



## Sonographic Evaluation of the Diaphragm in Critically Ill Mechanically Ventilated Pediatric Patients

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### ABSTRACT

**Background:** Various insults can render the diaphragm weak in ICU patients such as sepsis, electrolyte disturbances, hyperinflation, critical illness polyneuropathy and/or myopathy to name a few out of a long list, **Aim:** Aim of the work was using ultrasound to assess the function of the diaphragm in the mechanically ventilated pediatric patients. Detect the effect of mechanical ventilation on the infant and pediatric diaphragm muscle. Detect any association between diaphragm dysfunction and poor mechanical ventilation outcome. **Subject and Methods:** This cohort prospective study was performed in pediatric intensive care units of tertiary hospital (Abo El-Reesh Hospital, Cairo University, Egypt) from July 2018 to July 2021. This study was approved by the scientific ethics committee of pediatric department, Faculty of medicine, Cairo University, and the guardians of all enrolled children gave an informed consent form. **Results:** Median baseline thickness of diaphragm on admission was 1.50mm (IQR 1.40, 1.80). Compared to baseline thickness, the last recorded measurement of the diaphragm thickness before the moment of extubation, tracheostomy, death, end of study at day 14 showed mean decreased of 10.26% (SD  $\pm$ 12.95 %). The mean rate of diaphragm thickness decline was 1.71% per day (SD  $\pm$ 2.54%). **Conclusion:** Diaphragm measurements especially the diaphragm thickening fraction could predict the success of the extubation trial. Although it is important to monitor and prevent VIDD to improve patient outcome, it is more logic to consider that diaphragm dysfunction and weaning failure is multifactorial and that the patient would benefit more with holistic multi-organ assessment and treatment plan.

**Key Words:** Sonographic; diaphragm; critically ill; mechanically ventilated; pediatric.

### Introduction

Mechanical ventilation (MV) is one of the most frequently used critical care technologies; approximately 10–15% of critically ill patients will require prolonged mechanical ventilation and an elective tracheostomy [1]. While ventilated, patients may develop critical illness that leads to substantial skeletal muscle weakness, disability, and poor health-related quality of life [2].

Muscle weakness and dysfunction are common problems in patients hospitalized in the intensive care unit (ICU) [3]. This process affects striated muscles: dysfunction and atrophy are observed, often simultaneously, in muscles of the limbs and

of the diaphragm [4]. Whereas general limb muscle wasting is a more gradual and slow process, reaching its peak after the first 2–3 weeks of ICU stay, diaphragmatic dysfunction appears to occur much more rapidly [5].

Various insults can render the diaphragm weak in ICU patients such as sepsis, electrolyte disturbances, hyperinflation, critical illness polyneuropathy and/or myopathy to name a few out of a long list [6]. There is increased awareness that diaphragmatic weakness is common in critically ill patients on mechanical ventilation and is likely cause of weaning failure and prolonged hospital stay. Recent studies have suggested that the ventilator -

with its associated diaphragm muscle inactivity and unloading- is a likely cause of the decreased diaphragm force generating capacity seen in mechanically ventilated patients; a condition referred to as ventilator-induced diaphragmatic dysfunction (VIDD). Diaphragmatic dysfunction refers to altered force and structure [7].

To our knowledge few studies addressed this topic in the pediatric age group. We studied diaphragmatic characteristics by ultrasonography in critically ill pediatric patients those on mechanical ventilation.

Aim of the work was using ultrasound to assess the function of the diaphragm in the mechanically ventilated pediatric patients. Detect the effect of mechanical ventilation on the infant and pediatric diaphragm muscle. Detect any association between diaphragm dysfunction and poor mechanical ventilation outcome.

#### **PATIENTS AND METHODS**

This cohort prospective study was performed in pediatric intensive care units of tertiary hospital (Abo El-Reesh Hospital, Cairo University, Egypt) from July 2018 to July 2021. This study was approved by the scientific ethics committee of pediatric department, Faculty of medicine, Cairo University, and the guardians of all enrolled children gave an informed consent form.

**Study population:** Children aged 1 month to 14 years of both sexes who were newly intubated for MV were screened for enrollment into this study. This study included 50 patients who were invasively mechanically ventilated during this period. Fifty healthy non-mechanically ventilated children of matched age were also included as a control group.

**Inclusion criteria:** Selection of patients was based on the likelihood of prolonged mechanical ventilation more than 48 hours.

