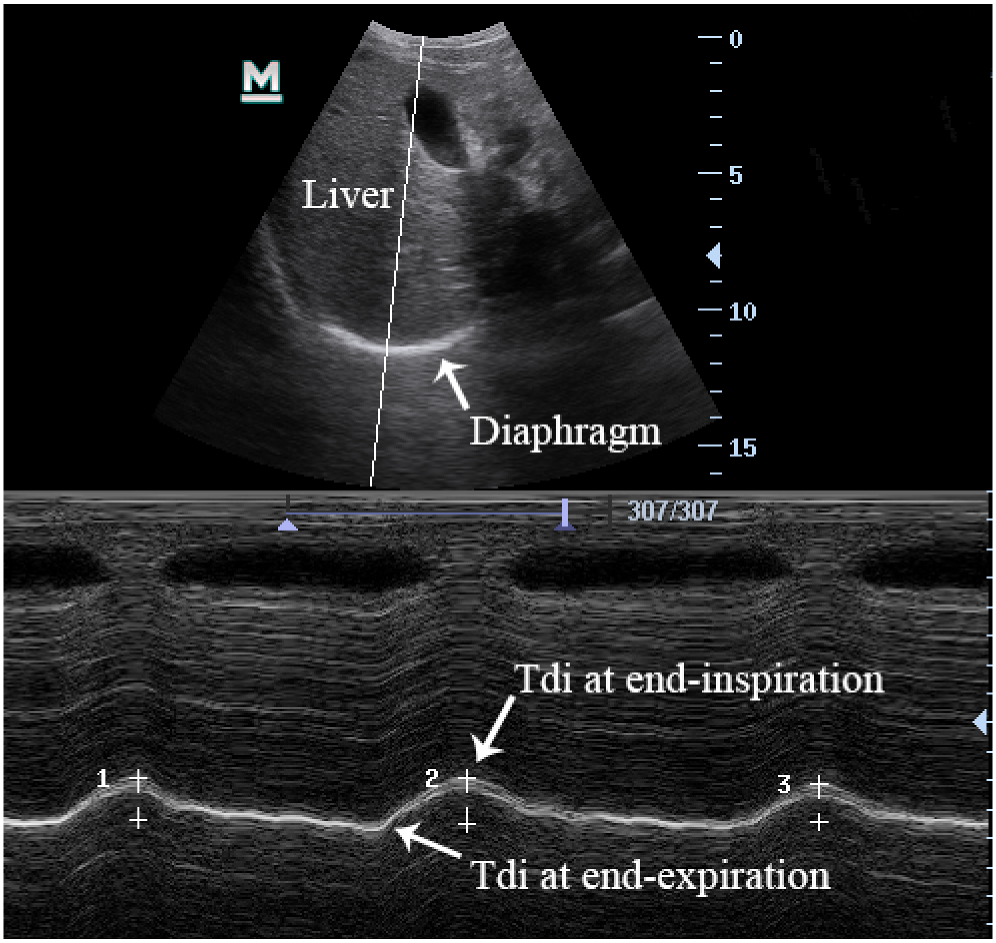

Figure 3

Ultrasound assessment of diaphragm diaphragmatic excursion in M-mode

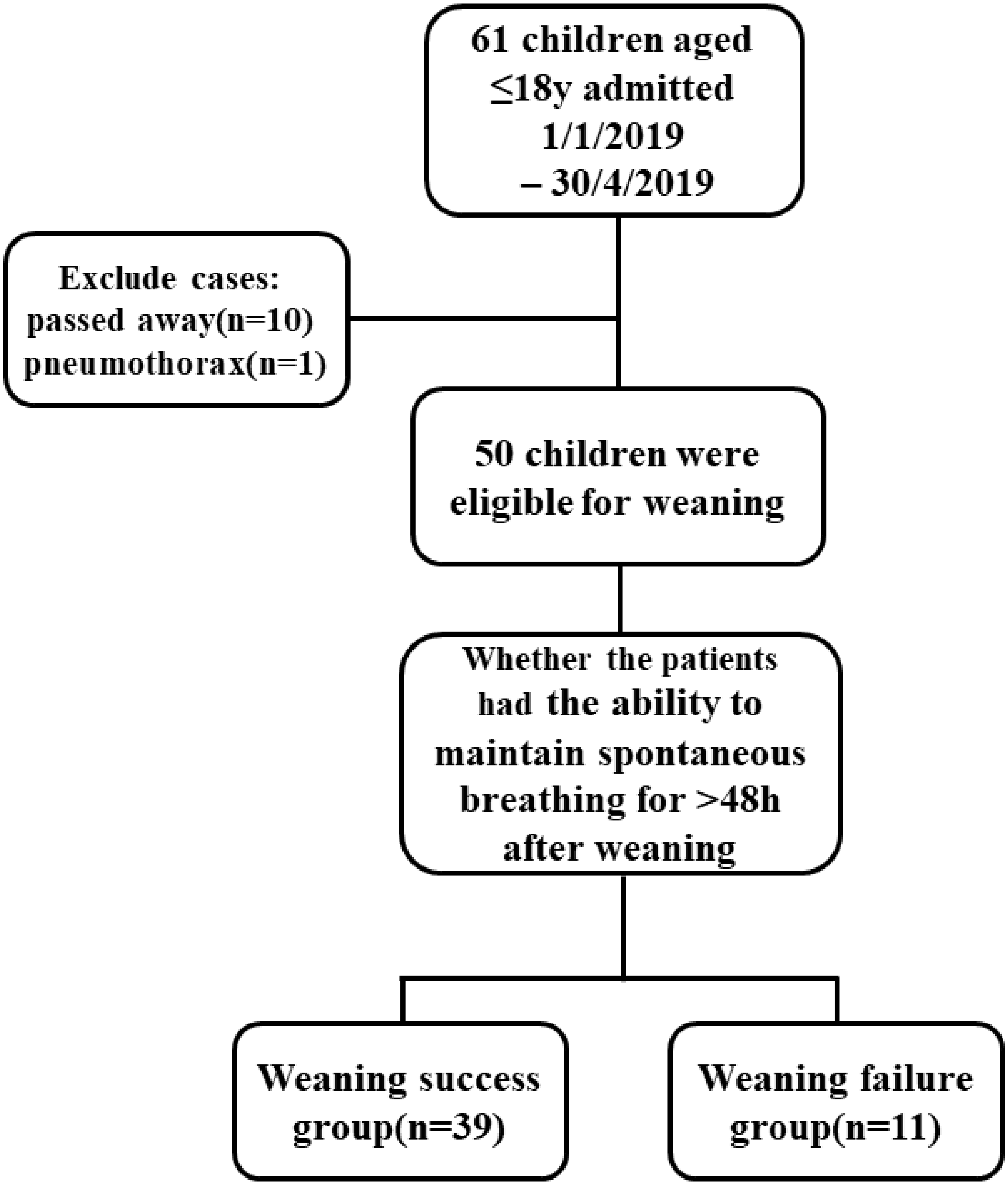

Figure 4

Flow chart of this study.

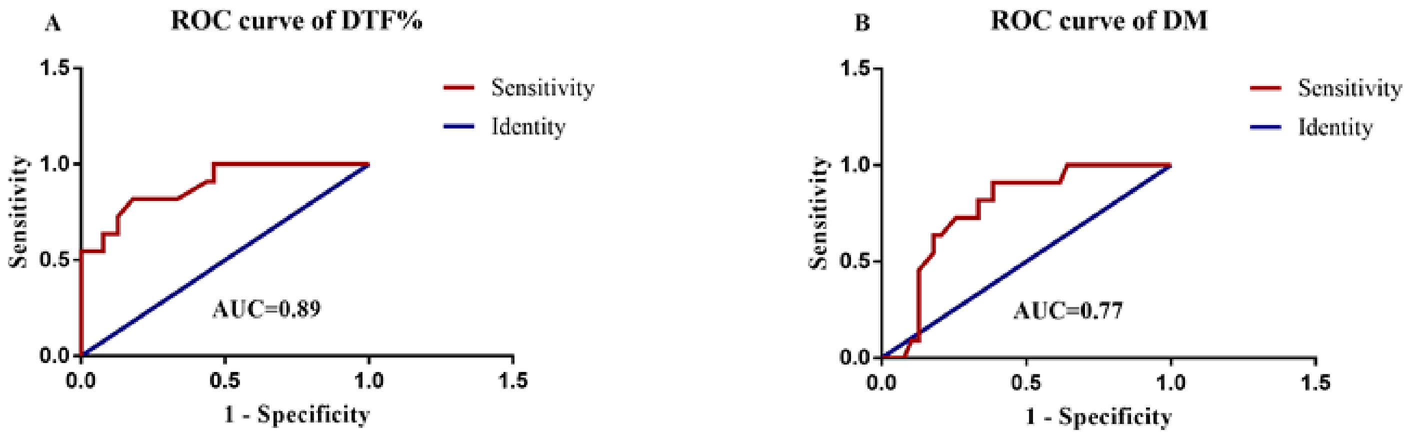

Figure 5

5A Area under receiving operating characteristic curve for DTF% to predict weaning success. The optimum cut-off value of DTF% was ≥ 21% with an AUC of 0.89 (95% CI [0.78 to 0.99]); 5B Area under receiving operating characteristic curve for DE to predict weaning success. The optimum cut-off value of DE was ≥ 8.40 mm with an AUC of 0.77 (95% CI [0.64 to 0.91]).