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ORIGINAL WORK

Ultrasonographic Assessment of Diaphragm Function to Predict Need for Mechanical Ventilation and its Liberation in Patients with Neuromuscular Disorders: An Observational Cohort Pilot Study

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Abstract

Background: Management of assisted ventilation and determining the optimal timing for discontinuation presents a significant clinical obstacle in patients affected by neuromuscular (NM) diseases. This study aimed to evaluate the efficacy of ultrasound in appraising diaphragmatic function for predicting the necessity of intubation and determining the opportune moment to discontinue mechanical ventilation (MV) in patients with NM disorders.

Methods: The study was conducted in adult patients with NM diseases requiring inpatient care in the high-dependency neurology ward and the intensive care unit. Ultrasonographic assessment of diaphragmatic excursion (DE) and diaphragmatic thickness fraction (DTF) was conducted at the patient's bedside every 48 h for ventilated patients and every 72 h for nonventilated patients until they were weaned from the ventilator or discharged home. Qualitative data are expressed as percentages or numbers, and quantitative data are represented as mean ± standard deviation. Unpaired *t*-tests were employed to compare continuous variables, and χ^2 tests were used for categorical variables. Contingency table analysis was used to compute relative risks in comparing the baseline DE and DTF with the sequential changes in these values.

Results: In cases in which the baseline left DE measured less than 1 cm, the relative risk for the requirement of ventilation was 2.5 times higher, with a confidence interval of 0.62–0.99 ($P = 0.19$). Notably, a bilateral reduction in DE within the initial 48 h of admission was identified as predictive of need for intubation. When comparing ventilated and nonventilated patients, it was observed that the mean DE values for the left and right sides in ventilated patients (0.74 and 0.79) were significantly lower than those in nonventilated patients (1.3 and 1.66), with corresponding *P* values of 0.05 and 0.01, respectively. Furthermore, a decline in right DE by more than 50% within 72 h of admission presented a relative risk of 3.3 for the necessity of ventilation, with a confidence interval of 1.29–8.59 ($P = 0.01$). Duration of ventilation ranged from 2 to 45 days, with an average of 13.14 days, whereas the mean ventilator-free days recorded was 13.57. Notably, a sequential increase in bilateral DE correlated with an extended duration of ventilator-free days.

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Conclusions: The presence of a baseline left DE of less than 1 cm, a consecutive decrease in DE measurements within 48 h, and a comparative reduction in right DE of more than 50% within the initial 3 days are indicators associated with the requirement for MV in patients with NM disease. Furthermore, the upward trajectory of DE in mechanically ventilated patients is linked to an increased number of days free from ventilator support, suggesting its potential to forecast earlier weaning.

Keywords: Ultrasound assessment of diaphragm function, Neuromuscular disease, Prediction of need for intubation, Prediction of weaning, Diaphragmatic excursion, Diaphragmatic thickening fraction

Introduction

Patients with neuromuscular (NM) diseases, particularly myasthenia gravis (MG) and Guillain–Barré syndrome (GBS), commonly experience rapid deterioration of respiratory status, leading to the need for intensive care unit (ICU) admission in nearly 30% of cases [1–3]. Various clinical and pulmonary function assessment tools have been used to anticipate declining lung function. Predictors for the requirement of mechanical ventilation (MV) include bulbar weakness, bilateral facial palsy, early admission within a week of symptom onset, and deteriorating lung function based on parameters such as vital capacity < 20 mL/kg, maximal inspiratory pressure < 30 cm H_2O, and maximum expiratory pressure < 40 cm H_2O, known as the 20–30–40 rule [4, 5]. However, these parameters have limitations in terms of sensitivity and bedside applicability. Following intubation, approximately 75% of patients with GBS and MG require continued ventilator support by the seventh day [6], and they contribute to more than 30% of extubation failures [7]. Conventional extubation criteria, borrowed from general critical care, are nonspecific and fail to account for specific challenges in this patient population, such as bulbar dysfunction, which is manifested only after extubation and often cannot be predicted. Moreover, traditional bedside pulmonary function tests are inadequate in predicting respiratory status, with diaphragmatic function being a crucial aspect overlooked by these assessments. In the context of intensive care, conventional tools for evaluating diaphragmatic function, such as fluoroscopy, phrenic nerve conduction study, and transdiaphragmatic pressure measurement, have limited applicability [8]. Conversely, bedside ultrasonographic assessment of diaphragmatic function offers advantages in terms of ease of execution, reproducibility, and sensitivity [9]. Parameters such as diaphragmatic excursion (DE) < 25 mm and reduced diaphragmatic thickness fraction (DTF) during maximal inspiratory effort have shown promise in predicting the need for MV in NM diseases [10]. Additionally, a study by Krishnakumar et al. [11] demonstrated that the trend of improving DTF and increased DE, assessed through ultrasound and neurally adjusted ventilatory assist mode, can predict successful weaning in patients with GBS and MG requiring more than 7 days of ventilation. This study aims to assess whether bedside ultrasonographic evaluation of diaphragmatic function can help predict two key challenges in the management of NM cases: the need for MV and the appropriate timing for weaning patients with MG and GBS off ventilation.

