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Impact of pressure-targeted modes of ventilation on diaphragmatic function as assessed using ultrasonography in critically ill patients with cerebral insult: a randomized clinical trial

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Abstract

Background Mechanical ventilation causes diaphragmatic atrophy and reduces diaphragmatic efficiency. Patients with diaphragmatic dysfunction have longer mechanical ventilation durations and intensive care unit stay. There is currently a scarcity of data on the effect of different modes of mechanical ventilation on diaphragmatic function and ultrasound-guided assessment of diaphragmatic efficiency.

Results Sixty mechanically ventilated patients were randomly divided into four equal groups (15 each): patients were ventilated using either assist control pressure-controlled mode (group A), synchronized intermittent mandatory ventilation pressure-controlled mode (group S), bi-level-positive airway pressure mode (group B) or pressure support ventilation mode (group P). The primary outcome was to assess the diaphragmatic excursion, while the secondary outcomes were to assess the diaphragmatic thickness fraction and the duration of the ICU stay. Patients in the P group had the highest diaphragmatic excursion indicating better diaphragmatic function.

Conclusions When compared to other pressure-targeted ventilation modes, the pressure support ventilation mode may have the least risk of diaphragmatic dysfunction as preserves diaphragmatic structure and strength.

Trial registration The clinical trial was retrospectively registered at <http://www.pactr.org> PACTR202112653971335.

Keywords Diaphragmatic, Dysfunction, Ventilation, Cerebral, Excursion, Thickness

Background

Mechanical ventilation (MV) induces muscle fibre atrophy, which leads to a decrease in the diaphragm's force-generating capacity, a condition known as diaphragmatic dysfunction (DD) (Vassilakopoulos and Petrof 2004).

The use of ultrasound (US) to monitor the diaphragm's dynamic function by diaphragmatic excursion (DE) and structure by diaphragmatic thickness fraction (DTF) showed promising results for being accurate, safe and not emitting ionizing radiation (Chavhan et al. 2010). This study aimed to compare the effect of pressure-targeted modes of ventilation on DE and DTF in critically ill patients with cerebral insult.

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Methods

The present study was a randomized, prospective, observational, double-blind study. In February 2020, it was approved by the research ethics committee. It was registered in Pan African Clinical Trials Registry, identifier: PACTR202112653971335. After the study procedure was explained to the relatives of the patients, they signed a written informed consent. The study was performed at the ICU between February 2020 and February 2022, where 60 patients were eligible for the study.

The inclusion criteria of patients included the following: age above 21 years, mechanically ventilated because of neurological insult, fair chest condition with normal diaphragmatic function on admission (DE more than 10 mm and DTF more than 20%), eligible for proposed pressure-targeted modes of MV, afebrile, hemodynamically stable and unsedated and body mass index (BMI) less than 40. The exclusion criteria were patients on neuromuscular blockers, with DD on ICU admission and with history of diaphragmatic palsy or diaphragmatic hernia, brainstem injury or cervical spine injury, neuromuscular diseases, psychiatric disease, pulmonary disease or cardiac disease; hemodynamically unstable patients and morbidly obese patients ($BMI > 40$); and marked abdominal distention, pregnancy or sepsis.

Assessment of the included patients and the decision of extubation were performed by an ICU physician who was blinded to the ultrasonographic measurements and was not involved in the study.

Patients were randomly assigned to one of four groups using a computer-based randomization programme:

- Group A: Patients were ventilated using assist control pressure-controlled mode.
- Group S: Patients were ventilated using synchronized intermittent mandatory ventilation pressure-controlled mode.
- Group B: Patients were ventilated using bi-level-positive airway pressure mode.
- Group P: Patients were ventilated using pressure support ventilation mode.

The ventilatory settings were adjusted to achieve the following: a tidal volume of 6–8 ml/kg, a plateau pressure ≤ 30 mmHg, normocapnia (PaCO₂ between 35 and 45 mm) and SpO₂ $\geq 92\%$. After enrollment of mechanically ventilated patients, MV was stopped for 30 min of spontaneous ventilation. The diaphragmatic function was assessed in the plateau level of constant tidal volume. They underwent a US examination of the right hemidiaphragm in the supine position for three respiratory cycles on admission in the first, second

and third days (T1, T2 and T3, respectively) by the same operator. All the patients were examined by the US machine (Mindray, M7; China). The right hemidiaphragm was chosen for examination because the liver afforded a better sonographic image (Boussuges et al. 2009). Precautions were taken to ensure that the patients were lying flat on their backs. The head of the bed was lowered to 0° incline. In cases where the head of the bed could not be laid completely flat due to patient condition, the degree of incline (usually between 10 and 20°) during baseline reading was noted, and the same degree of incline was set for all subsequent readings (Cohn et al. 1997).