**Exclusion criteria:** Patients were excluded from this study if they: were below 1 month or above 14 years age, were chronically ventilated patients, had neuromuscular disease or spinal paralysis, had diaphragmatic malformation or known diaphragmatic paralysis, were on continuous neuromuscular

blockers (NMB) and likely to be extubated before 24 hours; if they had marked abdominal distention or if they had dressing or burn covering right thoracic area.

#### **Methods**

**The study was performed for each patient for up to 14 days** from time of enrolment; given the patient had not develop new condition which would exclude him/her from the study (e.g. new development of pneumothorax or marked ascites), until 2 days after extubation, tracheostomy or death, whichever comes first.

**All patients followed our protocols** for nutrition, sedation and weaning from mechanical ventilation. Ventilator variables was not standardized and studied among the variables that could affect the diaphragmatic function (All measurements were performed during tidal breathes at 6-12 ml/kg excluding smaller or deeper ones trying to minimize the inspired volume effect on the diaphragmatic excursion to express the work load).

**Routine sedative medications used** at our unit if needed to avoid fighting or unwanted events like unplanned extubation included benzodiazepine (midazolam), starting dose 1 mic/kg/min and titrated to obtain a State Behavioral Scale (SBS) score of 0/1. Opioids (e.g.: fentanyl) can be added or used as first line if poor response to benzodiazepines was obtained for short durations to avoid side effects of prolonged use. Adjuvant analgesia is provided as 5-25 mic/kg/min of ketamin.

**No one of the patients was placed on mechanical ventilation or sedated for the purposes of this study.** Participants may already have been mechanically ventilated and sedated (for management of their medical condition) prior to commencement of our measurement intervention and/or were awake during their weaning phase.

**Weaning process usually started after resolution of the primary disease that necessitated mechanical ventilation.** The patient should have an adequate general condition, gas exchange, appropriate neurological and muscular state, normal electrolytes and hemodynamic stability.

Weaning failure was considered if the patient needed mechanical ventilation within 48 hours after successful extubation.

**All the following data were collected for each patient:** Complete history taking and physical examinations on admission, primary diagnosis on admission and associated comorbidities, PRISM III score on admission, associated organ failure and number of organ failure on admission and on daily basis during the study interval using PELOD score, sepsis grade on admission, use of steroids, aminoglycosides and shots of neuromuscular blocking agents during study interval. Laboratory and radiological evaluation including: Arterial blood gases (ABG) (on admission, daily, and before Spontaneous Breathing Trial). Routine investigation: (complete blood count (CBC), sodium (Na), potassium (K), urea, creatinine, liver enzymes, coagulation profile). X-ray chest done on admission and before weaning and CT chest when indicated. Mechanical ventilation related data including: Starting type and mode of MV (Controlled modes, assisted modes and spontaneous modes) and any change in them during study interval. Average Rate, Peak inspiratory pressure, positive end expiratory pressure, Mean airway pressure (MAP) per day. Fraction

inspired oxygen average per day, oxygenation index (OI) and PaO<sub>2</sub>/FiO<sub>2</sub> ratio daily during study interval, duration of mechanical ventilation, weaning trials, duration and type. Mortality and duration of PICU stay.

**All patients were subjected to daily sonographic evaluation of the diaphragm.**

**Diaphragm ultrasound (D-US)**

Researcher had a training session on the use of diaphragmatic us before the start of this study. Daily measurements were performed by the same researcher.