Methods

A prospective observational cohort pilot study was conducted in adult patients with NM diseases admitted to the neurology department's ward and ICU from August 2021 to June 2022. The study, which obtained ethical clearance from the institutional review board (IRB Min. No.14203 dated 25.08.2021) adhered to the institute's ethical standards and the Helsinki Declaration of 1975.

Inclusion criteria encompassed all adult patients diagnosed with either MG or GBS during the study period with consent provided by the patients or their relatives. Exclusion criteria involved patients with sepsis or infection and those who did not consent, as well as patients with NM diseases transferred on ventilators from elsewhere.

The study recorded demographic data from patient charts and electronic databases, including admission diagnosis, symptom duration, partial pressure of carbon dioxide (pCO_2) at admission, and ventilation history. Criteria for ICU admission or transfer included bulbar weakness, worsening pulmonary function tests, increased pCO_2, or signs of sepsis. Serial ultrasonographic diaphragmatic measurements were taken, and diaphragmatic function was assessed both with and without sedation.

Diaphragm ultrasound measurements were conducted using a Sonosite Extend ultrasound machine (Fujifilm Sonosite Inc, Bothell, WA), with DE and DTF measured using low-frequency (1–5 MHz) and high-frequency probes (7–13 MHz), respectively. DTF was calculated using the following formula: (thickness at the end of inspiration − thickness at the end of expiration)/(thickness at the end of expiration) [12]. These measurements were taken bilaterally, on admission and then at intervals of 48–72 h (48 h for ventilated patients and 72 h for nonventilated patients) until discharge or weaning off ventilation.

Patients with bulbar weakness indicating aspiration or increased work of breathing with CO_2 retention were directly shifted to the ICU and initiated on MV. Those not improving or worsening after treatment for NM disease were intubated within 2–3 days of admission. Weaning from ventilation was based on generated minute volume, absence of increased work of breathing, and specific bedside pulmonary function tests, such as shoulder shrug, neck holding, and forward arm abduction time. A 30-min T-piece trial was attempted before extubation. Successful extubation without the need for intubation or noninvasive ventilation for more than 48 h was considered liberation from ventilation.

The data were organized in a spreadsheet format using Microsoft Excel version 2010, and statistical analysis was performed using SPSS software. Qualitative data are presented as percentages or numbers, and quantitative data are represented as mean ± standard deviation. Unpaired *t*-tests were conducted to compare continuous variables, and χ^2 tests were used to compare categorical variables. Individual line graphs were generated for each patient, depicting the serial readings of DE and DTF for each side as well as the timing of initiation of MV and extubation. Contingency table analysis for relative risks was employed to compare the baseline DE and DTF and changes in DE and DTF relative to the baseline over the first week in predicting the need for MV. Additionally, a classification-based approach was used to analyze the relationship between the initial change in DE/DTF and the outcome variables. Patients were categorized based on the change in DE or DTF on each side, considering an increase or decrease of more than 50% between readings and from baseline for DE and of more than 10% for DTF. This approach was adopted based on previous relevant studies [11–13]. The threshold for statistical significance was set at $P < 0.05$.

Results

In this study, 20 patients were enrolled, as illustrated in Fig. 1. The demographic and clinical characteristics of the patients are detailed in Table 1. Among them, seven patients underwent MV, with two being successfully extubated, four requiring tracheostomy, and one dying. All four patients who underwent tracheostomy were successfully weaned off ventilation, and 75% of them were decannulated at discharge. The mean age of ventilated patients (30.4 years) was lower than that of nonventilated patients (45.2 years). Additionally, the average duration of hospital and ICU stay was longer for ventilated patients (33 and 15.4 days, respectively) compared to nonventilated patients (14.9 and 3.3 days, respectively).

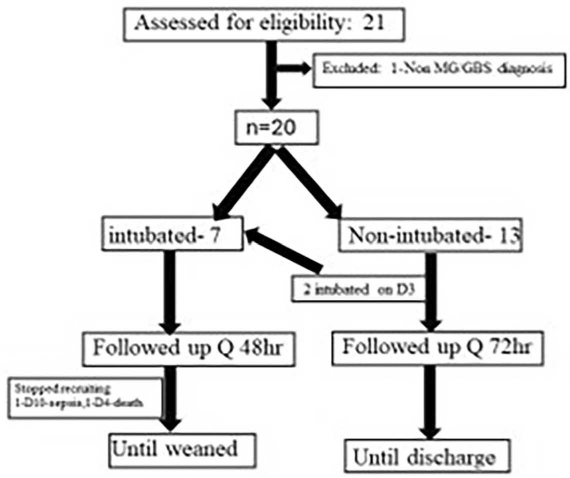

Fig. 1 Consolidated Standards of Reporting Trials diagram: observational study. *GBS*, Guillain Barre Syndrome, *MG*, Myasthenia Gravis

Ventilated patients presented with a higher mean pCO_2 at admission (45.6 vs. 22.7 mm Hg) and required more extensive immunosuppression, indicating a more severe disease, than nonventilated patients. The median monitoring period for ventilated patients (up to 11 days) exceeded that for nonventilated patients (8 days).