The primary outcome was to assess the DE, while the secondary outcomes were to assess the DTF and the duration of the ICU stay. The DE was assessed during the patients' spontaneous breathing trials. The convex probe (bandwidth 2–5 MHz) was placed below the right costal margin in the right anterior axillary and adjusted to be perpendicular on the right hemidiaphragm. The M-mode was activated. The DE was recorded by measuring the difference in the diaphragmatic positions during inspiration and expiration (Boussuges et al. 2009; Matamis et al. 2013).

The DTF was also assessed. A linear probe (8–10 MHz) was placed on the right anterior axillary line perpendicular to the diaphragm and adjusted to achieve the best diaphragmatic image (Cohn et al. 1997). Using M-mode, the diaphragmatic thickness was measured in the zone of apposition between the two layers of the pleura and the peritoneum (Haji et al. 2016). The DTF was measured by calculating the following: (end inspiratory thickness-end expiratory thickness)/(end expiratory thickness). A DTF of less than 20% or DE of less than 10 mm were used as cut-off parameters to identify diaphragmatic dysfunction (Vivier et al. 2017).

The length of ICU stay and results of ABG and lung US at T1, T2 and T3 were also recorded. Throughout the study, the modes and settings of ventilation were sometimes changed due to non-convenient clinical outcomes, and the patients were shifted to more convenient modes of ventilation than the proposed mode in our study. In the event of a change in ventilatory mode, the patient was dropped from the study, and an equivalent number of patients was recruited to substitute the dropped cases.

Statistical analysis

The primary outcome of the study was to assess the DE. Based on a study conducted by Saeed et al. (2018), the sample size was calculated using PASS 11–0 (power analysis and sample size). A sample size of 15 patients per group was used to compare the DE and DTF means.

Using an *F*-test with a 0.05 significance level, the whole sample of 60 patients had 80% power to detect differences between means. The standard deviation (SD) was 1.93, and the common SD was considered to be 4.37 (Saeed et al. 2018).

Data were collected, revised, coded and entered into version 22 of the Statistical Package for Social Sciences (SPSS; SPSS Inc., Chicago, IL, USA). Quantitative data which were presented as means, SDs and four groups were compared using the one-way analysis of variance test (ANOVA), and this ANOVA test was repeated for intergroup comparison. The qualitative data, on the other hand, were presented as numbers and were compared

among groups using the chi-square (χ^2) test. The confidence interval was set at 95%, and the accepted margin of error was set at 5%. Therefore, the *P*-value was considered significant at a level less than 0.05 and was considered highly significant at a level less than 0.001. Lastly, the *P*-value was considered nonsignificant at a level more than 0.05.

Results

Sixty patients have completed the study (Table 1, Figs. 1 and 2). Patients in group P had higher DE compared with other groups; however, in all groups, the DE was impaired over time (Table 2). The DTF was not

Table 1 Comparison of demographic data and admission diagnosis between the four groups

Demographic data	Group A (n = 15)	Group S (n = 15)	Group B (n = 15)	Group P (n = 15)
Age (years)	41.7 (11.3)	41.2 (11.5)	41.9 (12.1)	42.8 (11.7)
BMI (kg/m ²)	24.4 (2.8)	23.33 (3.1)	22.9 (2.49)	22.47 (2.6)
Sex (male)	8	7	8	9
Admission diagnosis	7	8	6	7
• Cerebral haemorrhage	8	7	9	8
• Cerebral stroke				