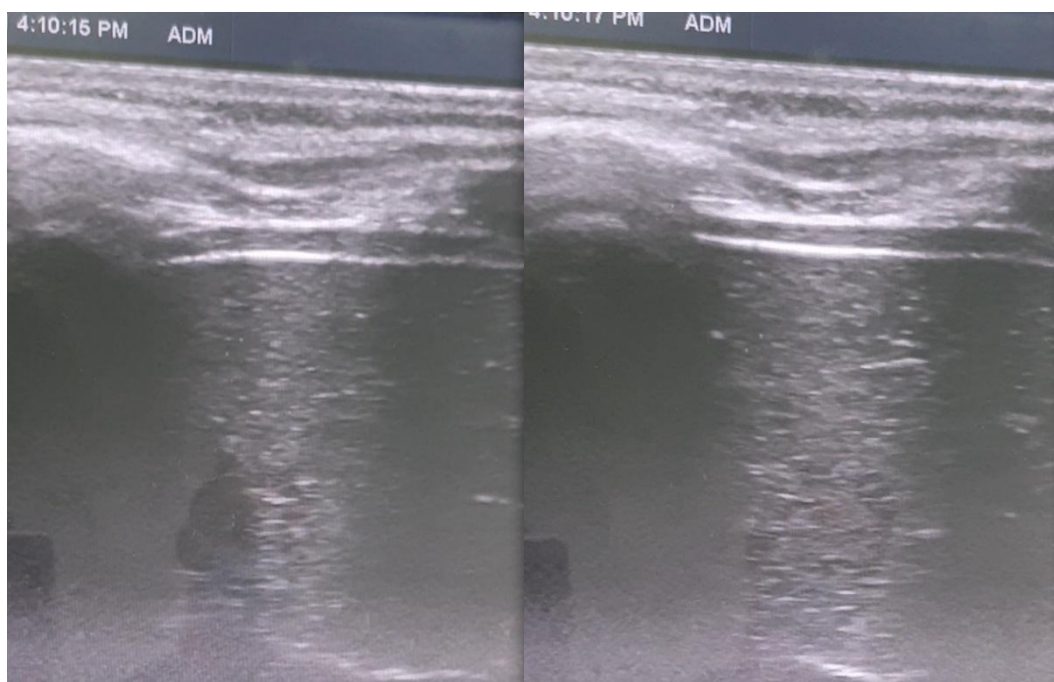
**Timing:** The first Ultrasonographic measurement was performed within 24 hours (hrs) of start of mechanical ventilation for enrolled patients. The subsequent recordings were acquired daily within a  $24 \pm 4$  hrs time frame. After extubation diaphragmatic measurements were taken within  $\pm 12$  hrs and for 2 days.

**First approach for assessment of the diaphragm thickness (DT) as well as the thickening fraction (DTF):**

A linear high frequency probe, was used by all the authors, due to its high superficial spatial resolution, in B-mode or M-mode at the zone of apposition (ZOA).



**Figure1: Photo image showing high linear probe position during measurement of the diaphragm thickness and thickening fraction**



**Figure 2: Ultrasound image showing appearance of the diaphragm at the ZOA. (a) at end of inspiration, (b) at end of expiration.**

**Second approach for assessment of diaphragmatic motion by measuring diaphragmatic inspiratory excursion (DE):**

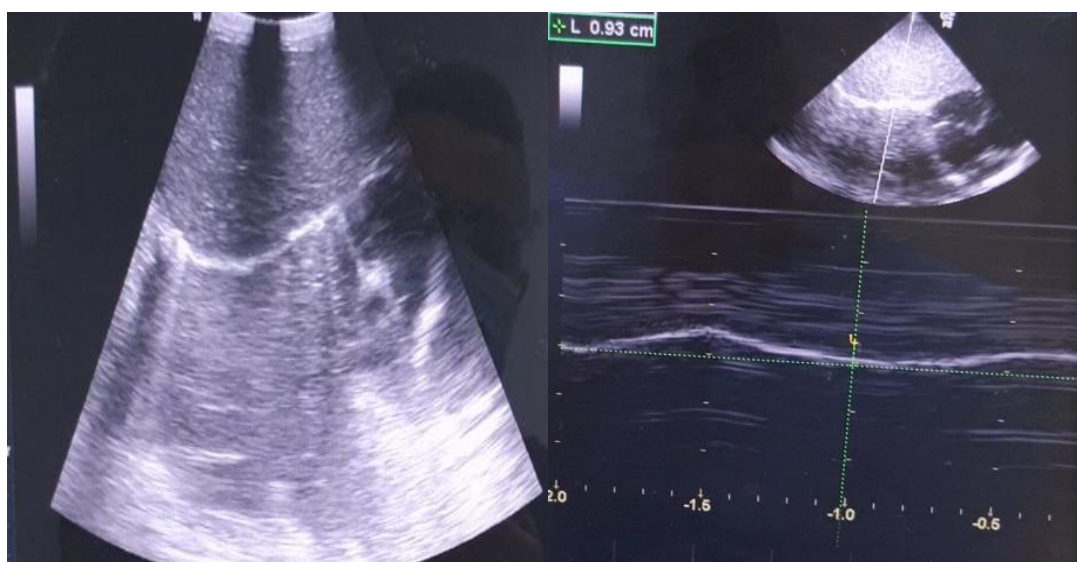
Liver was used as acoustic windows with a convex (cardiac or abdominal) lower frequency curvilinear probe in anterior subcostal view.



**Figure 3: Photo image showing the abdominal convex probe position for measurement of the diaphragm motion excursion**



**Figure 4: Photo image showing the position of cardiac curvilinear probe for measurement of the diaphragm motion excursion**



**Figure 5:**Ultrasound images showing diaphragm appearance during motion excursion assessment. (a) in B-mode and M-mode. (b) in M- mode.