Diaphragmatic Readings for Ventilated Patients

The line graphs in Fig. 2 illustrate the serial readings and mean values of left and right DE and DTF in individual ventilated patients. Data points highlight the timing of initiation of MV, tracheostomy, and liberation from MV. The graphs show a decreasing trend in DE on both sides for the first 2 days, followed by a rising trend. DTF did not exhibit a discernible pattern of change.

Table 2 presents the results of the contingency table analysis, showing relative risks for the need for MV based on cutoff values of baseline DE and DTF on each side and for changes in DE and DTF between serial readings. A baseline left DE < 1 cm was associated with 2.5 times the relative risk for the need for ventilation (confidence interval: 0.62–0.99; $P = 0.19$). A decrease in right DE by > 50% from baseline had a relative risk of 3.3 for the need for ventilation (confidence interval 1.29–8.59; $P = 0.01$). However, a similar 10% change in DTF between serial readings and baseline values did not show significance.

Supplementary Table 1 displays outcome variables in the study participants, segmented by categories based on changes in DE and DTF. Notably, there was a significant difference in the total number of ICU days between ventilated and nonventilated patients ($P = 0.06$). The duration of ventilation varied from 2 to 45 days, with a mean of 13.14 days. The mean ventilator-free days were

Table 1 Demographic and clinical characteristics of study population

	Total (*N* = 20)	Assisted ventilation (*n* = 7)	No assisted ventilation (*n* = 13)	*P* value
Age, mean (SD), y	40.1 (16.9)	30.4 (15.5)	45.2 (15.8)	0.06
Male sex, *n* (%)	12 (60)	5 (41.7)	7 (58.3)	0.44
Duration of symptoms, mean (SD), wk	30.7 (21)	10 (19.6)	3.3 (3.6)	0.20
History of prior ventilation, *n* (%)	2 (10)	1 (14.3)	1 (7.7)	0.63
Diagnosis, *n* (%)				
MG	9 (45)	3 (42.9)	6 (46.2)	0.88
GBS	11 (55)	4 (57.1)	7 (53.8)	0.88
pCO_2 at admission, mean (SD), mm Hg	30.8 (21)	45.6 (16.4)	22.7 (19.2)	**0.01**
Treatment, *n* (%)				
Steroids	4 (20)	1 (14)	3 (23)	0.63
IVIG	5 (25)	4 (57)	1 (7.7)	**0.01**
Rituximab	3 (15)	2 (28)	1 (7.7)	0.21
Plasma exchange	9 (45)	6 (85)	3 (23)	**0.007**
Thymectomy	3 (15)	2 (28.6)	1 (7.7)	0.21
Extubation failure, *n* (%)		5 (71.4)		
Extubation success, *n* (%)		2 (38.6)		

GBS Guillain–Barré syndrome, *IVIG* intravenous immunoglobulin, MG, myasthenia gravis, pCO_2, partial pressure of carbon dioxide

