RESEARCH PAPER

Evaluation of Diaphragmatic Thickness and Dysfunction by Ultrasonography in Mechanically Ventilated Children for Assessment of Extubation Success

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Objectives: This study aimed to evaluate diaphragm thickness (DT) and diaphragmatic thickening fraction (DTF) in mechanically ventilated children and study the association of these measurements with extubation success. **Methods:** Consecutive children aged one month to 18 years, who required mechanical ventilation (MV) for more than 24 hours at our institution, were enrolled between April, 2019 to October, 2020. Ultrasonographic measurements of DT were documented, and DTF was calculated from baseline (within 24 hours of MV) until 14 days of MV, and up to three days post-extubation. **Results:** Of the 54 children-enrolled, 40 underwent planned extubation trial, of which 9 (22.5%) had extubation failure. Pre-extubation and post-extubation DTF between children in extubation-success and extubation-failure groups were comparable (*P*=0.074). There was no significant difference in the diaphragm atrophy rate between the two groups (*P*=0.819). Binary logistic regression showed significantly decreased probability of successful extubation with total ventilation duration (*P*=0.012) and mean DTF% before extubation (*P*=0.033). **Conclusion**: Despite evidence of diaphragmatic atrophy in critically ill children receiving mechanical ventilation, there was no significant difference in DTF between extubation success and failure groups.

Keywords: *Diaphragm atrophy, Diaphragmatic thickening fraction, Mechanical ventilation*.

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Critically ill children requiring ventilation support account for one-third of patients admitted to pediatric intensive care units (PICUs) [1]. In mechanically ventilated patients, the diaphragm muscle undergoes disuse atrophy, also known as ventilator induced diaphragmatic dysfunction (VIDD). It is known to occur in nearly 44% of children within 24 hours to 4 days after the initiation of mechanical ventilation (MV) [1,2]. VIDD leads to extubation failure, defined as the failure to withstand spontaneous breathing, requiring re-intubation within 48 hours of extubation [3,4].

Diaphragmatic ultrasonography has recently been used in children to quantify the changes in diaphragmatic parameters and correlate them with the weaning outcomes. Limited literature is available in children on mechanical ventilation admitted to PICU [1,2,5]. Some diaphragmatic parameters used to assess VIDD include static measurements such as diaphragm thickness (DT) and dynamic measurements such as diaphragm thickening fraction (DTF).

This study aimed to evaluate the use of DT and DTF in predicting extubation failure in mechanically ventilated children.

METHODS

This prospective observational single-center study was conducted in the PICU of our tertiary care public hospital in Western Rajasthan between April, 2019 to October, 2020, after approval from the institutional ethics committee. All children aged one month to 18 years, requiring mechanical ventilation for more than 24 hours, were enrolled after written informed consent from parents. Children who required less than 24 hours of mechanical ventilation, those with neuromuscular disease, cerebral palsy, diaphragm paralysis, congenital lung or pleural malformation, any fluid or air collection between pleural spaces, and chronic respiratory failure were excluded from the study. The baseline demographics and clinical data were obtained for all enrolled patients.

The primary outcome was the assessment of DT and

DTF. The secondary outcome was to compare the number of patients who underwent reintubation, tracheostomy, prolonged ventilation (≥14 days), and death in successful-extubation and extubation-failure groups. The first ultrasound assessment (baseline) was done within 24 hours of mechanical ventilation. The study pediatrician (trained in diaphragm ultrasound for 4 weeks) and radiologist performed independent ultrasound assessments of diaphragmatic thickness parameters daily to measure DT and DTF until 14 days of mechanical ventilation, and up to three days post-extubation. The inter-rater reliability for sonography done by pediatrician and radiologist was assessed by intraclass correlation coefficient (ICC), which showed excellent absolute agreement (ICC varied from 0.939 (0.831-0.978) to 0.987 (0.968 -0.995), *P*-value <0.001).

Ultrasound was performed using a portable ultrasound machine (Sonosite M Turbo, Fujifilm Sonosite) with a 6-13 MHz linear probe. The horizontal view of the diaphragm was obtained by placing a linear probe perpendicular to the right chest wall and below the costal margin in the intercostal space between the eighth and tenth ribs (between anterior axillary and mid-axillary lines) in the zone of apposition of the muscle. Using the M mode image, the DT was measured from the middle of the pleural line to the center of the peritoneal line at the end of inspiration (DTi) and expiration (DTe). DTF was calculated using the formula:- (DTi- DTe) /DTe x 100. In recent studies, this index has served as an accurate parameter for evaluating diaphragmatic function in ventilated and non-ventilated patients [6].