Images of the measurement were taken for revision by experienced radiologist researcher. If there was problem with the ultrasound machine printer, mobile photos or videos were taken.

#### **Outcome parameters**

**Primary outcome Parameter:** Diaphragmatic function assessment by ultrasonography in critically ill mechanically ventilated pediatric patients and change in diaphragmatic function during mechanical ventilation.

**Secondary outcome parameters:** Assessing the prevalence of diaphragmatic atrophy and dysfunction, effect of diaphragmatic dysfunction on the weaning process, mean time to the Nadir of diaphragmatic measurements and diaphragm ultrasound can predict successful extubation.

**Statistical analysis:** All the collected data were revised for completeness and logical consistency. Pre-coded data was entered on the computer using Microsoft Office Excel Software Program 2019. Pre-coded data was then transferred and entered into the Statistical Package of Social Science Software program, version 26 (SPSS) to be statistically analyzed. The quantitative variables were described as mean, standard deviation SD, median, interquartile range IQR (25<sup>th</sup> and 75<sup>th</sup> percentiles), and number N, percent %. Independent groups were

compared using Mann Whitney U test, and Kruskal Wallis test while, the paired groups were compared using Friedman test; where the p value was significant at 0.05.

#### **RESULTS**

Of the eligible patients identified during the period of study, 60 consented and were enrolled in the study. Each of these subjects underwent the baseline diaphragm measurement, but only 50 underwent the second diaphragm measurement and thus were evaluable.

Of these 50 subjects, 38 were considered survivors; 34 were extubated, 2 underwent tracheostomy, 2 reached study duration limit without tracheostomy. And 12 were no survivors; 2 were referred outside and 10 died during the study duration

Comparing the studied 50 patients and 50 healthy control groups of children of matched age, sex, weight and BSA showed no significant statistical correlation between the base line diaphragmatic measurements diaphragm thickness (**DT**), diaphragm thickening fraction (**DTF**) and diaphragm excursion (**DE**).

**Table 1: Comparing patient characteristics and base line measurements with controls**

	Cases		Control		P value
	Mean	Standard Deviation	Mean	Standard Deviation	
Age in months	16	21	24	32	0.341
Weight in kg	9.6	8.6	10.9	7.7	0.191
BSA (mm <sup>2</sup> )	0.43	0.25	0.48	0.24	0.176
DT (mm)	1.57	0.32	1.50	0.25	0.166
DTF (%)	37.2	8.5	35.3	7.6	0.262
DE (mm)	9.42	2.19	9.83	2.44	0.627
DT/Weight (mm/kg)	0.24	0.14	0.20	0.14	0.096
DT/BSA (mm/mm <sup>2</sup> )	4.46	2.02	3.84	1.99	0.074
DE/Weight (mm/kg)	1.40	0.78	1.21	0.61	0.299
DE/BSA (mm/mm <sup>2</sup> )	25.9	11.0	23.6	9.2	0.334

BSA, body surface area; DT, diaphragm thickness; DTF, diaphragm thickening fraction; DE, diaphragm excursion

For the 50 enrolled cases the median initial measurement was 35% (IQR 32, 34) diaphragm thickness at end expiration was 1.5 mm (IQR 1.40, 1.80) at base line. The median diaphragm thickening fraction at the initial measurement was 35% (IQR 32, 34) while the initial median diaphragm excursion was 9.00 mm (IQR 8.10, 10.40) as shown in table2.

**Table 2: Baseline measurements of the diaphragm**

	Case (N=50)	
	mean ± sd	median (IQR)
DT (mm)	1.57 ± 0.32	1.50 (1.40, 1.80)
DTF (%)	37.2 ± 8.5	35.0 (32.0, 42.0)
DE (mm)	9.42 ± 2.19	9.00 (8.10, 10.40)
DT/Weight (mm/kg)	0.24 ± 0.14	0.19 (0.14, 0.32)
DT/BSA (mm/mm <sup>2</sup> )	4.45 ± 2.02	3.79 (3.02, 5.94)
DE/Weight (mm/kg)	1.39 ± 0.79	1.21 (0.75, 1.86)
DE/BSA (mm/mm <sup>2</sup> )	25.9 ± 11.0	23.8 (16.9, 33.3)

BSA, body surface area; DT, diaphragm thickness; DTF, diaphragm thickening fraction; DE, diaphragm excursion

To follow the change in diaphragm function and thickness, the first and last diaphragm ultrasound measurement on mechanical ventilation were used and percentage of change was calculated as shown in following table3