Bold indicate *p* values < 0.05 was considered significant

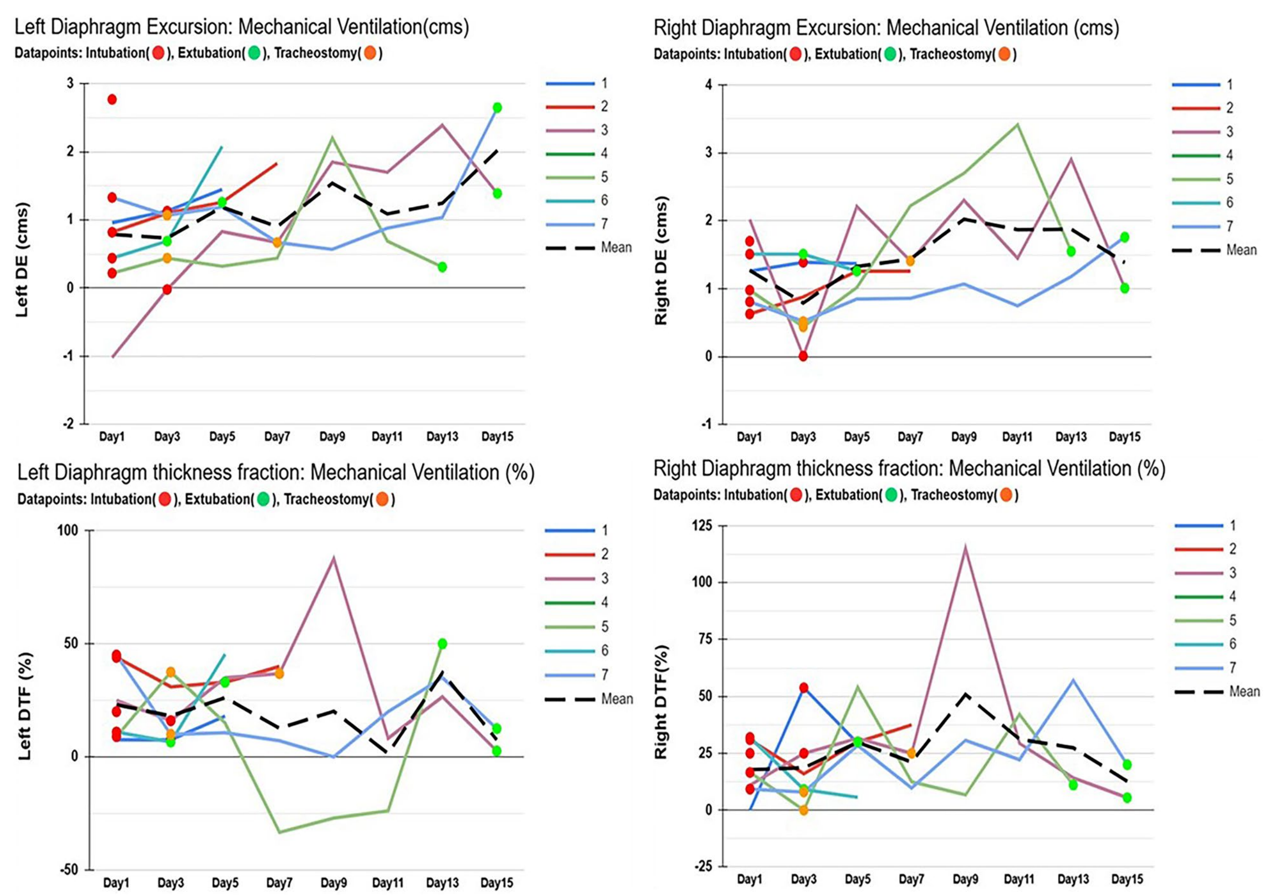

Fig. 2 Diaphragmatic function for mechanically ventilated patients. *DE* Diaphragmatic excursion, *DTF* Diaphragmatic thickness fraction

Table 2 Prediction of need for ventilation using change in DE and DTF

	Ventilation, RR (CI)
Baseline cutoff	
Left DE < 1 cm	2.5 (0.62–0.99)
Right DE < 1 cm	0.91 (0.27–3.07)
Left DTF < 30%	0.62 (0.18–2.11)
Right DTF < 30%	0.44 (0.14–1.30)
Left DE change	
Increase > 50%	1.66 (0.26–10.33)
Decrease > 50%	0.55 (0.3–9.72)
Right DE change	
Increase > 50%	0.55 (0.07–4.20)
Decrease > 50%	3.33 (1.29–8.59)
Left DTF change	
Increase > 10%	3.27 (0.22–48.13)
Decrease > 10%	3.33 (0.21–52.68)
Right DTF change	
Increase > 10%	1.90 (0.93–27.68)
Decrease > 10%	3.00 (0.21–41.89)

CI, confidence interval, DE, diaphragmatic excursion, DTF, diaphragmatic thickness fraction, RR, relative risk

13.57. Death was considered as zero ventilator-free days. Among the ventilated patients, considerable variations were found in the number of ventilator-free days across categories based on changes in DE and DTF.

Prediction of Ventilator-Free Days

In Fig. 3, the depicted data illustrate the changes in DE and DTF for each ventilated patient alongside their corresponding ventilator-free days. A consistent incremental pattern in bilateral DE readings correlated with higher ventilator-free days. The ventilator-free days exhibited variability in conjunction with positive or negative DTF changes on both the left and right sides, displaying no discernible pattern. Following a consecutive rise in bilateral DE readings, patients underwent a successful T-piece trial within 2 days. Subsequently, patients were extubated within 24 h of the successful trial, with the decision-maker being blinded to diaphragmatic readings.

In contrast to the trends observed in ventilated patients, nonventilated patients demonstrated a progressive enhancement in both left and right DE and DTF values from the initial to the fifth day, as highlighted in Fig. 4.

Comparison of Changes in Diaphragmatic Readings in Ventilated and Nonventilated Patients

Comparisons were made regarding the mean values for the first three readings of DE (and DTF over a period of 5 days for both sides). The comparison also involved the mean change from the first to the second and the first to the third readings for ventilated and nonventilated patients, as detailed in Table 3. The readings of the first 3 days were compared, and of the 13 nonventilated patients, 12 had a maximum of three readings of DE and DTF.

The analysis revealed that the mean values for the second readings of bilateral DE in ventilated patients (0.74 and 0.79) were significantly lower compared to that for nonventilated patients (1.3 and 1.66), with associated P values of 0.05 and 0.01, respectively. Additionally, the mean change from the first to the second reading for right DE in ventilated patients (−0.23%) differed significantly from that in nonventilated patients (31.91%) ($P = 0.05$). The third day readings of right DE between ventilated and nonventilated patients (1.33 vs. 2.02; $P = 0.06$) also showed a trend toward significant difference. This could imply the potential for predicting the need for ventilation based on changes in DE and DTF over the second and third days (1.33 vs. 2.02; $P = 0.06$). It is important to note that although other readings, including baseline values, exhibited differences between ventilated and nonventilated patients, these differences did not reach statistical significance.

Discussion

This study is distinguished by its comprehensive monitoring of diaphragmatic function in patients from admission to discharge. Its unique approach uses sequential diaphragmatic parameters to assess deteriorating respiratory conditions and predict the need for intubation. The study underscores the significance of these parameters in ventilated patients as a means of determining the optimal timing for successful weaning.