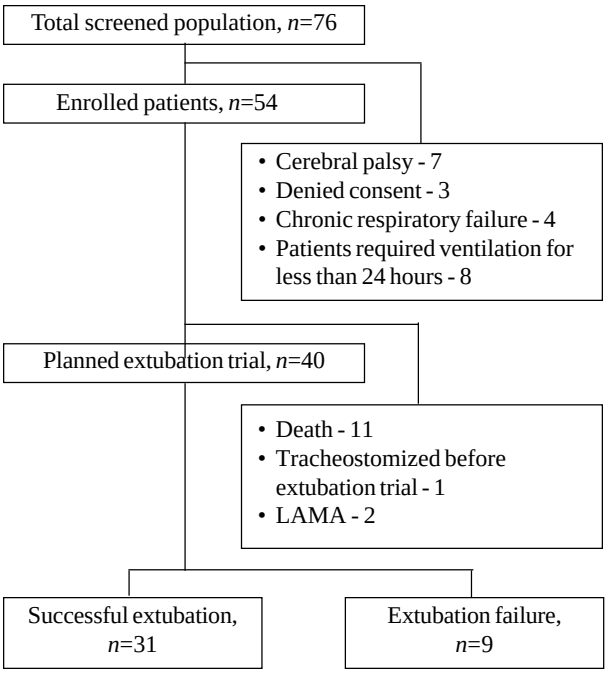


Fig. 1 Study flow chart.

The sample size calculation was derived from the study done by Lee, et al. [1]. Considering the success of extubation in study group to be 70% and precision of 85% with significance level of 0.05, a sample size of 36 patients was calculated. With a dropout rate of about 10%, 40 children were planned to be included in study.

Statistical analysis: Binary logistic regression for probability of successful extubation with independent clinical parameters was performed. All statistical analyses were performed using SPSS version 23, and a *P*-value of <0.05 was considered statistically significant.

RESULTS

During the study period, 76 patients admitted to the PICU were screened and 54 mechanically ventilated patients of age one month to 18 years were found eligible (**Fig. 1**). Eleven patients (20.3%) died before extubation. The baseline characteristics of the study population are detailed in **Table I.** A planned extubation trial was done on 40 patients, of which 31 patients were successfully extubated, and nine patients had extubation-failure

Table I Baseline Characteristics of Mechanically Ventilated Children Enrolled in the Study (*N*=54)

Characterstics	*Value*
Infants (<1 y)	21 (39)
Children (1-14 y)	30 (56)
Adolescents (15-18 y)	3 (5)
Age (y)[a]	3.5 (0.5, 7)
Male gender	33 (61.1)
Weight (kg)[a]	12 (5.1, 16)
Length (cm)[a]	65.3 (52.6, 116.8)
Weight for age, *z*-score[a]	-1.57 (-2.21, -1.04)
Length for age, *z*-score[a]	-1.74 (-2.06, -0.84)
Weight for length, *z*-score[a]	-1.48 (-2.15, -0.97)
PIM-3 predicted mortality (%)[a]	6.75 (2.9, 14.42)
Patients survived	41 (75.9)
Deaths	11 (20.4)
Primary diagnosis	
Respiratory	14 (26)
Sepsis	14 (26)
Cardiovascular	8 (15)
Central nervous system	6 (11)
Renal	5 (9)
Gastrointestinal	2 (4)
Others	5 (9)

Data represented as no. (%) or [a]median (IQR). PIM-Pediatric index of mortality.

Table II Profile of Mechanically Ventilated Children With Extubation Success and Extubation Failure (*N*=40)

Characteristics	*Extubation success (n=31)*	*Extubation failure (n=9)*	*P value*
Age (y)	5 (1, 8.5)	0.33 (0.25, 1)	0.031
Males [a]	18 (58.1)	7 (77.8)	0.440
Weight (kg)	14.5 (5.7, 19.7)	5.7 (4, 6.8)	0.021
Length (cm)	74.2 (48.5, 97.1)	52 (34.2, 64)	0.038
Weight for age (*z*-score)	-1.54 (-2.19, -1.05)	-1.79 (-2.38, -0.59)	0.185
Length for age (*z*-score)	-1.76 (-2.27, -0.86)	-1.35 (-2.6, -1.02)	0.670
Weight for length (*z*-score)	-1.35 (-2.05, -0.94)	-1.81 (-2.43, -1.53)	0.580
Total duration of PICU stay (d)	14 (9, 17.5)	26 (22, 37)	<0.001
Total duration of ventilation (d)	6 (5, 8)	17 (8, 30)	<0.001
PIM-3 predicted mortality (%)	9.2 (4, 18.1)	0.8 (0.7, 4.9)	0.094
Prolonged ventilation (≥14 d) [a]	16 (51.6)	8 (88.9)	0.046
Number tracheostomized [a]	0	2 (22.2)	0.006
Steroid use [a]	1 (3.2)	3 (33.3)	0.007
Duration (d)	3.2 (0, 5)	14 (4, 22)	0.041
Average Penn State sedation scale	3.5 (3.2, 3.8)	3.7 (3.6, 4)	0.489
Neuromuscular blocker use [a]	0	2 (22.2)	0.006
Duration (d)	0	5.5 (3, 9)	0.032
Maximum PEEP (cm of H_2O)	5 (5, 5)	5 (4.7, 5.3)	0.452
Maximum PIP (cm of H_2O)	15.2 (14.2, 16.7)	14 (13.5, 16.1)	0.434
Maximum FiO2 (%)	0.35 (0.3, 0.47)	0.3 (0.25, 0.35)	0.374
DTF before extubation (%)	30 (27.58, 35.55)	34.07 (30.85, 37.5)	0.074
DTF after extubation (%)	31 (25.83, 33.35)	34.33 (30.42, 35.5)	0.702