**Table 3: Percentage change over total duration of mechanical ventilation and average daily rate of change**

	Mean	Standard Deviation	Median	Minimum	Maximum
Change over duration in DT	-10.26%	12.95%	-10.56%	-36.84%	18.18%
Change over duration in DTF	-21.96%	22.47%	-25.76%	-58.62%	63.16%
Change over duration in DE	-10.04%	19.56%	-10.36%	-50.00%	38.30%
Daily rate of change in DT	-1.71%	2.54%	-2.03%	-9.26%	4.55%
Daily rate of change DTF	-4.48%	4.25%	-4.10%	-15.15%	7.89%

<b>Daily rate of change DE</b>	-2.15%	4.64%	-1.74%	-13.99%	9.57%
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DT, diaphragm thickness; DTF, diaphragm thickening fraction; DE, diaphragm excursion  
 Median baseline thickness of diaphragm on admission was 1.50mm (IQR 1.40, 1.80). Compared to baseline thickness, the last recorded measurement of the diaphragm thickness before the moment of extubation, tracheostomy, death, end of study at day 14 showed mean decreased of 10.26% (SD  $\pm 12.95$  %). The mean rate of diaphragm thickness decline was 1.71% per day (SD  $\pm 2.54$ %) as shown before in **table 3**.

To follow the change in diaphragm during duration of mechanical ventilation, ultrasound measurements of the diaphragm on mechanical ventilations on admission, after 72 hours, after one week and weekly thereafter for the duration of mechanical ventilation were used as shown in **table 4**. Only evaluable subjects with two or more measurements performed during the course of MV were chosen.

**Table 4: Average ultrasound measurements over time during mechanical ventilation**

	Day1(n=50)	Day3(n=49)	Day7(n=17)	Day14(n=4)	Before extubation trial
<b>DT(mm)</b>	1.58 $\pm$ 0.32	1.49 $\pm$ 0.29	1.46 $\pm$ 0.26	1.40 $\pm$ 0.12	1.40 $\pm$ 0.2
<b>DE(mm)</b>	9.13 $\pm$ 2.57	7.73 $\pm$ 2.19	7.94 $\pm$ 2.73	5.20 $\pm$ 2.80	8.3 $\pm$ 1.9
<b>DTF(%)</b>	37.18 $\pm$ 8.49	29.59 $\pm$ 7.74	28.26 $\pm$ 6.40	19.25 $\pm$ 3.5	29.3 $\pm$ 8

DT, diaphragm thickness; DTF, diaphragm thickening fraction; DE, diaphragm excursion; n, number

The diaphragm thickening fraction decreased substantially after intubation from 37.18% to 29.59% on day3 (a daily rate of decrease 3.79 per day). Subsequently, the diaphragm thickening fraction decreased to 28.26 % on day7 (nearly the same). Then continued to show a gradual decrease from day7 to be 19.25 % on day14 (a daily rate of decrease 1.28 per day) as shown in **table4**.

Validation of diaphragmatic US measurements, and their corrections for weaning from the ventilator showed that diaphragm thickening fraction, diaphragm excursion/weight, and diaphragm excursion/BSA can distinguish between successful and failed extubation (p value 0.019, 0.022, 0.016) as shown in the following **table 5**.

**Table 5: Validation of diaphragmatic US measurements, and their corrections for weaning from the ventilator**

Test Result Variable(s)	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
		Lower Bound	Upper Bound
DT day before	.964	.345	.663
DTF day before	.019	.551	.835
DE day before	.395	.413	.727
DT/weight day before	.113	.468	.792
DT/BSA day before	.079	.485	.803
DE/weight day before	.022	.532	.844
DE/BSA day before	.016	.545	.849

DT, diaphragm thickness; DTF, diaphragm thickening fraction; DE, diaphragm excursion; BSA, body surface area

Correlating the duration of mechanical ventilation to the overall change in different diaphragm measurements showed moderate negative correlation with the change in diaphragm thickness with P value of

0.009 and no correlation to the diaphragm excursion or the diaphragm thickening fraction as illustrated in the following **table 6**.

**Table 6: Correlation between duration of mechanical ventilation and overall change in diaphragm measurements**

mv duration days		
change over duration DT	R	-.365 <sup>***</sup>
	P	0.009
change over duration DTF	R	0.007
	P	0.959
change over duration DE	R	0.055
	P	0.705

DT, diaphragm thickness; DTF, diaphragm thickening fraction; DE, diaphragm excursion; R, correlation; P, p value

### Discussion

Changes in diaphragm thickness and motion are common in patients on mechanically ventilation. These changes occur early in the course of ventilation, and seem to be affected by the intensity of respiratory muscle work done by the patient, even under partially assisted modes of mechanical ventilation [8].