In a study involving myasthenic patients from the Chinese population, Liu et al. identified age > 50 years and early treatment with plasma exchange as predictors of early liberation from MV [14]. However, in a study on patients with GBS, Lawn et al. did not find age to be a predictor of MV requirement. Instead, they found that a vital capacity of less than 20%, rapid disease progression, and bulbar involvement were predictive of the need for MV [4]. Our own observations revealed that ventilated patients were younger and had higher baseline pCO_2 values compared to nonventilated patients.

Ultrasound-based bedside diaphragmatic measurements using DE and DTF have been suggested as indicators of successful weaning, yielding mixed results. A DE measurement greater than 1.0 cm and a DTF measurement exceeding 29% were associated with a high probability of successful extubation [12]. Our findings align with this pattern as well. Specifically, a baseline left DE

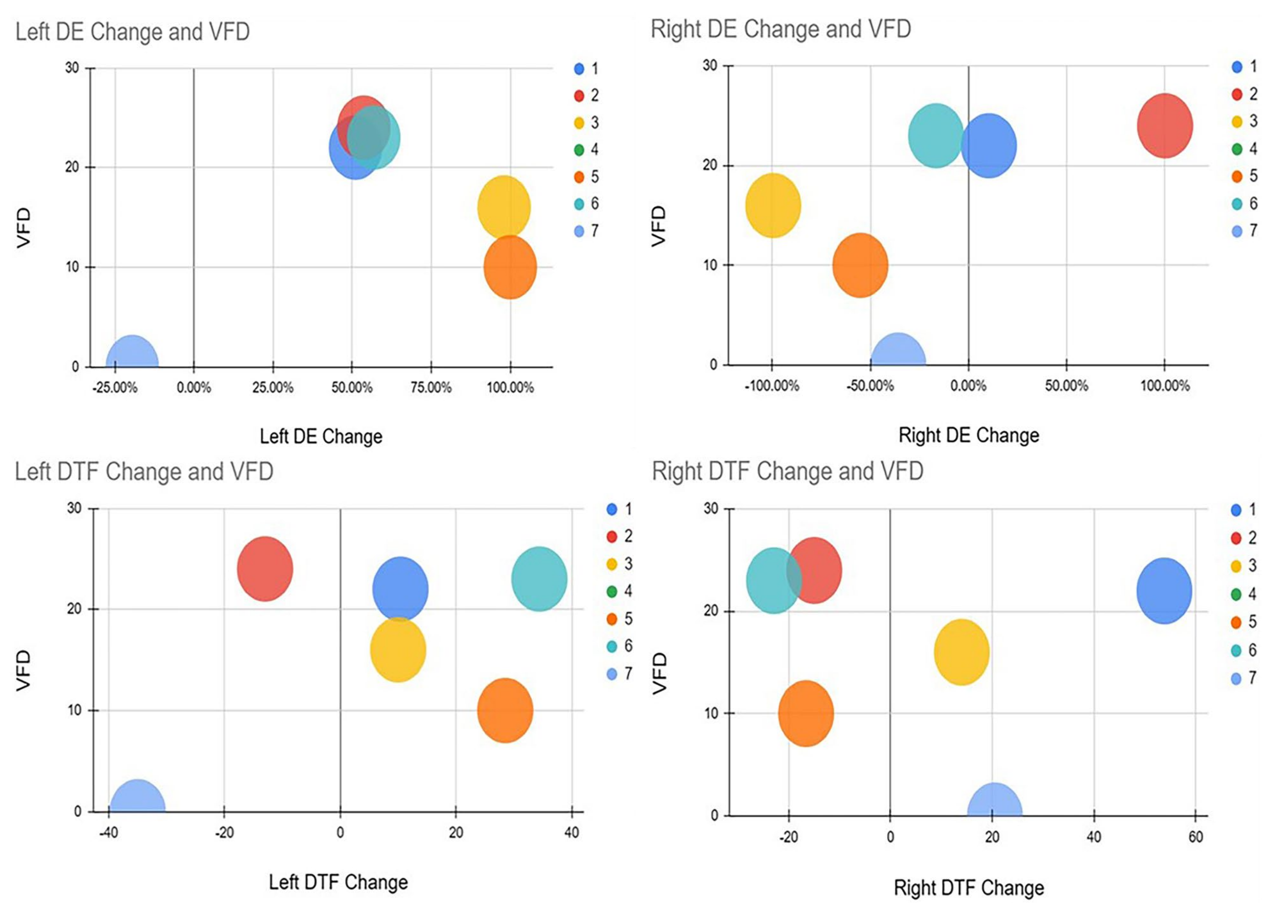

Fig. 3 Change in diaphragmatic function for predicting ventilator-free days. *DE* Diaphragmatic excursion, *DTF* Diaphragmatic thickness fraction, *VFD* ventilator free days

measurement of less than 1 cm was associated with a 2.5 times relative risk for the need for ventilation, and a decrease in right DE of more than 50% from baseline demonstrated a relative risk of 3.3 for predicting the need for ventilation on admission and over the subsequent 48 h. This study underscores the importance of serial bedside diaphragmatic assessment in effectively identifying NM cases that are likely to deteriorate and require ventilation promptly on admission or within a short period of 2–3 days.