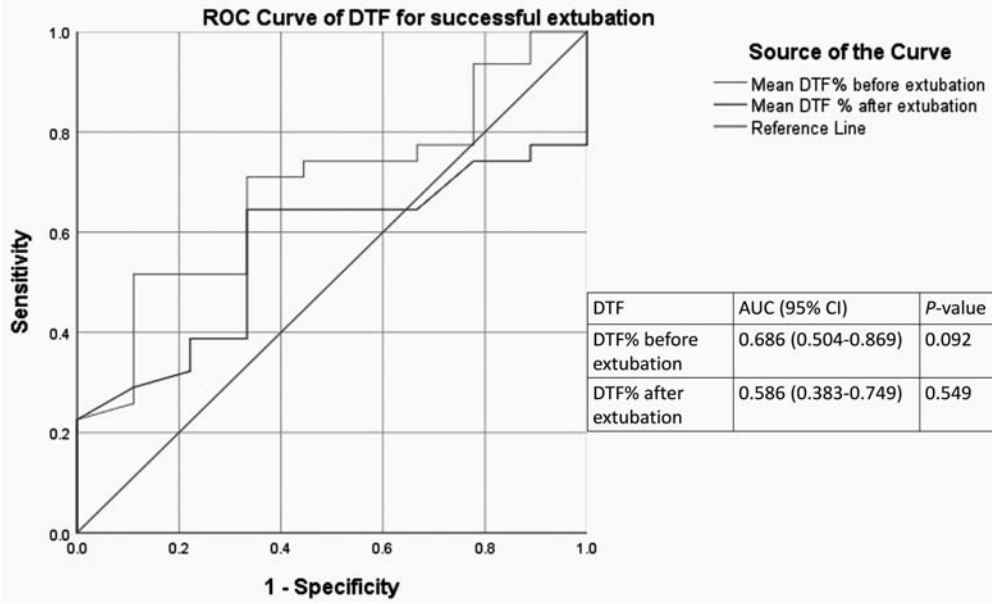
**Data presented as median (IQR) or [a]no. (%). DTF-diaphragmatic thickening fraction. FiO2-fraction of inspired oxygen. NMB-neuromuscular blocker. PEEP-peak end expiratory pressure. PICU-pediatric intensive care unit. PIM 3-pediatric index mortality score. PIP-peak inspiratory pressure.*

requiring re-intubation within 48 hours. The baseline characteristics and clinical profile of extubation success and extubation failure groups are detailed in **Table II**.

There was a significant reduction in daily DTe and DTi compared to baseline values. DTF decreased to a maximum of 6% in the first 24 hours following baseline measurement. The median DTF before extubation was 30% (27.58%,35.55%) and 34.1% (30.85%, 37.5%) (*P*=0.074) and after extubation was 31% (25.83%,33.35%) and 34.3% (30.42%, 35.5%) (*P*=0.702) in the extubation-success and extubation-failure groups, respectively. There was no significant difference in the diaphragmatic indices between the two groups. The median (IQR) diaphragm atrophy (decrease in DTe from its baseline) was 11.4% (7.8%, 19.6%). The percentage decrease in DTe each day was calculated as the diaphragm atrophy rate, and the median (IQR) diaphragm atrophy rate was 1.43% (0.9, 1.98) per day. There was no significant difference in diaphragm atrophy rate between successfully extubated and extubation-failure groups [3.1% (1.22%, 3.97%) vs 3.4% (1.8%, 4.07%); *P*=0.819].

Only age had a moderate correlation with baseline DTe (r=0.677, *P*<0.001). Among the factors affecting diaphragm atrophy rate, high PEEP had moderate correlation (r=0.471, *P*=0.002). There was no correlation of diaphragm atrophy rate with age, sex, weight for age, length for age and weight for length; duration of MV; duration of PICU stay and neuromuscular blocking agent use.