**This study included 50 mechanically ventilated children** with eligible evaluable readings of them; 34/50 (68%) were males and the remaining 16/50 (32%) were females with median age 8 months (IQR 4, 17). The median PICU stay was 10 days (IQR 7, 14) in our study. Comparable result of 9 (IQR 7, 23) days median PICU stay reported by Lee et al., [9]

The median MV duration was 6 days (IQR 4, 7), which is similar to the 6 days reported by Khemani et al., [10] and similar to another study which reported that average MV duration was 6 days [11] in a South African PICU.

Lee et al., [9] in a study of thirty-one mechanically ventilated children found the median MV duration was 7 days (IQR, 4–15), which is slightly higher. Wielenga et al., [12] reported a median duration of MV of 4 days which is lower.

**Baseline measurements in the current study** found that for the 50 enrolled cases the mean diaphragm thickness at end expiration was  $1.5 \pm 0.32$  (mm) at base line after intubation. This was in concordance to the mean end expiratory thickness  $1.5 \pm 0.38$

(mm) reported by Lee et al., [9] in a study of thirty-one mechanically ventilated children.

The mean diaphragm thickening fraction at the initial measurement was  $37.2 \pm 8.5$ (%) in our study. This was different from Lee et al., [9] study which demonstrated the DTF in children averaged  $25.8 \pm 3$  (%) immediately after intubation but consistent with the DTF range of 25%–40% during resting tidal breathing in healthy adults [8,13].

The initial median diaphragm excursion in our study was 9.00 mm (IQR 8.10, 10.40). This was in concordance to the reference values for sonographic diaphragm excursion measurements in healthy children reported by El-Halaby et al., [14].

**In the present study when correlating the initial diaphragmatic measurements together** showed only positive moderate correlation between diaphragm thickening fraction and diaphragm excursion. A lack of correlation between diaphragm thickening fraction and diaphragm thickness further confirms that muscle activity, as represented by diaphragm thickening fraction, should not be confused with muscle atrophy, as represented by diaphragm thickness [15].

**Correlating the initial measurements of the diaphragm on admission with the patient characteristics on admission** in our study showed significant positive correlation between diaphragm excursion and patient's age, weight and BSA.

Hida et al., [19] and El-Halaby et al., [14] mentioned a positive correlation between patients' weight and the diaphragm excursion



in agreement with our study. Also, Ishak and Sakr (2022) mentioned that diaphragm excursion is positively correlated with patients' age, weight, height in pediatric patients.

**There was no statistical significant difference in the initial diaphragmatic measurements between patients of different admission diagnoses and illness severity.** Diaphragm excursion on admission was significantly low in patients with sepsis. Sepsis induced inflammation may have had effects on contractile dysfunction of diaphragm without associated additional atrophy on admission.

**Over the total duration of MV** all results of our study suggest decrease pattern change in diaphragm measurements of thickness, motion and activity, as represented by thickness, excursion and thickening fraction, over mechanical ventilation in pediatric population. Also, these changes occurred early in the course of mechanical ventilation starting from the second measurement at days 2.

These results are in agreement with **Lee et al., [9]** study which described decrease in the diaphragm thickness and diaphragm thickening fraction within the first 2 days of mechanical ventilation. Also, it was in agreement with adult study of Goligher et al. who found that changes in diaphragm thickness are common in mechanically ventilated patients, occur early in the course of ventilation and seem to be modulated by the intensity of respiratory muscle work done by the patient [8].

On the other hand, **terhart et al., [17]** disagreed with these results and suggested that there is no identifiable pattern of change in diaphragm thickness or activity (thickening fraction) over period of MV in pediatric patients.

**Assessment of the diaphragmatic activity in our study** showed that over the study period median baseline thickening fraction of diaphragm on admission decreased by 21.96% (SD  $\pm$ 22.47%). This was comparable to results of Lee et al. in his study who described 17.7 % decrease in the

diaphragm thickening fraction over study period [9].

**Moreover,** our study showed that the mean diaphragm thickness also decreased substantially from 1.58mm on admission to 1.49mm on day3 of intubation (a 6% decrease). Subsequently, diaphragms decreased to 1.46mm on day7 of intubation (nearly stationary). Then continued to show a gradual reduction of the thickness from day7 to reach 1.40mm on day 14 (a 4.10% decrease from day 7). Also, The DTF decreased substantially in the first 3 days (a daily rate of decrease 3.79 per day) compared to the more gradual rate of decrease from day 3 to day 7 and from day 7 to the end of study day 14.