Research in this cohort has addressed the challenge of high extubation failure rates by investigating several parameters. Goligher et al. conducted a study on ventilated patients, measuring DTF and DE daily, and observed that a DTF between 15 and 30% during the initial 3 days of ventilation predicted a shorter duration of ventilation. Additionally, both an increase and decrease in diaphragm thickness during MV were associated with prolonged ventilation needs. The authors suggested that inadequate respiratory muscle unloading may lead to diaphragm injury, resulting in increased diaphragm thickness and subsequent diaphragm atrophy, manifested as reduced diaphragm thickness [13].

Krishnakumar et al. assessed serial DE and DTF during spontaneous breathing trials in patients with NM diseases and discovered that an increase in DE predicted successful extubation. They also noted that decreased DTF measurements and a slower rate of decline were correlated with an extended duration of weaning [11]. However, Rittayamai et al. [15] and Vivier et al. [16] did not find an association between DE and DTF measurements and an increased risk of extubation failure.

In our research, we observed that ventilated patients with a bilateral increase in DE experienced higher ventilator-free days. Consistent with our findings, a meta-analysis of ten studies assessing weaning failure prediction in mechanically ventilated patients indicated that DE had a sensitivity and specificity of 75% [17]. Furthermore, in patients who underwent tracheostomy and a T-piece trial, a DTF greater than 36% predicted successful weaning with a sensitivity of 88% and a specificity of 71% [18]. However, a study by Dubé et al. reported

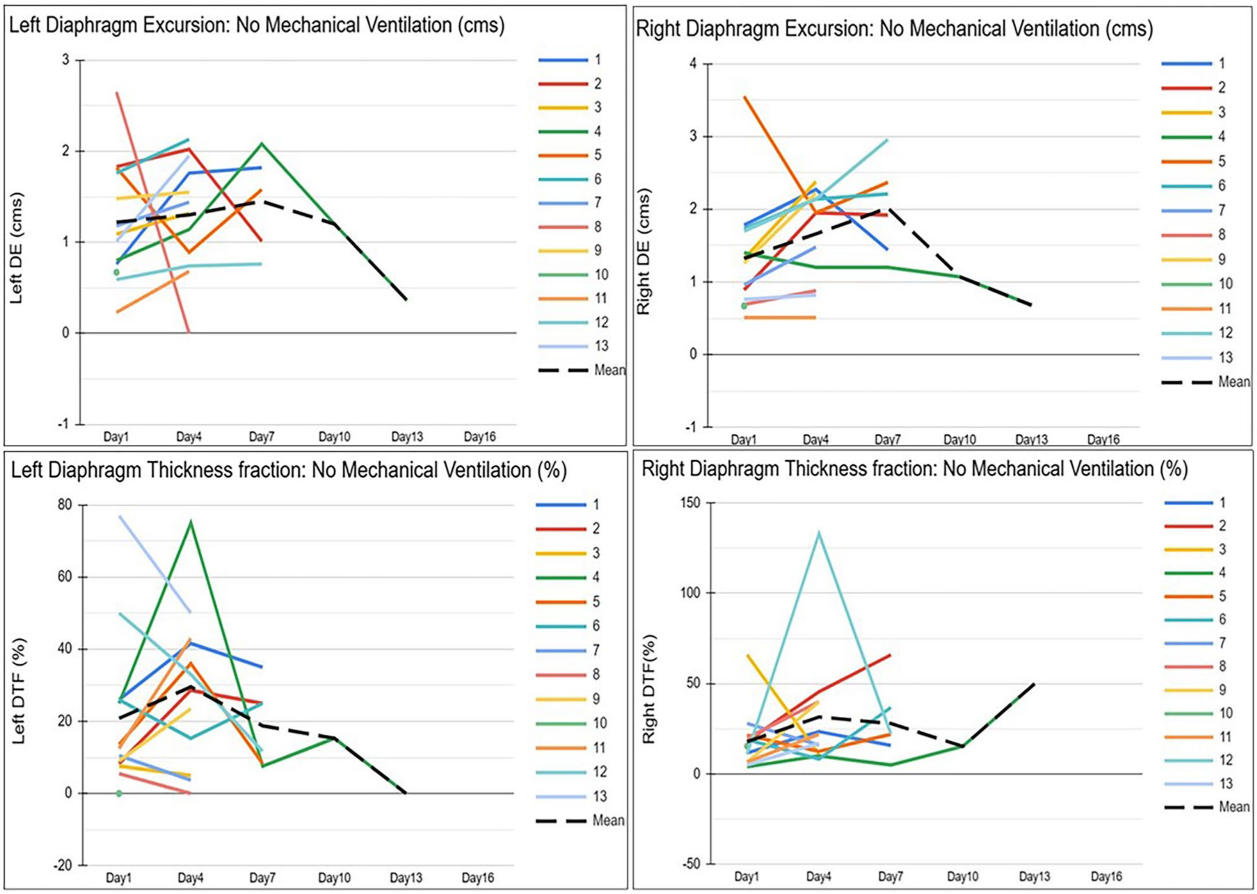

Fig. 4 Diaphragmatic function for nonventilated patients

variable baseline and subsequent DTF readings on either side, and the differences in DTF between ventilated and nonventilated patients did not demonstrate statistical significance [19].