Data expressed as mean (SD) number. *BMI*, body mass index

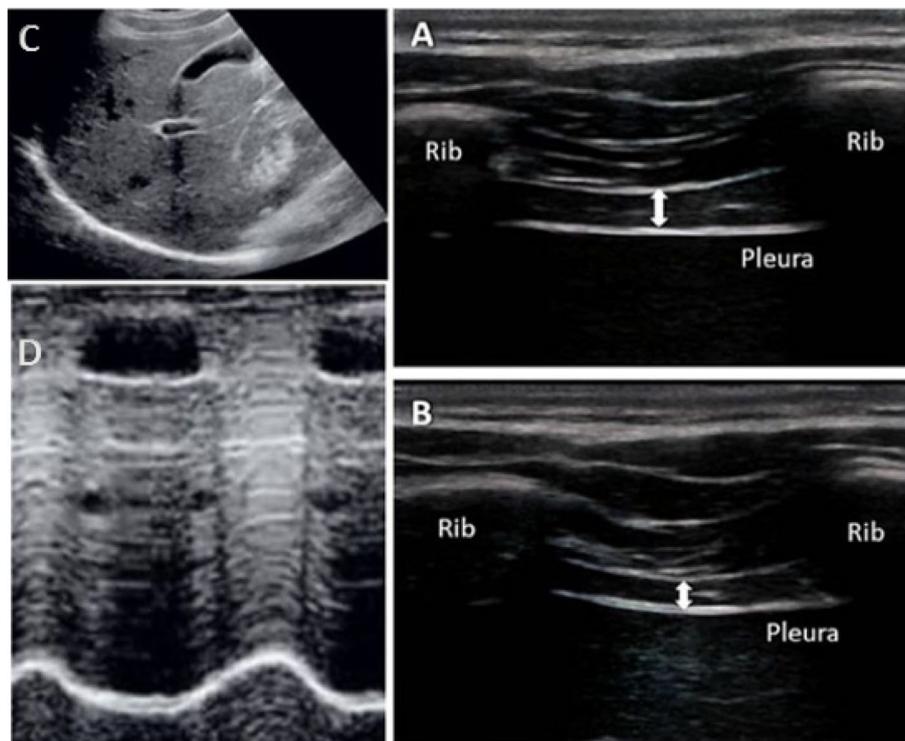


Fig. 1 The ultrasound diaphragmatic assessment. **A** and **B** To assess the DE, the right hemidiaphragm was identified. Then the M-mode was activated. **C** and **D** The DTF was assessed by calculating the ratio of the increase in diaphragmatic thickness at the end of inspiration compared with that at the end of expiration. DE, diaphragmatic excursion; DTF, diaphragmatic thickness fraction