This was in agreement with the study of Lee et al. who motioned that the mean diaphragm thickness decreased significantly within the first 2 days and decreased steadily thereafter but it was more rapid than the average decrease in ventilated adults reported by Grosuet al. . Also, he reported that mean DTF decreased substantially in the first two days and then decreased more steadily from day 3 to day 7 [9, 18].

**Prediction of the outcome of mechanical ventilation weaning by D-US before extubation** was proven possible in our study. The cut off value for diaphragm thickening fraction was **26.5 %** in predicting successful extubation with sensitivity (73.5%), specificity (55.0%), PPV (73.5%), NPV (55.0%) and total accuracy (67%). Cut- off value for corrected diaphragm excursion for weight was 0.64 mm/kg in predicting successful extubation with sensitivity (88.2%), specificity (45.0%), PPV (73.2%), NPV (69.2%) and total accuracy (72%).

Several studies have reported the utility of diaphragm US for predicting successful weaning from MV in adults. However, limited data are available in children, with only few studies published [19].

In a cohort of 50 children, diaphragm thickening fraction was significantly higher in patients that were successfully extubated. The optimal cutoff value associated with successful extubation was a diaphragm

thickening fraction > 21%, with a positive predictive value of 94% and a negative predictive value of 56%. In this study, diaphragm excursion (which was normalized to body weight (mm/kg)) -like our study- had limited value in predicting weaning success[20].

In a larger study involving 106 children, the optimal cutoff value associated with weaning success was a diaphragm thickening fraction of >23%. In contrast to the prior study, diaphragm excursion was significantly associated with weaning success, with a cutoff value of >6.2 mm [21].

On the other side, Lee et al. in his study of 31 mechanically ventilated children found no significant difference between successful and failed extubation groups [9].

**To study the risk factors of diaphragm dysfunction we correlated the duration of mechanical ventilation to the degree of change in different diaphragm measurements.** The results showed moderate negative correlation with only the change in diaphragm thickness with P value of 0.009 and no correlation to the diaphragm motion and activity (diaphragm excursion and diaphragm thickening fraction).

This might be explained by the fact that morphological characteristic, and atrophy represented by diaphragm thickness is not necessarily linked with muscle strength or activity which may be affected by patient level of sedation and level of ventilator support [22].

**Study limitations:**Our study had some limitations to mention. First, because no reference values for diaphragm measurements have been established it is difficult to determine whether the initial measurements of our cases and 50 healthy controls are normal or abnormal. Second, ideally all measurements of the diaphragm would have taken on spontaneous breathes to obtain more accurate measurement of the diaphragm activity.

## **Conclusion**

Diaphragm measurements especially the diaphragm thickening fraction could predict the success of the extubation trial. Although it is important to monitor and prevent VIDD to improve patient outcome, it is more logic to consider that diaphragm dysfunction and weaning failure is multifactorial and that the patient would benefit more with holistic multi-organ assessment and treatment plan.

## **REFERENCES**

1. **Hooijman PE, Beishuizen A, Witt CC, de Waard MC, Girbes AR, Spoelstra-de Man AM, et al.** Diaphragm muscle fiber weakness and ubiquitin–proteasome activation in critically ill patients. *American journal of respiratory and critical care medicine.* 2015 May 15; 191(10):1126-38.
2. **Van der Schaaf M, Dettling DS, Beelen A, Lucas C, Dongelmans DA, Nollet F.** Poor functional status immediately after discharge from an intensive care unit. *Disability and rehabilitation.* 2008 Jan 1; 30(23):1812-8.
3. **Jaber S, Petrof BJ, Jung B, Chanques G, Berthet JP, Rabuel C, et al.** Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. *American journal of respiratory and critical care medicine.* 2011 Feb 1; 183(3):364-71.
4. **De Jonghe B, Bastuji-Garin S, Durand M-C, Malissin I, Rodrigues P, Cerf C, et al.** Respiratory weakness is associated with limb weakness and delayed weaning in critical illness. *Critical Care Medicine.* 2007; 35(9):2007–15.
5. **Demoule A, Jung B, Prodanovic H, Molinari N, Chanques G, Coirault C, et al.** Diaphragm dysfunction on admission to the Intensive Care Unit. prevalence, risk factors, and prognostic impact—a prospective study. *American Journal of Respiratory and Critical Care Medicine.* 2013; 188(2):213–9.
6. **Sigala I, Vassilakopoulos T.** Diaphragmatic ultrasound as a monitoring tool in the intensive care unit. *Annals of Translational Medicine.* 2017 Feb; 5(4).
7. **Azuelos I, Jung B, Picard M, Liang F, Li T, Lemaire C, et al.** Relationship between autophagy and ventilator-induced diaphragmatic dysfunction. *Anesthesiology.* 2015; 122(6):1349–61.
8. **Goligher EC, Fan E, Herridge MS, Murray A, Vorona S, Brace D, et al.** Evolution of diaphragm thickness during mechanical ventilation. Impact of inspiratory effort. *American journal of respiratory and critical care medicine.* 2015 Nov 1; 192(9):1080-8.
9. **Lee EP, Hsia SH, Hsiao HF, Chen MC, Lin JJ, Chan OW, et al.** Evaluation of diaphragmatic