Ultrasound assessment of the left hemidiaphragm is known to be more challenging than that of the right hemidiaphragm because of the smaller acoustic window of the spleen and the presence of stomach gas [20, 21]. Additionally, regional variations in diaphragmatic movement exist, with the middle and posterior parts exhibiting maximum excursion during spontaneous breathing [22]. These factors may explain why measurements on the right side showed a stronger association with the need for MV in our study. Various factors, including diaphragmatic workload, patient effort, and intrinsic muscle weakness, can influence the assessment of diaphragm function through DE and DTF measurements in patients with MG and GBS. Furthermore, DTF measurements may be affected by diaphragmatic injury and atrophy, which could elucidate the absence of an association between DTF measurements and the need for MV in our study [11–13].

It is important to acknowledge several limitations in our study. As a pilot study, the size of the study population is relatively small. Therefore, future large-scale studies are necessary to validate these findings. The duration of 30 min for stopping sedative agents may have been insufficient. Nonetheless, we were able to confirm satisfactory respiratory effort, indicated by a minute volume of at least 4L/min, with minimal pressure support during spontaneous ventilation. It is essential to recognize the inherent limitations associated with ultrasound diaphragm measurements, including operator dependence and anatomical variations in diaphragm insertion [23]. Factors such as diaphragmatic weakness, residual sedation, and patient effort, may impact the accuracy of these measurements [24]. To uncover the correlation between sequential DE and DTF measurements and the necessity for MV in MG and GBS, further extensive studies are imperative.

Table 3 DE and DTF changes over the first three readings between ventilated and nonventilated patients

	Ventilated, mean (SD)	Not ventilated, mean (SD)	*P* value
Baseline (R1)			
Left DE (cm)	0.79 (1.15)	1.12 (0.66)	0.39
Right DE (cm)	1.27 (0.50)	1.32 (.080)	0.86
Left DTF (%)	23.09 (15.89)	20.85 (21.30)	0.79
Right DTF (%)	17.84 (12.00)	17.9 (16.18)	0.99
R2			
Left DE (cm)	0.74 (0.46)	1.3 (0.64)	**0.05**
Right DE (cm)	0.79 (0.58))	1.66 (0.65)	**0.01**
Left DTF (%)	18.12 (13.08)	29.56 (21.84)	0.19
Right DTF (%)	18.65 (19.16)	31.57 (34.42)	0.32
R3			
Left DE (cm)	1.19 (0.59)	1.45 (0.55)	0.47
Right DE (cm)	1.33 (0.47)	2.02 (0.64)	0.06
Left DTF (%)	26.18 (13.60)	18.77 (11.18)	0.33
Right DTF (%)	29.87 (15.31)	27.97 (21.30)	0.86
Change R1–R2			
Left DE (%)	47.86 (46.81)	34.7 (77.68)	0.66
Right DE (%)	− 0.23 (50.23)	31.91 (44.92)	**0.05**
Left DTF (cm)	− 5.48 (20.62)	6.97 (22.22)	0.26
Right DTF (cm)	2.00 (28.61)	13.45 (41.45)	0.50
Change R1–R3			
Left DE (%)	115.62 (140.91)	54.05 (91.45)	0.41
Right DE (%)	18.43 (41.09)	25.16 (59.21)	0.82
Left DTF (cm)	2.58 (23.17)	− 6.05 (19.69)	0.50
Right DTF (cm)	17.68 (21.82)	2.38 (34.35)	0.35

DE, diaphragmatic excursion, DTF, diaphragmatic thickness fraction, R, reading

Bold indicate *p* values < 0.05 was considered significant

Conclusions

Continuous bedside ultrasonic diaphragmatic assessment may serve as a valuable tool in predicting the necessity for ventilation and gauging the potential for successful extubation in patients with NM diseases. Specifically, a left DE of less than 1 cm on admission and a decline of more than 50% in serial right DE over the initial 3 days could assist in identifying patients likely to require MV. Additionally, a bilateral increase in serial DE in ventilated patients is correlated with an increase in ventilator-free days and could facilitate the prediction of early weaning.

Supplementary Information

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Author Contributions

SN: study design, data collection, data analysis, manuscript writing, manuscript revision; AM: data collection, data analysis, manuscript writing, manuscript revision; RK: data collection, data analysis, manuscript writing; AS: study design, data analysis, manuscript writing, manuscript revision; SA: study design, data analysis, manuscript writing, manuscript revision.

Source of Support

None.

Data Availability

The data sets used and analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no competing interests.

Ethical approval/informed consent

Ethical clearance for the study was obtained from the institutional review board (IRB Min. No.14203 dated 25.08.2021 for the study titled "Ultrasonographic assessment of diaphragm function to predict need for assisted ventilation and liberation from mechanical ventilation in patients with neuromuscular disorders: an observational cohort pilot study") in accordance with the institute's ethical standards on human experimentation and with the Helsinki Declaration of 1975.