Binary logistic regression showed significantly decreased probability of successful extubation with increase in total ventilation duration [(aOR (95% CI) 0.76 (0.62, 0.94); *P* = 0.012)] and mean DTF% before extubation [(aOR (95% CI) 0.79 (0.64, 0.98); *P* = 0.033)]. Receiver operating characteristic (ROC) curve showed poor diagnostic accuracy of DTF% before [(AUC (95% CI) 0.686 (0.504,0.869); *P*=0.092) and after extubation [AUC (95% CI) 0.586 (0.383, 0.749); *P*=0.549) for successful extubation (**Fig. 2**).



DTF	AUC (95% CI)	*P*-value
DTF% before extubation	0.686 (0.504-0.869)	0.092
DTF% after extubation	0.586 (0.383-0.749)	0.549

Fig. 2 Receiver operating characteristics curve of diaphragmatic thickening fraction (DTF) for successful extubation.

DISCUSSION

This study evaluated the utility of diaphragmatic thickness parameters (DTe, DTi, DTF) in mechanically ventilated children and their association with successful extubation. We found a significant and progressive decrease in DT during MV with the onset of diaphragmatic atrophy and reduction of DTF as early as the second day of MV. There was a decrease in DT starting within the first 48 hours and decreasing steadily thereafter. There was no significant difference in DTF between extubation-success and extubation-failure groups.

In contrast to our findings, previous authors [1,4,7] were able to demonstrate a significant difference in DTF between successful-extubation and extubation-failure groups. The increased levels of inspiratory effort reflecting load-induced muscle injury may explain the higher value of pre-extubation DTF in the extubation-failure group [8]. Similar results were also published by Goligher, et al. [9], in which 24% of the study population had increased DT predicting prolonged ventilation. The reasons for these differences could be different characteristics of the study cohorts. Similar to our findings, a reduction in three serial readings of DTe in the first week of mechanical ventilation has been documented by Glau, et al. [5]. In the post-extubation period, diaphragm tends to move cranially due to loss of PEEP, this leads to lengthening and thinning of diaphragmatic fibers resulting in smaller DTe and higher DTF [10]. This was noted in our cohort, and also by other authors [1].

Previous studies had defined cut-off values of DTF >36%, 20%, and 30%, respectively as a favorable predictor of successful extubation [4,11,12]. A study by Rahman, et al. [7] in children has shown that DTF at a cut-off value of >23.17% had sensitivity and specificity of 100% and 76.2%, respectively, for predicting weaning failure.

The median (IQR) diaphragmatic atrophy and atrophy rate over the first week of ventilation were 11.4% (7.8,19.6) and 1.43% (0.9, 1.98) per day, respectively. Glau, et al. [5] reported a diaphragmatic atrophy rate of 3.4% per day with a median age of 16 months in their study participants. Mistri, et al. [13] reported a diaphragmatic atrophy rate of 2% per day, with a median age of 6 years. The latter shares similar age characteristics as our study, with a median age of 5.8 years. In our study, age had moderate correlation with baseline DTe. This could be explained by the fact that infants have thinner diaphragm and with age diaphragm thickness increases [14]. Moreover, in our study, high PEEP had moderate correlation with diaphragm atrophy rate. This could be explained by the fact that children with higher PEEP were sedated to a higher degree and hence developed more diaphragm atrophy. Like previous studies, we did not find any correlation between diaphragm atrophy rate and nutritional status of children or duration of mechanical ventilation [13].

Diaphragm ultrasound can be easily done bedside in intensive care settings. The role of diaphragm ultrasound should be explored further in mechanically ventilated children for assessment of extubation success.

WHAT THIS STUDY ADDS?

- Ultrasonography measurement of diaphragm thickness and diaphragmatic thickening fraction did not predict extubation success in mechanically ventilated children.

To conclude, the use of DTF in predicting extubation outcomes cannot be concluded from this study. Hence, more extensive, well-designed studies are needed to assimilate evidence about the role of diaphragmatic indices in mechanically ventilated children.

Ethics clearance: EIC, AIIMS, Jodhpur; No. AIIMS/IEC/2018/779, dated Dec 24, 2018.
Contributors: SV: involved in developing the protocol, data collection, data analysis and manuscript writing; DK: involved in supervision of protocol development, data collection, data analysis and manuscript writing; BC: supervision of protocol development, data collection and manuscript writing; NT: involved in supervision of manuscript writing; BS: involved in training and supervision of diaphragmatic ultrasonography and supervision of manuscript writing; KS: involved in supervision of protocol development and manuscript writing; SS: involved in statistical analysis of the data and supervision of manuscript writing.
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