- function in mechanically ventilated children: an ultrasound study. *PLoS one*. 2017 Aug 22; 12(8):e0183560.
10. **Khemani RG, Markovitz BP, Curley MAQ. Epidemiologic factors of mechanically ventilated PICU patients in the United States.** *Pediatr Crit Care Med*. 2007; 8:A39.
  11. **Morrow BM, Mowzer R, Pitcher R, Argent AC.** Investigation into the effect of closed-system suctioning on the frequency of pediatric ventilator-associated pneumonia in a developing country. *Pediatric Critical Care Medicine*. 2012 Jan 1; 13(1):e25-32.
  12. **Wielenga JM, van den Hoogen A, van Zanten HA, Helder O, Bol B, Blackwood B.** Protocolized versus non-protocolized weaning for reducing the duration of invasive mechanical ventilation in newborn infants. *Cochrane Database of Systematic Reviews*. 2016(3).
  13. **Baldwin CE, Paratz JD, Bersten AD.** Diaphragm and peripheral muscle thickness on ultrasound: Intra-rater reliability and variability of a methodology using non-standard recumbent positions. *Respirology*. 2011 Oct; 16(7):1136-43.
  14. **El-Halaby H, Abdel-Hady H, Alsawah G, Abdelrahman A, El-Tahan H.** Sonographic evaluation of diaphragmatic excursion and thickness in healthy infants and children. *Journal of Ultrasound in Medicine*. 2016;35(1):167-75.
  15. **IJland MM, Lemson J, van der Hoeven JG, Heunks LMA.** The impact of critical illness on the expiratory muscles and the diaphragm assessed by ultrasound in mechanically ventilated children. *Ann Intensive Care*. 2020; 10(1):115. <https://doi.org/10.1186/s13613-020-00731-2>
  16. **Hida T, Yamada Y, Ueyama M, Araki T, Nishino M, Kurosaki A, et al.** Time-resolved quantitative evaluation of diaphragmatic motion during forced breathing in a health screening cohort in a standing position: dynamic chest phrenicography. *European Journal of Radiology*. 2019 Apr 1; 113:59-65.
  17. **Terhart M, Hanekom S, Lupton-Smith A, Morrow B.** Abstract P-609: the effect of mechanical ventilation on diaphragm functions in infants and children: an exploratory study. *Pediatric Critical Care Medicine*. 2018 Jun 1;19(6S):237.
  18. **Grosu HB, Im Lee Y, Lee J, Eden E, Eikermann M, Rose KM.** Diaphragm muscle thinning in patients who are mechanically ventilated. *Chest*. 2012 Dec 1; 142(6):1455-60.
  19. **Weber MD, Lim JK, Glau C, Conlon T, James R, Lee JH.** A narrative review of diaphragmatic ultrasound in pediatric critical care. *Pediatric Pulmonology*. 2021 Aug; 56(8):2471-83.
  20. **Xue Y, Zhang Z, Sheng C-Q, Li Y-M, Jia F-Y.** The predictive value of diaphragm ultrasound for weaning outcomes in critically ill children. *BMC Pulm Med*. 2019; 19(1):270. <https://doi.org/10.1186/s12890-019-1034-0>
  21. **Abdel Rahman DA, Saber S, El-Maghraby A.** Diaphragm and lung ultrasound indices in prediction of outcome of weaning from mechanical ventilation in pediatric intensive care unit. *The Indian Journal of Pediatrics*. 2020; 87(6):413-20.
  22. **Ali ER, Mohamad AM.** Diaphragm ultrasound as a new functional and morphological index of outcome, prognosis and discontinuation from mechanical ventilation in critically ill patients and evaluating the possible protective indices against VIDD. *Egyptian Journal of Chest Diseases and Tuberculosis*. 2017; 66(2):339-51.