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References

1. The French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. Appropriate number of plasma exchanges in Guillain–Barré syndrome. Ann Neurol. 1997;41(3):298–306.
2. Hadden RD, Cornblath DR, Hughes RA, Zielasek J, Hartung HP, Toyka KV, et al.; Plasma Exchange/Sandoglobulin Guillain-Barré Syndrome Trial Group. Electrophysiological classification of Guillain-Barré syndrome: clinical associations and outcome. Ann Neurol. 1998;44(5):780–8.
3. Rees JH, Thompson RD, Smeeton NC, Hughes RA. Epidemiological study of Guillain-Barré syndrome in south east England. J Neurol Neurosurg Psychiatry. 1998;64(1):74–7.
4. Lawn ND, Fletcher DD, Henderson RD, Wolter TD, Wijdicks EF. Anticipating mechanical ventilation in Guillain–Barré syndrome. Arch Neurol. 2001;58(6):893–8.
5. Hughes RA. Management of acute neuromuscular paralysis. J R Coll Physicians Lond. 1998;32(3):254–9.
6. Thomas CE, Mayer SA, Gungor Y, Swarup R, Webster EA, Chang I, et al. Myasthenic crisis: clinical features, mortality, complications, and risk factors for prolonged intubation. Neurology. 1997;48(5):1253–60.
7. Varelas PN, Chua HC, Natterman J, Barmadia L, Zimmerman P, Yahia A, et al. Ventilatory care in myasthenia gravis crisis: assessing the baseline adverse event rate. Crit Care Med. 2002;30(12):2663–8.

8. American Thoracic Society/European Respiratory Society. ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med. 2002;166(4):518–624.
9. Lerolle N, Guérot E, Dimassi S, Zegdi R, Faisy C, Fagon JY, et al. Ultrasonographic diagnostic criterion for severe diaphragmatic dysfunction after cardiac surgery. Chest. 2009;135(2):401–7.
10. Remérand F, Dellamonica J, Mao Z, Ferrari F, Bouhemad B, Jianxin Y, et al. Multiplane ultrasound approach to quantify pleural effusion at the bedside. Intensive Care Med. 2010;36(4):656–64.
11. Krishnakumar M, Muthuchellappan R, Chakrabarti D. Diaphragm function assessment during spontaneous breathing trial in patients with neuromuscular diseases. Neurocrit Care. 2021;34(2):382–9.
12. Parada-Gereda HM, Tibaduiza AL, Rico-Mendoza A, Molano-Franco D, Nieto VH, Arias-Ortiz WA, et al. Effectiveness of diaphragmatic ultrasound as a predictor of successful weaning from mechanical ventilation: a systematic review and meta-analysis. Crit Care. 2023;27(1):174.
13. Goligher EC, Dres M, Fan E, Rubenfeld GD, Scales DC, Herridge MS, et al. Mechanical ventilation-induced diaphragm atrophy strongly impacts clinical outcomes. Am J Respir Crit Care Med. 2018;197(2):204–13.
14. Liu Z, Yao S, Zhou Q, Deng Z, Zou J, Feng H, et al. Predictors of extubation outcomes following myasthenic crisis. J Int Med Res. 2016;44(6):1524–33.
15. Rittayamai N, Hemvimon S, Chierakul N. The evolution of diaphragm activity and function determined by ultrasound during spontaneous breathing trials. J Crit Care. 2019;51:133–8.
16. Vivier E, Muller M, Putegnat JB, Steyer J, Barrau S, Boissier F, et al. Inability of diaphragm ultrasound to predict extubation failure: a multicenter study. Chest. 2019;155(6):1131–9.
17. Llamas-Álvarez AM, Tenza-Lozano EM, Latour-Pérez J. Diaphragm and lung ultrasound to predict weaning outcome: systematic review and meta-analysis. Chest. 2017;152(6):1140–50.
18. DiNino E, Gartman EJ, Sethi JM, McCool FD. Diaphragm ultrasound as a predictor of successful extubation from mechanical ventilation. Thorax. 2014;69(5):423–7.
19. Dubé BP, Dres M, Mayaux J, Demiri S, Similowski T, Demoule A. Ultrasound evaluation of diaphragm function in mechanically ventilated patients: comparison to phrenic stimulation and prognostic implications. Thorax. 2017;72(9):811–8.
20. Santana PV, Cardenas LZ, Albuquerque AL, Carvalho CR, Caruso P. Diaphragmatic ultrasound: a review of its methodological aspects and clinical uses. J Bras Pneumol. 2020;46(6): e20200064.
21. Boussuges A, Gole Y, Blanc P. Diaphragmatic motion studied by m-mode ultrasonography: methods, reproducibility, and normal values. Chest. 2009;135(2):391–400.
22. Harris RS, Giovannetti M, Kim BK. Normal ventilatory movement of the right hemidiaphragm studied by ultrasonography and pneumotachography. Radiology. 1983;146(1):141–4.
23. Yeh HC, Halton KP, Gray CE. Anatomic variations and abnormalities in the diaphragm seen with US. Radiographics. 1990;10(6):1019–30.
24. Vivier E, Roche-Campo F, Brochard L, Mekontso DA. Determinants of diaphragm thickening fraction during mechanical ventilation: an ancillary study of a randomised trial. Eur Respir J. 2017;50(3):1700783.