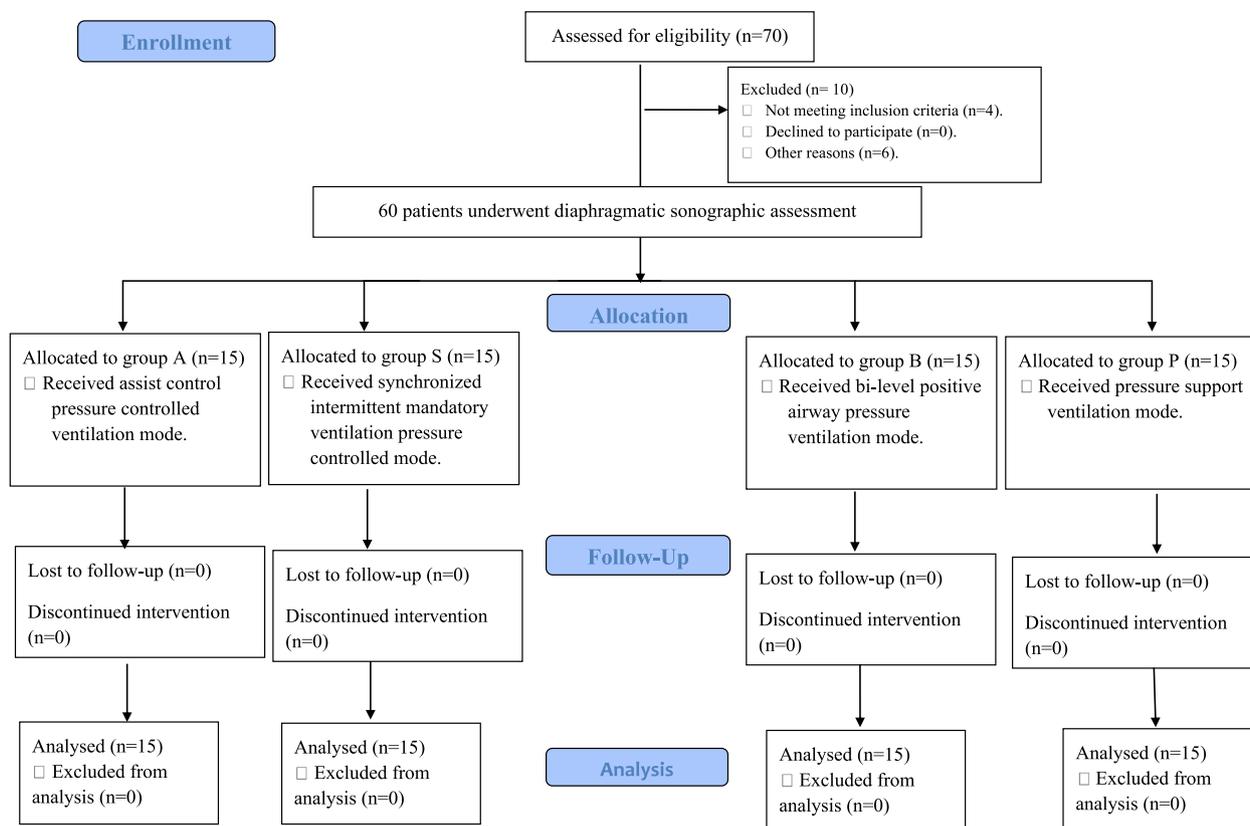


Fig. 2 Flow chart for patient enrollment

Table 2 Comparison between groups as regards DE

DE (mm)	Group A (n = 15)	Group S (n = 15)	Group B (n = 15)	Group P (n = 15)	p-value	
T1	25.2 (2.3)	23.6 (1.9)	25.6 (2.2)	29.7 (1.3)	<0.001	
T2	24.9 (2.2) ^a	23.1 (1.9) ^a	25.2 (2.2) ^a	29.5 (1.3) ^a	<0.001	
T3	24.7 (2.2) ^{a,b}	22.8 (1.9) ^{a,b}	24.8 (2.2) ^{a,b}	29.2 (1.3) ^{a,b}	<0.001	
P-value	<0.001	<0.001	<0.001	<0.001		
Post hoc analysis by LSD						
	P1	P2	P3	P4	P5	P6
T1	0.026	0.550	<0.001	0.005	<0.001	<0.001
T2	0.016	0.660	<0.001	0.005	<0.001	<0.001
T3	0.013	0.903	<0.001	0.009	<0.001	<0.001

Data expressed as mean (SD). T1 1st day, T2 2nd day, T3 3rd day

^a difference from T1

^b difference from T2, DE diaphragmatic excursion. P1, group A vs group S; P2, group A vs group B; P3, group A vs group P; P4, group S vs group B; P5, group S vs group P; P6, group B vs group P

affected by the mode of ventilation but with duration of ventilation (Table 3). Also, patients in group P had shorter ICU admission (Table 4). However, there was no difference regarding the gas exchange parameters (SpO2, PaCO2 and hypoxia index).

Discussion

Our study was conducted on 60 mechanically ventilated patients due to cerebral insult. Each patient was subjected to one pressure-targeted mode of ventilation appropriate to his respiratory pattern. Our study found that DE was

Table 3 Comparison between groups as regards DTF

DTF (%)	Group A (n = 15)	Group S (n = 15)	Group B (n = 15)	Group P (n = 15)	p-value
T1	25.4 (2.9)	22.8 (3)	24.59 (3)	23 (2.6)	0.051
T2	24.8 (3.1) ^a	22.3 (3.1) ^a	24.01 (3.2) ^a	22.5 (2.6) ^a	0.068
T3	24 (3) ^{a,b}	21.7 (3) ^{a,b}	23.5 (3.2) ^{a,b}	22.1 (2.6) ^{a,b}	0.059
P-value	<0.001	<0.001	<0.001	<0.001	

Data expressed as mean (SD). T1, 1st day, T2 2nd day, T3 3rd day

^a difference from T1

^b difference from T2, DTF diaphragmatic thickness fraction

Table 4 Comparison between groups as regards the length of ICU stay

	Group A (n = 15)	Group S (n = 15)	Group B (n = 15)	Group P (n = 15)	p-value
ICU stay (days)	10.6 (0.99)	10.8 (1)	9.67 (1.4)	9.33 (1.8)	0.008
Post hoc analysis by LSD					
	P1	P2	P3	P4	P5
ICU stay	0.681	0.059	0.011	0.023	0.004

Data expressed as mean (SD). T1 1st day, T2 2nd day, T3 3rd day, ICU intensive care unit. P1, group A vs group S; P2, group A vs group B; P3, group A vs group P; P4, group S vs group B; P5, group S vs group P; P6, group B vs group P

impaired over time, DTF was affected by the duration of ventilation rather than mode and the P group had the best outcome.

US evaluated the structure and dynamic function of the diaphragm. It provided accuracy, reproducibility, convenience for critically ill patients on MV and safety with no ionizing radiation (Chavhan et al. 2010). The use of M-mode provides images that visualize the movement of the diaphragm over time and enables accurate diaphragmatic displacement measurement over a breathing cycle (Testa et al. 2011).

We assumed that increasing the duration of ventilation caused diaphragmatic thinning and a decrease in DTF, resulting in DD. DTF is an indicator of the work of breathing. DTF was found to be more accurate than diaphragmatic thickness because it abolished the effect of body weight and height on diaphragmatic thickness.

PSV improves patient comfort, reduces patient's ventilatory work and provides a more balanced pressure which allows maximum diaphragmatic activity without fatigue. Additionally, it has been found that PSV unloads respiratory muscles preserving spontaneous contraction, thus avoiding atrophy and probably leading to partial restoration of diaphragm thickness in patients with prolonged durations of MV, and this seems to correlate to a better breathing pattern. When using PSV, a better response was observed in the measurements of the oxygenation and respiratory parameters regarding CO₂ elimination values and respiratory rate, as proven by many authors (MacIntyre 1986; Brochard et al. 1989; Costa et al. 2005; Grassi et al. 2020).

Saeed et al. studied patients with chronic obstructive pulmonary disease (Saeed et al. 2018). The authors reported that the PSV has the lowest DTF but highest DE. They found that the DE was significantly affected with the ventilation mode. It was higher with PSV mode (29.7 mm) compared with Bi-PAP (25.3 mm), SIMV (23.8 mm) and volume-controlled (231.7 mm) modes. The better DE with PSV was associated with improved lung volumes, ventilation and accelerating the weaning process. Regarding DTF measurements, they contradicted our findings, where the DTF in group B was 24 while having the same value (22.9) in both groups S and P. They also found a statistically significant change in DTF, where the thickness of the diaphragm decreased significantly at PSV. Their study differed from our study in the type of patients recruited (chronic obstructive pulmonary disease patients).

Umbrello et al. evaluated the DE and DTF in comparison to traditional indices of inspiratory muscle effort during PSV using different support levels (Umbrello et al. 2015). They found that the use of the higher-pressure support was associated with more impairment of DTF without affecting the DE.

Although Farghaly and Hasan deduced that US evaluation of diaphragmatic excursion and thickness at end inspiration could be a good predictor of extubation outcome, their results differed from ours. In their study, DTF was significantly higher (58.9) at pressure support of MV in the patients successfully weaned from ventilation when compared with those who failed extubation trials (30.8). These differences between their results and our results may be due to the following: (1) Difference in the type of

patients recruited (patients with underlying pulmonary disease causing acute respiratory failure such as bronchiectasis, interstitial lung disease, extensive pneumonia complicated by the development of respiratory distress, hypoventilation with respiratory acidosis) and those patients were excluded from our study and (2) the degree and extent to which airways were affected in each type of pulmonary disease (Farghaly and Hasan 2017).

Some factors may limit the generalizability of our results. This study was conducted in a single centre. We assessed patients with cerebral insults. Patients with other disorders may have different responses to different modes of MV. In our patients with cerebral insults, it was difficult to assess the effect of MV modes on the ventilatory weaning. The diaphragmatic assessment was performed for 3 days; therefore, our result may or may be not valid with longer periods of MV.

Conclusions

When compared to other pressure-targeted ventilation modes, the pressure support ventilation mode may have the least risk of diaphragmatic dysfunction as preserves diaphragmatic structure and strength.

Abbreviations

ABG	Arterial blood gases
ANOVA	Analysis of variance
BMI	Body mass index
US	Ultrasound
DD	Diaphragmatic dysfunction
DE	Diaphragmatic excursion
DTF	Diaphragmatic thickness fraction
HI	Hypoxic index
ICU	Intensive care unit
MV	Mechanical ventilation
PAAS	Power analysis and sample size
PSV	Pressure support ventilation
P-value	Probability value
SD	Standard deviation
SpO ₂	Arterial saturation
SPS	Statistical Package for the Social Sciences

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Not applicable

Authors' contributions

AME designed the study, revised literature, followed the patients and critically reviewed the manuscript. RHM designed the study, revised literature, followed the patients and critically reviewed the manuscript. MMK revised literature and followed the patients. MMM revised literature, followed the patients and helped with revision and submission. HM collected the data, performed the analysis and wrote the manuscript. All authors approved the final version of the manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due [publishing the clinical data about any study conducted

in our hospitals and approved by the institutional ethical committee is against the policy of the Faculty of Medicine, Ain Shams University, unless there is a reasonable request] but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee at the Faculty of Medicine, Ain Shams University (FMASU MD 59a/2020/2021/2022) and registered retrospectively with Pan African Clinical Trial Registry, identifier: PACTR202112653971335. Written informed consent was obtained from the relatives of the patients.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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